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# Demographic Changes and the Challenge for a Healthy Ageing

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**Abstract:** Demographic changes bring about a wide range of new research fields including policy topics, health, social welfare, work & productivity, urban & rural development, communication tools, and mobility. This new situation requires a new multi-disciplinary approach bringing together different research programs in order to provide solutions for the upcoming challenges. National Health services are now facing a huge shift in the population structure with a predominance of older generations in the total number of citizens. Good health is the most important factor to live independently in old age. A better understanding of ageing processes and the related "plasticity" of individual performance for environmental adaptation, the prevention for age-related illnesses and healthcare strategies are the basis for keeping very old people healthy and active throughout the course of their lives. We will face mainly the biological, cognitive and psychological dimensions of ageing. Afterwards, we will focus on the relationships linking various biological and lifestyle factors -such as nutrition- that are crucial to obtain a comprehensive picture of ageing and to promote preventing strategies against degenerative neurological diseases. Finally we will investigate which interventions - nutritional and physical - could help in keeping people healthy, in particular which factors could promote people's physical, social and psychological functional abilities and the systemic multilevel consequences induced by a healthy ageing.

**Keywords.** Demographic Change, Healthy Ageing, Innovation, Research, Healthcare Strategies, Elderly, Health

## Introduction

In all industrialized and more advanced countries the "Demographic Change" of the population is one of the most important societal challenges that Governments will have to face in the next future.

The Demographic Change is a direct consequence of the simultaneously rise in life expectancy and of the decrease in birth rates leading to a huge shift in the population structure of communities and to a prevalence of older generations in the total number of citizens. Epidemiological studies [1-2] report that at the beginning of the 20th century the average life expectancy of a woman born in Western Europe was 48 years, and that of a man was 45 years; today, they can expect to live 82 and 77 years, respectively.

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Around 1900, 60-year-olds had another 13 to 14 years to live on average, whereas today, they can expect about 23 further years, 25 among women and 21 among men.

This demographic trend has an exceptional impact, with only few exception (Ireland), mainly on Europe.

It is clear that most societal field will be impacted by this change significantly with unpredictable consequences on structures of society, social cohesion and equity, productive systems, mobility, connection changes, services needs, communication systems, economic policy and distribution of resources. Researchers of all scientific fields should provide an analyses of the biological, social and economic consequences of ageing to cope with these changes and in order to supply the technical and societal adaption, the economical and policy adjustments, and finally the adequate prevention strategies in order to contrast the impact due to lack of validity, decrease of productivity and of all general abilities in the population.

Meanwhile, ageing does not represent per se a burden, but it can also represent an opportunity to be explored; within this frame a positive vision of ageing in Europe requires joining forces in ageing-related research and establishing coordination and collaboration between the national research programs in several key areas.

Indeed, several research fields are involved ranging from health, welfare, education and social programs, to financial reforms, to technology improvement. Health care programs aiming at developing prevention strategies for a optimized ageing will have a pivotal role in reducing the needs of social and financial interventions and in reducing the general costs of the societal policy for the elderly people in the future.

High relevance must be addressed to the research in the field of prevention and in the studies aiming at delaying the onset of degenerative diseases in the elderly. The plan of interventions requires a transnational, multi-disciplinary approach, bringing together different research programs and researchers from various disciplines to approach crosscutting topics in order to understand the different facets of the phenomenon of individual and societal ageing as well as to provide solutions for the upcoming challenges.

## 1. The Challenge of Healthy Ageing

Good health is the most important factor to live independently in old age. A better understanding of ageing processes and the related plasticity of individual performance, the prevention for age-related illnesses and healthcare strategies are the basis for keeping people healthy and active throughout the course of their lives. In spite of these premises oldest-old people (aged > 85 years) has been the most rapidly expanding fragment of the population in developed countries in the last decades. This group is also the most susceptible to disease and disability; as a consequence an increase of costs for health services should be expected with fundamental effect on the future sustainability of modern society [3-5].

The multisistemic physiological ageing involving sensorial abilities (hearing, vision, taste, proprioception etc.), motor system (for both neural loss and muscle sarcopenia), and cognition for a progressively longer period of time increases the need of health and social services as well as of technical aids in a progressively larger percentage of population.

The main challenge in this situation is to intercept as early as possible the "grey zone" separating the physiological from the pathological ageing in order to counterbalance the development of degenerative diseases by means of dedicated health policies, prevention, early diagnosis and strict monitoring and follow-up in those people "at high risk" (i.e. with a familiarity for degenerative disease or carrying genetic modifications, susceptibility or polymorphisms, with personal history –for instance severe head trauma- that could lead to the onset of degenerative disease).

Some encouraging data stem from the evidence that in several epidemiological studies, concerning older people up to age 85, the trend of delayed disability is increasing but at a lesser extent than the increment of chronic diseases [6]. Some factors could influence the reduction in disability in younger and older people. Better accessibility to care and treatment has also played a role in delaying disability, together with increasing levels of educational attainment and increased income level in large segments of society. Better occupation, workplace conditions, physical activities, nutritional changes, and the reduction in poverty may have all contributed to the decline in disability in the last decades.

For the oldest-old group the situation is less clear. The prevalence of disease in the elderly population has generally increased disability over time [6]. Neurodegenerative diseases such as Alzheimer's disease and other types of dementia, as well as Parkinson's disease typically recognize age as the main risk factor. Neurodegenerative disease all share the same lifestyle and related risk factors common to the major chronic diseases. In all neurodegenerative diseases there is a balance between the various environtmental/lifestyle risk factors and the genetic predisposition. Thus considering nutrition, lifestyle and environment is crucial to obtain a comprehensive picture of the boundaries separating an "healthy" from a "pathological" ageing. The investigation of which factors keep people healthy, in particular which factors promote people's physical, social and psychological functioning is crucial for the correct application of preventive strategies This also includes greater knowledge about potentially reversible processes that might be used to preserve or restore lost capabilities.

An example of this state of affair has been provided for Alzheimer disease (AD) in recent epidemiological report on the incidence of AD in American population [7]. The major evidence is that in the last years, an inverted trend with a reduction of incidence/year of AD in the population over 80 years has been observed; thus suggesting the possibility that some environmental factors could have positively interfered in the previous decades with the onset of the disease in the oldest old people.

On this purpose researchers have to devote their efforts in multidisciplinary research aimed at exploring the biological basis of ageing and the modulatory effect of environmental factors (nutrition, exercise, inflammation amongst the others) on the biochemical and genetic basis of ageing. The final aim is to reach a better comprehension about how environmental interplay with genetic factors in modulating the onset of the degenerative processes in human populations. From this perspective we should pass from a research focused on the early diagnosis and treatment, to the study of those factors that could promote mental and physical health in older age, life expectancy and primary prevention.

## 2. Factors Promoting Healthy Ageing: the Basis for Preventing Strategies

At the present, the main issues that have to be investigated to increase the knowledge on how to promote good health in the elderly and to reach useful preventing strategies to increase quality of life involve the following areas:

a) Social role, lifestyle, socioeconomic, cultural, genetic, and biological determinants that produce an healthy ageing.
b) Research on the plasticity of human development and successful ageing in various domains of physical and cognitive functioning.
c) Role and efficacy of preventing strategies in age related diseases in order to investigate different strategies for successful ageing for maintaining good social contacts and independent living in the elderly.
d) The role of technological aids in reducing disability and replace the decline of functions in the elderly. In particular, research should focus on innovative technology, improved communication system, and Tecno-care assistance at home, as well as for indoor/outdoor mobility in order to provide technologies for dependent older persons to help themselves in coping with daily life in a way more similar to their original life styles.
e) Investigation on the effect of sensorimotor and cognitive rehabilitation in very old age in order to maintain social engagement and a productive life.

When examining possible preventing strategies in the elderly, several fields that have provided recent evidences of efficacy in counterbalancing the effect of the age correlated degenerative diseases can be identified. In particular, some key measures seem particularly effective in decreasing the development of neurodegeneration:

a) food quality and diet;
b) physical and cognitive exercise;
c) oligo-elements and oxidative stress

### *2.1 The Dietary Effect*

Among the modifiable lifestyle related factors, associated with degenerative disease, in the elderly people, diet has been proven to interfere with the onset of degenerative disease in elderly people. Also in AD the preventing strategies are more successful in the late onset of the disease.

Diet, and in particular Mediterranean-type diet, has shown some interesting effect in the delay of AD onset [8] and reducing the incidence of AD [9]

Two nutrition-related links could connect diet and the development of AD, i,e., micronutrients and macronutrients. Deficiencies of some micronutrients, especially those related to antioxidant and amino acid metabolism mechanisms (e.g., vitamin B1, B2, B6, B12, C, copper and folate), have been associated with cognitive impairment in elderly people [10] (see 2.3).

As concern macronutrients, a high intake of specific dietary factors (e.g., saturated fatty acids) enhances the amyloid-beta (Aβ) deposition in the animal model brain and increases oxidative stress. Some preventing strategies have been proposed in order to limit the effect of 'wrong nutrients' on the developing of degenerative disease in particular some general warning have been proposed in order to limit the use of some nutrients

Among other information provided by the guidelines, a reduction in the intake of saturated and trans fatty acids (contained in meat, for example, those "red" in particular), which produce an increase in cognitive impairment, is desirable. A decreased intake of saturated fats and trans fats is a powerful preventing strategy for AD. Saturated fat is found primarily in dairy products, meats and certain oils (coconut and palm oils). Trans fats are found in many snack pastries and fried foods and are listed on labels as "partially hydrogenated oils."

On the other hand, it is advisable to increase the consumption of plant foods, especially vegetables: the metals they contain are indeed treated based on the needs of the organism. Vegetables, legumes (beans, peas, and lentils), fruits, and whole grains should replace meats and dairy products as primary staples of the diet. Another recommendation also relates to the consumption of foods containing vitamin E (seeds, spinach or other vegetable broadleaf), which is able to increase the resistance of neurons to degenerative processes and that instead it is not properly taken in the form of vitamin complex. Important for the production of neurotransmitters and the improvement of cognitive faculties are vitamins B12 and B6, also effective if taken as multivitamin complex.

The future fields of research activities should point at the exploration of the modality by which these nutritional factors act on ageing, in general, and on neurodegeneration, in particular, in order to determine:

a) the relationships between fatty acids, oxidative stress and developing of neuroinflammation in the brain

b) how the nutrients can modulate, increase or decrease the effect of some patterns of genetic susceptibility or also modify the effects of well known risk factors for AD (APOE; BDNF, etc)

c) which are the nutrients and other components of metabolism that could represent risk factors for neurodegeneration, or, at the variance, protective factors, is an issue that deserves further investigations. Moreover researchers should address their efforts in establishing what is the level of diurnal intake of nutrients potentially dangerous or protective, and how age and gender could interplay with the intake of these nutrients, triggering some patients, but not others, to a neurodegenerative process.

### *2.2 Physical/Cognitive Exercise*

Lifestyle is strongly associated with the risk of dementia. One of the top prominent issue at the last G8 summit, held in London on December 2013, was the effect on European population of the longevity related increasing of degenerative disease and in particular of AD. As mentioned above one of the most important environmental factors able to modify the expression of AD in people affected by genetic susceptibility or genetic risk factors is the regular physical and cognitive exercise. In fact several researchers have demonstrated that not only longevity and genetic risk factors are the only cause for an increasing incidence of AD. There is evidence that different lifestyle factors including obesity, stress, smoking, physical inactivity and low level of education and of cognitive burden are associated not only with the risk of cardiovascular disease but also of increased incident late-life dementia [11]. In particular physical exercise during midlife seems to exert a neurobiological modification leading to a delay of neurodegeneration in general and AD onset specifically [12-14].

Although some studies indicate enhanced behavioural performances in AD patients after only three month of physical exercise [15] little is known about how this effect would be exerted on the progressive neuropathology of AD after disease onset.

One possible explanation is that regular physical/cognitive exercise acts also as a promoter of a healthy brain by the activation of restorative mechanisms, plasticity, and the production of neuroprotective factors including endorphins good for mood. In the last ten years the literature on the preventing strategies for AD has enormously increased. Researchers have focused their attention on the final outcome of the physical exercise both on the cognition and on the delay the onset of AD. In spite of these evidences there is poor comprehension about the modality of this effect on neurodegenerative processes. In particular researchers activity should be devoted in the future at exploring:

a) The neurobiological effects of physical/cognitive exercise on metabolism and on the reduction of risk factors linked to the diet.

b) The relation between physical/cognitive exercise and the reduction of inflammation patterns both in blood and in SNC of MCI (=Mild Cognitive Impairment, a prodromic stage of AD) and AD patients

c) The role played by physical/cognitive exercise in promoting neural/synaptic plasticity in the human cortex and in increasing connectivity between brain regions.

From an operational point of view, some other points need to be clarified, in particular:

a) The amount of physical/cognitive exercise able to exert a positive effect on the human health and the minimum and the maximum of motor and cognitive activities beyond which the effects are less evident.

b) What are the optimal physical/cognitive exercises needed to obtain favorable effects on the neurodegeneration?

c) The study of gender and race roles is of critical value to understand if the effect of the physical/cognitive exercise could be generalized or restricted to particular subjects, geographical areas or personal condition.

The clarification of these issues could provide the basic information to check which modalities of interventions could produce the best outcomes in planning preventive policy programs for a healthy ageing.

### *2.3 Oligo Elements and Oxidative Stress*

In the last years several micronutrients have been demonstrated to interfere with degenerative processes in humans.

One of the most studied is the effect of some vitamins. Vitamin E has been proposed as supplement in diet to avoid o decrease neurodegeneration. However, vitamins should come from foods, rather than supplements.

Healthful food sources of vitamin E include seeds, nuts, green leafy vegetables, and whole grains. The RDA for vitamin E is 15 mg per day.

A reliable source of vitamin B12, such as fortified foods or a supplement providing at least the recommended daily allowance (2.4 mcg per day for adults) should be part of any daily diet. Blood levels of vitamin B12 and folate should be checked regularly as many factors, including age, impaired assimilation.

A general warning should be made when using vitamins supplements. If using multiple vitamins integrators, is advisable to choose those without iron and copper, and consume iron supplements only when directed by a physician.

While aluminum's role in Alzheimer's disease remains a matter of investigation, those who desire to minimize their exposure can avoid the use of cookware, antacids, baking powder, or other products that contain aluminum.

In a similar way, copper is a micronutrients that works as a cofactor in several basic enzymes of the cell. Some of these are the cytochrome C oxidase (involved in energy generation), copper-zinc superoxide dismutase, or SOD (responsible for detoxification), lysyl oxidase (responsible for the connective functioning). In particular copper counterbalance iron mobilization by ceruloplasmin activity. If the presence of copper is too high, its uncontrolled redox activity can lead to the harmful generation of free radicals and to the increase of oxidative activity, thus compromising cellular function and causing oxidative damage to the body. Moreover one other unsafe effect of copper is due to its implication in inflammatory conditions and in the interactions with the productions of many cellular growth factors, interleukins, and pro-inflammatory cytokines, such as TNFalfa and C-reactive protein.

The role of copper seems to be central in the regulation of several patterns of ROS activity, and metals clearance, and its unbalancing in plasma could lead a cascade of harmful events. [16-18]

One of the most relevant new research fields in the future could be the exploration of the relationship between copper and the onset of Alzheimer disease and its pathophysiological mechanism.

Recent studies have clearly shown a role of "free" Copper (non-ceruloplasmin bound) in the cascade leading to Beta Amyloid plaques formation in excess as in the AD brain [19]. This excess is partly determined by being genetically a "good" or a "bad" Copper metabolizer [20-21]. It is noteworthy that such copper excess can be modified by an appropriate diet poor in Copper as well as by chelating drugs [22].

On these premises, a wider comprehension of the modality that determines the increasing production of Beta Amyloid in human brain, mediated by copper and the study of the antioxidant patterns in the brain could provide relevant information on the mechanisms triggering the onset of AD from one hand and the potential preventing strategies to inhibit the disease onset from the other.

Another crucial field of research could be devoted to the potential use of Zinc that is copper's primary antagonist. Zinc helps to reduce copper toxicity and also removes excess copper from the body naturally so people could maintain a proper zinc-copper balance. According to a National Health and Nutrition Examination Survey, an extensive cohort population study, aimed at explore if zinc dietary supplementation could modify the prevalence of AD, could have an enormous relevance for the health policies in the future.

## 3. Perspective and Conclusion

Very long lives is no more a mirage of future generations, but represent the probable destiny of most people alive now in developed countries. Increasing numbers of people at old and very old ages will be a major challenge for health-care systems, economic policy, and public health plans in the western countries. However elderly people can also be a new "resource" for future societies. From this point of view is critical for public administrations to promote healthy lifestyles among populations in order not only to avoid premature morbidity and mortality due to chronic diseases but also to

prevent or postpone mental and physical disability among elderly people. Unfortunately less is known about the further potential of reducing disabilities and diseases among elderly. Therefore, it is a key challenge to understand the contribution and interaction of the determinants that shape ageing across the life course and develop strategies and interventions to improve and extend cognitive and physical functions and quality of life at an older age.

The new knowledge, that environmental preventing factors could play an epigenetic role in inducing modification of the phenotype of degenerative diseases, provides the evidence that ageing is no more a permanent and unstoppable decay process leading to a progressively disabling condition. These data stress the importance of maintenance of physical and mental performance of older people through prevention and interventions which ensure that the additional gained years result in healthier, more active, productive and enriching years.

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