

Challenges of longevity :

ILC-France perspective

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Longevity is a remarkable venture at the individual, social and national level as long as the aging population remains healthy and active. It is not disputable that tomorrow will be old and female. But tomorrow will be healthy if we do promote prevention of age-related diseases and tomorrow will be wealthy if the aging population is allowed to fully take part in the economic circuit.

Before addressing the French issues, let us consider the world population: It will grow from 6.1 billion in 2000 to 8.1 billion in 2050 but mainly in strongly emerging nations (India, Africa, and Asia). In contrast, in the most developed nations, the European, North American and Japanese populations will decrease. So will the Chinese population but it will nevertheless stay one of the largest in the world.

All populations share at least the same characteristics: a progressive increase in their dependency ratio, defined by the ratio of the 65 + over the 15-64 years old population.

In France, more than 20% of the 62.9 million inhabitants are 60 years old and over. The mean life expectancy at birth is continuously progressing up to nearly 77 years for men and nearly 84 years for women. As in other nations, there will be a continuous increase in the 65 +, 75 +, and 85 + populations until 2020 but, the percentage of the population under the age of 60 years, though decreasing, remains

rather high, probably thanks to the maintained fertility ratio at 1.9, one of the greatest in Europe (Table 1).

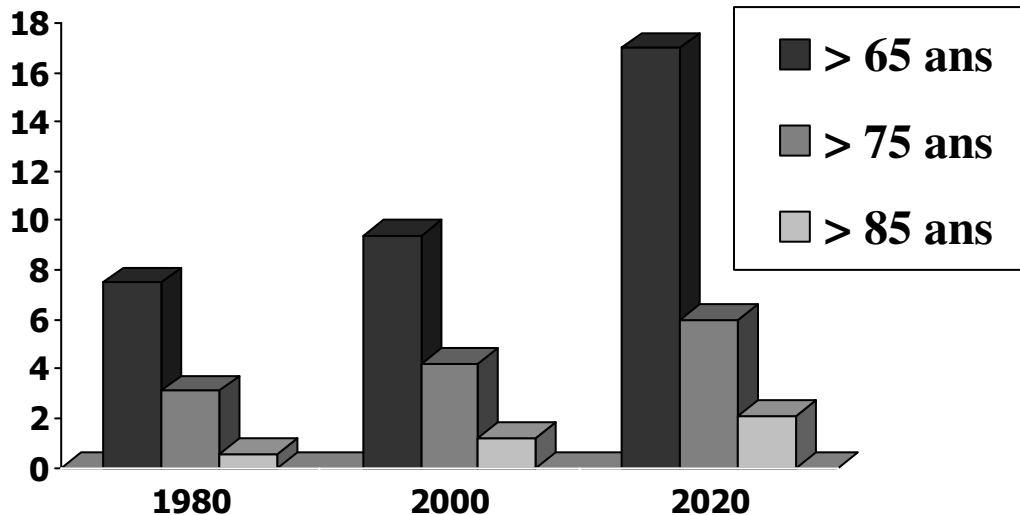


Table 1 : Evolution of the elderly population in France

The female advantage in life expectancy remains nearly universal and widened in the twentieth century. Precise explanation of the gender difference is not clear because of the interplay of biological and social factors¹. But this difference explains the large predominance of women in the elderly world population: 237 millions females and 182 millions men. It must be noted that a majority of elderly women live in developing countries.

The same trend is observed in France: At each age and period, the mean life expectancy is significantly higher in females than in men. But there seems to be a slight stagnation in women probably due to the increase in lung cancers in female smokers. Nevertheless, the demographic pyramid clearly shows the predominance of women in the older population.

¹ Kinsella K, Velkoff V. *Life expectancy and changing mortality. Aging Clin Exp Res. 2002; 14:322-332*

All people do not equally enjoy this excellent health status: For example in France, there is a five year difference in life expectancy at 60 between the white collar and blue collar workers. But strikingly, the difference is less marked in the female population, three years only. As well, the risk of mortality of unemployed men is for many reasons, of course threefold this of the active population. It is only twofold in women.

The place where you live may have an influence: the life expectancy at birth is five year lower in the North of France than in the Paris region, it is only 2.4 years in women , as if women were protected against a number of extrinsic factors (Table 2).

Region	Men	Women
North of France	73,6	81,8
Paris and around	78,4	84,5

Table 2: Mean life expectancy at birth in France, comparison of two regions (Insee2004-http://www.insee.fr/fr/ffc/chifcle_fiche.asp?ref_id=CMRSOS02219&tab_id=473)

The absolute number of frail elderly needing assistance or Long Term Care either at home or in institution seems high: In France, it is probably close to 1 million individuals but it must be emphasized that the percentage is low: 6% only of the population over 65 years of age, and 2% of the population between 60 and 69 years of age suffer from loss of autonomy due to disabling diseases. This percentage of course increases with age but it remains rather low until very high ages (table 3).

Age	Males	Females	Total
60-69	2.19	1.95	2.06
70-79	4.99	4.35	4.65
80-89	13.40	19.85	17.69
+ 90	29.31	46.45	42.55
Total	5.00	7.80	6.63

Table 3: Senior population of 60+ in France: 6, 63% of loss of autonomy (Insee –HID study -GIR 1-4) d’après: Etudes et résultats N°94-décembre 2000

It must be observed that the rate of loss of autonomy is higher in women than in men at very advanced ages. Only 30% of the males are dependant after 90 years of age versus 46% of women.

In order to increase the rate of autonomy we have to solve a tricky equation:

- 1 The aging population is increasing worldwide, particularly the female population.
- 2 Disability increases with age.
- 3 But disability decreases at each age (people at each age are less dependant that 20 years ago).
- 4 So, the increase in disability due to the aging of the population must be counterbalanced by the decrease of disability at each age so that the number of disabled elderly be stable or progressively reduced.

This is an objective that can be reached if prevention is strongly promoted in our countries. Women play a tremendous role in prevention.

When considering prevention, one must be aware that the health status is an heterogeneous process at the individual and population levels. Two types of factors, genetic and environmental, may be involved in this heterogeneity².

The variations at the level of genes are extensive; According to the Danish twin study, the genetic variance component to life span was estimated to account for about 25% of total life span variation.³ In addition, there is throughout life an accumulation of genetic mutations within the somatic cells over the course of a lifetime contributing to the large variation in health status and age at death⁴

The environmental factors may be more important because they are modifiable. They encompass the medical progress particularly in terms of prevention and access to care and the socio-economic factors, responsible of inside-country and between country differences. When you look at the differences in mean life expectancy in different countries and/or continents the responsibility of the socio-economic levels is overwhelming. Life expectancy has doubled at the end of the twentieth century in some developed countries. Life expectancy at birth exceeds 78 years in 28 countries. But deep inequalities do persist. In 2004⁵, the life expectancy at birth was 82,3 in Japan, 80,6 in Sweden, 79,7 in France, 78.7 in the UK, 77.6 in the USA, 71.9 in China, 70,2 in Brazil, 64,9 in Russia, 62.2 in India, 50,5 in Kenya, 41,4 in Malawi. and 35,7 in Zimbabwe.

To increase the life expectancy and promote healthy aging, lifestyles, prevention and medical progress are key determinants. The different components of

² Carnes BA, Olshanski SJ. *Heterogeneity and its biodemographic implications for longevity and mortality. Experimental Gerontol. 2001; 36: 419-430*

³ Herskind AM, McGue M, Holm NV, Sorensen TI, Harvald B, Vaupel JW. *The heritability of human longevity: a population-based study of 2872 Danish twin pairs born 1870-1900. Hum Genet 1996; 97: 319-323.*

⁴ Finch CE, Ruvkun G [Annu Rev Genomics Hum Genet. 2001;2:435-62](#)

healthy lifestyles are well known: Education throughout life, healthy nutrition, moderate and prolonged physical activity, mental activity, professional and leisure activity, personal commitment and responsibility. The challenge is to develop in citizens health literacy and preventative consciousness.

Indeed, most of age-related diseases may be related to modifiable risk factors and then accessible to prevention: cardiovascular diseases, strokes, osteoporosis and fractures, diminished hearing and vision, cancers, undernutrition, depression. Medical progress (and chips, cell therapy, biotechnologies) will accelerate the efficacy of prevention approaches. It is never too soon, never too late. Osteoporosis can be prevented in teenagers, by increasing physical activity and calcium intake in girls. Fighting obesity and smoking in boys may prevent the coronary diseases in the forties, fifties and over. Wearing sun glasses when sailing or skiing may postpone cataracts.

The role of young parents and particularly mothers is essential but prevention is a lifelong perspective and must be continued throughout life. Let us take the example of hypertension: Age-specific relevance of usual blood pressure to vascular mortality was addressed in a meta-analysis of individual data for one million adults in 61 prospective studies⁶. This meta-analysis shows that high blood pressure is still related to cardiovascular complications at higher ages. The randomised trials have demonstrated that treatment of hypertension significantly reduces the incidence of strokes and other cardiovascular complications before and after sixty years of age. In the meta-analysis by Insua⁷, the relative risk for strokes is decreased by 35%, for

⁵ http://www3.who.int/whosis/life/life_tables/life_tables_process.cfm?path=whosis,life_tables&language=english

⁶ Levington S, Clarke R, Qizibach N et al for the Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002;360:1903-13.

⁷ Insua JT-Drug Treatment of Hypertension in the Elderly A Meta-Analysis-*Annals of Internal Medicine* Drug 1 September 1994 Volume 121

cardiovascular complication by 25% and by 12% for all causes of mortality. Even if it does not prolong life at higher ages, antihypertensive treatment might preserve quality of life by preventing distressing invalidating diseases⁸.

Prevention of cardiovascular diseases remains the privilege of the most developed countries. A recent WHO report for Europe⁹ shows that the gap between western and eastern Europe is increasing. People in western Europe may expect to live 6 years longer than people in central Europe and 10 years longer than people of the New Independent States born after the dissolution of the Soviet Union. In eastern Europe, cardiovascular diseases represent 60% of the mortality causes as compared to 35% in western Europe. The huge decrease in the cardiovascular mortality from east to west emphasizes the absolute need for cardiovascular prevention in all countries.

Even dementia may be prevented. Given the increase with age of Alzheimer's disease and related disorders and the twofold prevalence in women, prevention has turned into a striking challenge. A number of risk factors have been identified including, besides age and sex, the level of education, genetic factors (history and genotypes) and vascular factors. Some of them cannot be modified but vascular risk factors and, in particular but not only hypertension, may be the target of prevention trials. Indeed, two randomized studies^{10 11 12} were able to demonstrate a reduction in the incidence of dementia by lowering blood pressure. In contrast, prevention using

⁸ Gueyffier F, Bulpitt C, Boissel J-P, et al. Antihypertensive treatment in very old people: a subgroup meta-analysis of randomised controlled trials. *Lancet* 1999; 353: 793-6.

⁹ *The health status of the European Union —Narrowing the health gap- Luxembourg: Office for Official Publications of the European Communities 2003 — 58 pp. — 21 x 29.7 cm- ISBN 92-894-3802-9*

¹⁰ Forette F, Seux ML, Staessen JA, et al. Prevention of dementia in randomised double-blind placebo-controlled Systolic Hypertension in Europe (Syst-Eur) trial. *Lancet*. 1998;352:1347-1351.

¹¹ Forette F, Seux ML, Staessen JA et al. The prevention of dementia with antihypertensive treatment. New evidence from the systolic hypertension in Europe (Syst-Eur) Study. *Arch Intern Med* 2002;162:2046-52

¹² Tzourio C., Anderson C., Chapman N., Woodward M., Neal B., MacMahon S. et al. PROGRESS Collaborative Group. "Effects of blood pressure lowering with perindopril and indapamide therapy on dementia and cognitive decline in patients with cerebrovascular disease". *Arch Intern Med*, 2003 ; 163 : 1069-75.

estrogens, anti-inflammatory agents, anti-oxidants and cholesterol-lowering agents remains to be confirmed.

Is it possible to go further and act on the cause of Alzheimer's disease? Based on the amyloid hypothesis, two approaches are being tested: the development of beta and secretase inhibitors and the beta amyloid immunisation. The original work by Dale Schenk¹³ on transgenic ADAPP mice engineered to produce human A beta amyloid protein was spectacular. The transgenic mice in the placebo group produce hippocampal amyloid deposition, neuritic plaques and plaque-associated astrocytosis comparable to one of the 2 Alzheimer lesions. The mice vaccinated with the human amyloid protein at 6 weeks do not develop the Alzheimer lesions.

The first phase 2 trial of the amyloid vaccine was stopped due to severe side-effects. Seventeen of the 300 patients developed an immune encephalitis¹⁴. However a recent paper by Nicoll in Nature¹⁵ shows that the immune response generated against the peptide elicited clearance of A beta plaques in the brain of a vaccinated patient, deceased of encephalitis. Extensive areas of cortex were devoid of plaques. Other trials based on fragments of the A beta protein will maybe prove that it is possible to produce the same effect without the immune inflammation.

All these studies show that the key of Alzheimer prevention is possibly not too far ahead. This is a fantastic hope for the future.

The randomized studies as well as the observational statistics show that prevention works: Over the past three decades major health gains attested by a significant reduction of premature mortality were observed. Premature mortality by

¹³ Shenk D et al. *J Neurosci*. 1996 Sep 15;16(18):5795-811

¹⁴ Gilman S, Koller M Black RS et al. *Clinical effects of Abeta immunization (AN1792) in patients with AD in an interrupted trial. Neurology*, 2005 ; 34 :1553-62

¹⁵ Nicoll et al, *Nature Medicine*, 9, 2003, 448-52

ischaemic heart disease was reduced by 42%, stroke by 57%, bronchitis and emphysema by 73% (Table 4).

Health problem (per 100 000 inhabitants)	EU average gain for the period 1970-1997
Life expectancy at birth (years)	+ 8,4 years
Premature mortality by cancer	- 12,0 %
Premature mortality by cancer of the lung	+ 6,0 %
Premature mortality by cancer of the female breast	+ 2,2 %
Premature mortality by ischaemic heart disease	- 42,3 %
Premature mortality by stroke	- 57,0 %
Premature mortality by diabetes mellitus	- 35,4 %
Premature mortality by asthma, bronchitis and emphysema	- 73,9 %

Table 4 : Health gains over the past three decades (The health status of the European Union : Narrowing the health gap 2003 (HFA Statistical Database, WHO Regional Office for Europe)

It is very interesting to consider which factors contributed to these gains. When you look for example at the life expectancy of males, the economic level is indeed important and accounts for 20% of the gain but the level of educations of females accounts for 30 % and the utilization of new knowledge for 50%. This emphasizes the important role of women in the development of prevention (Table 5).

Reduction	Percentage contribution of gains in		
	Income	Educational level of adult females	Generation and utilization of new knowledge
Under-5 mortality rate	17	38	45
Female adult mortality rate	20	41	39
Male adult mortality rate	25	27	49
Female life expectancy at birth	19	32	49
Male life expectancy at birth	20	30	50
Total fertility rate	12	58	29

Table 5 : Source of mortality reduction 1960-1990 (Wang J et al. Measuring country performance on health: Selected indicators for 115 countries. The World Bank, 1999 (Human Development Network, Health, Nutrition and Population Series).

Promoting health is important not only to reduce disability and suffering of the aging population, but also to promote wealth and wellness of the nations and then happiness of the individuals. The positive correlation between health, attested by the mean life expectancy, and income per capita is well known. As underlined by the economist David Bloom¹⁶, this positive correlation is commonly thought to reflect a causal link running from income to health. Indeed, a higher economic level allows access to goods and services that promote health (nutrition, sanitation, skilled health services, prevention...).

In fact, the income-health correlation could be partly explained by a causal link running the other way from health to income. Health improvement can lead to income growth due to several mechanisms: health improves productivity due to

¹⁶ David E. Bloom and David Canning. *The Health and wealth of nations- Science Vol. 287. no. 5456, pp. 1207 - 1209*

more energy and mental force, fewer lost workdays from illness or need of care for other members of the family. Healthier populations invest more in education that in turn promotes greater productivity and income. Higher education is correlated to better cognitive function and long term preservation of cognition. Higher education is also linked to a better compliance to prevention. An increased longevity leads to long term investment and saving that, in turn, stimulates economy. The transition from high to low rate of mortality is correlated to the progressive reduction in the fertility rate observed in developing countries. Mortality decline in the children and youths initiates this transition and increases progressively the proportion of future healthy workers.

A WHO report¹⁷ indicates that health status as measured by life expectancy is a significant predictor of subsequent economic growth.

Health is not enough. Tomorrow will be wealthy if the senior population and particularly the female population is allowed to take part in the economic circuit. Women highly contribute to the economy of the country : In France, they represent 45% of the active population in 2003 versus 35% in the sixties. But the rate of activity decreases significantly in the senior population. Only 39% of the 55/64 year population are working in spite of a rather good health status as compared to 50% in Europe. The rate of activity after 60 is particularly disastrous: 7% in men and 4% in women. In Sweden, 23% of males and 14% of women are still allowed to work, in the USA, 27% and 14% and in Japan 51% and 23% (Table 6).

¹⁷ World Health Organisation. (1999). *World Health Report 1999: Making a Difference*. Geneva: World Health Organisation.

Country	% 60 + in 2000	% 60 + in 2020	Life expectancy at birth in 2000	% activity at 60 + in 2000
India	7.6	11	M : 63 W : 64	M : 65 W : 14
China	10.1	16.7	M : 69 W : 73	M : 45 W : 15
USA	16.0	22.8	M : 74 W : 80	M : 27 W : 14
France	20.5	26.8	M : 75 w : 82	M : 7 w : 4
UK	20.6	26.7	M : 75 W : 80	M : 21 W : 8
Italy	22.3	33	M : 75 W : 81	M : 17 W : 4
Japon	23.2	33.7	M : 77 W : 85	M : 51 W : 23

Table 6: Longevity and activity, comparison 2000-2020 (UNO population)

Indeed, the rate of activity of women increases progressively while it slightly decreases in men but the difference remains very high. A comparable difference is observed in the purchasing power of women. In the private sector, wages are 25% lower in women than in men. As well the so-called “glass ceiling” prevent them to have access to the highest position. Only 6,5 of women are CEOs of companies. The same figure is observed in the public sector. The problem no longer lies in the education system: women represent 56% of the students in the French universities but only 30% in the scientific disciplines.

The time spent in child care and housekeeping is still significantly higher in women than in men. However the help given to parents by the “crèche” (day nursery) and the nursery school system allows many young mothers to stay at work. The help given by grand parents and particularly grand mothers must be emphasized. As well the senior female population represent 80% of the caregivers when a very old person

looses his/her autonomy. This non paid activity plays a very important role in the care of all dependant persons of all ages.

The discrimination toward women was striking in the political area but progress is being made. Women represented 2 % of the senators in the sixties and seventies. The percentage rose up to 16% at the last 2004 election. Elected members of the regional councils were 10% in the eighties and are now nearly 50% (2004 election). The election at the European parliament also demonstrated an important progress: 30% of the MEP (members of the European parliament) were women in 1999 versus 43% in 2004 (Table 7).

	1999-2004 (EU 15)		2004-2009 (EU 25)	
	Number of women /total	% of women	Number of women /total	% of women
France	26/87	29,9%	34/78	43,6%
Total	166/626	26,5%	222/732	30,3%

Table 7 : members of the European parliament

In conclusion, the evolution of the French shows the more and more important part played by the female population in all sectors of activity. Women take an important part in the promotion of health, children education, economic activity and policy. Promotion of women is an important challenge.

From 2000 to 2050 there will be a 30% increase in the active population in the USA. As a whole it will remain stable in the OECD countries but it will decrease by 10 to 15% in France and by nearly 30% in Japan. It is more than time to develop strategies to promote employment in healthy seniors and particularly in female seniors. The objectives are to encourage changes in attitudes of employers and workers and to promote training for upgrading skills and acquiring new ones. The

improvement of working conditions may be a powerful incentive for all generations. The reform of retirement and welfare systems is, as well indispensable.

The longevity revolution will be an opportunity and not a threat for women and for men if we are able to maintain equity and promote health, quality of life, activity and wealth of all generations living together. We must guarantee that the labor market fosters productive engagement and does not compromise the rights of the expanding aging population. A peaceful world also implies that all countries will equally benefit of the fantastic venture of longevity.