Pr. Athanase Benetos, MD, PhD

Born in Athens, Greece, on July 5, 1956
Married, 4 children

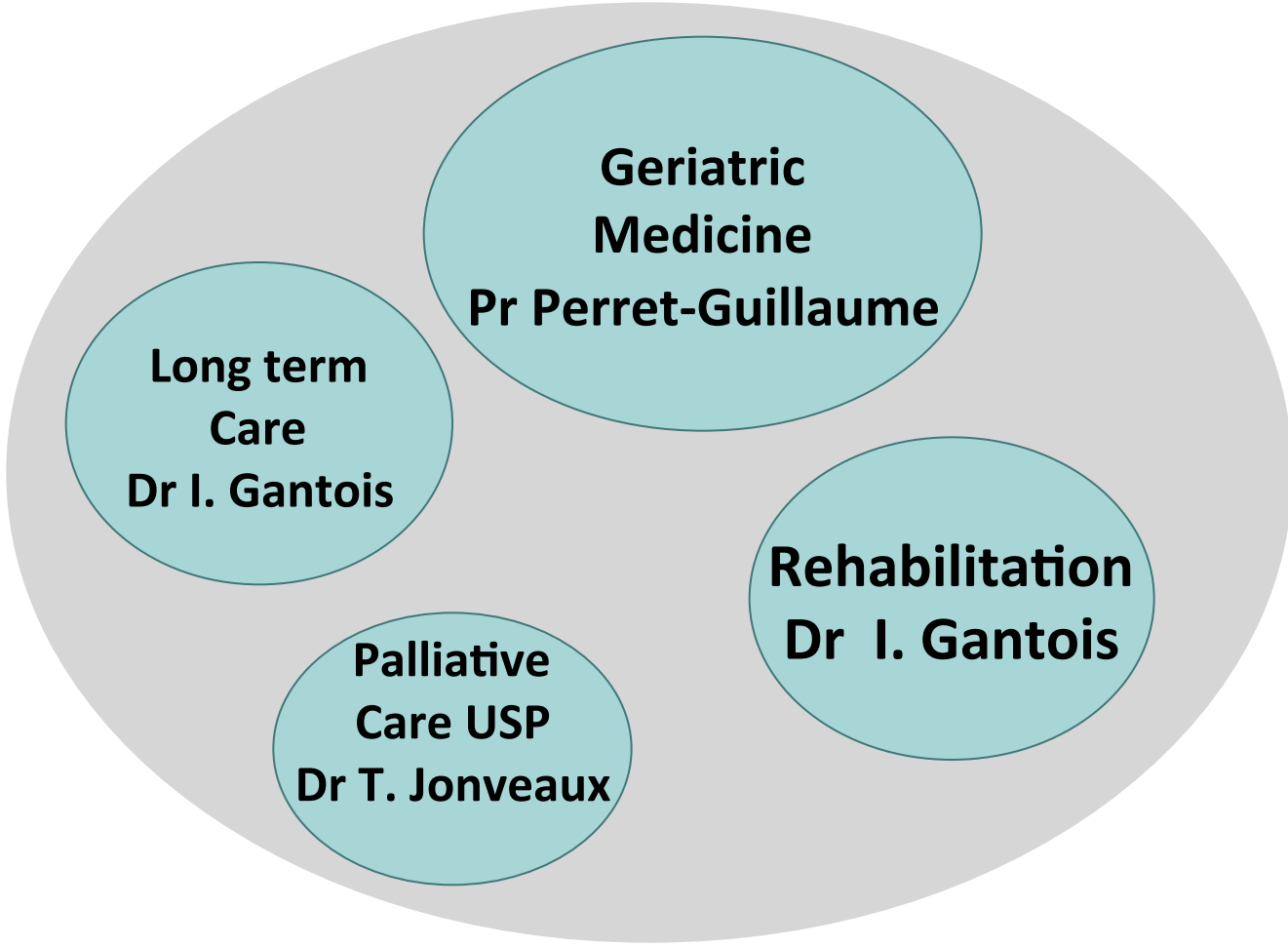
- ✓ MD: Medical School of the University of Athens Greece
- ✓ PhD: University Pierre et Marie Curie, Paris 6, France
- ✓ Clinical Specialties: Cardiologist and Geriatrician
- ✓ Academic Position : Professsor of Geriatric Medicine and Biology of Aging
- ✓ Clinical Position: Chief of the Dpt of Geriatric Medicine and Clinical Gerontology; Université de Lorraine
- ✓ European academic activity: President Elect EuGMS
- ✓ Professional address: Department of Geriatric Medicine, CHRU de Nancy, Hôpital de Brabois; 54511, Nancy, France, e-mail: a.benetos@chru-nancy.fr

Moscow, 25 October 2018


www.CartesFrance.fr
ROYAUME-UNI
BELGIQUE
LUXEMBOURG
ALLEMAGNE
SUISSE
ITALIE
ESPAGNE
ANDORRE
Manche
Océan Atlantique
Golfe de Gascogne
Mer Méditerranée
0 100 200 km
0 100 200 mi
62 59 80 02 08 76 60 55 57 50 14 95 51 27 67 78 61 91 77 54 22 88 29 35 53 28 10 52 72 45 68 56 89 70 41 90 44 49 37 25 21 58 18 36 85 39 71 79 86 03 23 01 74 63 42 69 87 73 17 16 19 43 38 24 15 26 33 05 46 07 12 48 04 47 82 84 40 30 06 34 13 81 32 31 83 64 65 11 2b 09 66 2a

Department of Age-Related Diseases, Clinical Gerontology and Palliative Care (MaVie-GSP)

Prof A. Benetos



MaVie-GSP: 227 beds, outpatient units, clinical research, teaching

CHU NANCY
www.chu-nancy.fr

Acute Hospitalisation Units: 62 beds

- Unit 1: 20 beds
- Unit 2: 20 beds
- Direct entrance unit (UGED): 15 beds
- Reinforced care Unit (SC): 7 beds

Day Hospital
5 beds

Out-patient Clinic

Geriatric Mobile Unit

Palliative Care Mobile Unit

Rehabilitation Hospitalisation Units: 44 beds

- General Geriatric Unit SSR: 32 beds
- Cognitivo-Comportemental Unit (UCC) 12 Beds

Thematic Units

- Memory Clinic (CMRR)
- Oncogeriatric (ULCOG)
- CV Aging and Frailty (MARCAGE.FR)

Palliative Care Hospitalisation Unit: 15 beds

Long-term Care Units: 106 beds

- General Geriatric LTC Unit (USLD) : 90 Beds
- Reinforced LTC Unit (UHR): 16 Beds

Geriatric Clinical Research Unit

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MaVie-GSP Staff

-24 Physicians-geriatricians (3 cardiologists, 1 neurologist, 1 vascular medicine, 1 psychiatrist, 2 internal medicine, 1 public health)
(3 Professors of medicine; 13 Senior geriatricians, 3 University assistants)

-10 Medical Residents, 1 Pharmacist Resident, 1 Dentist Resident
-10-20 Medical Students

-12 psychologists
-3 chief-nurses
->100 nurses, assist. nurses
-10 secretaries
-6 social assistants
-physiotherapists, ergotherapist, nutritionist, speech therapist

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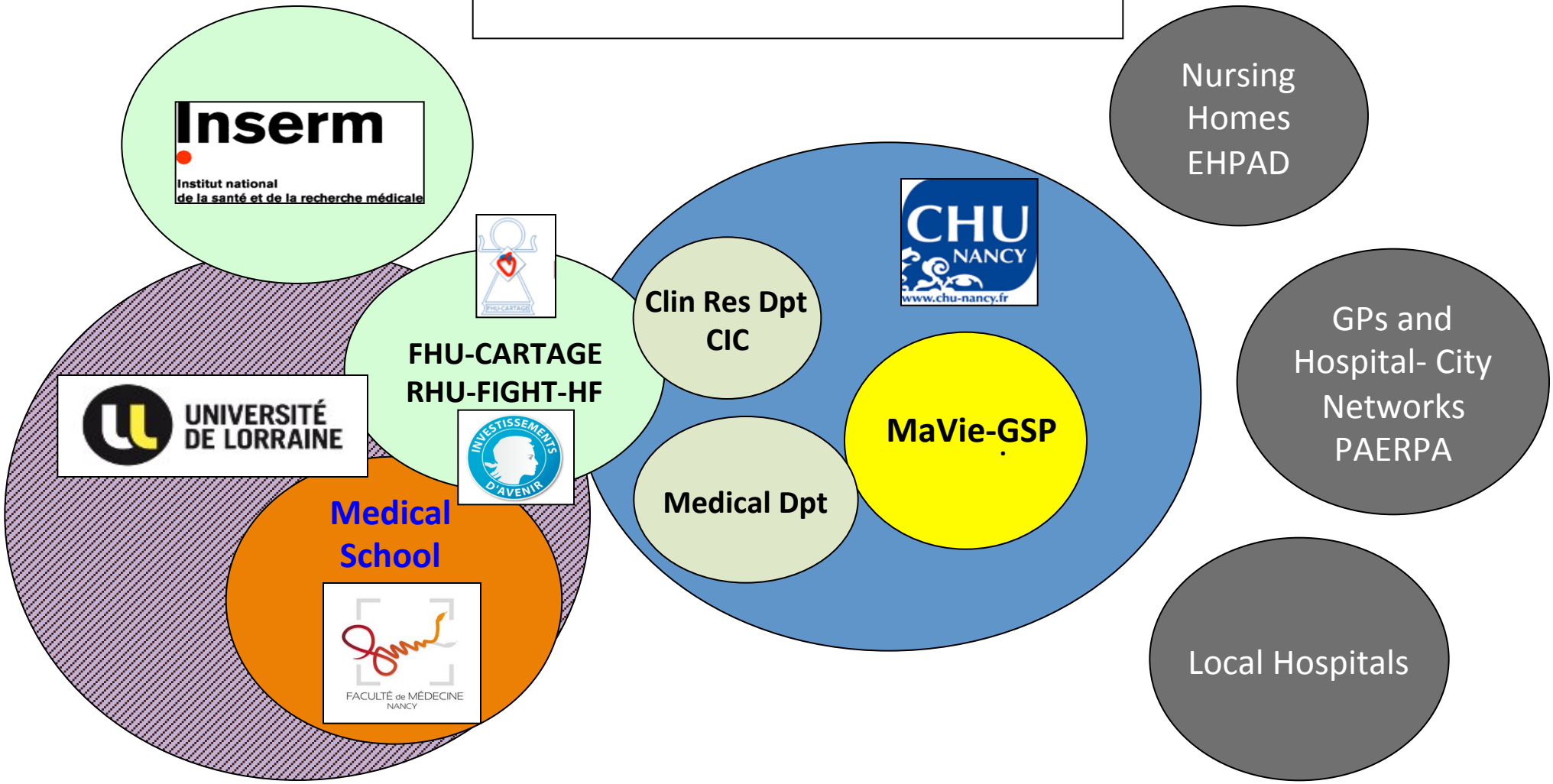
Clinical and Academic Connections



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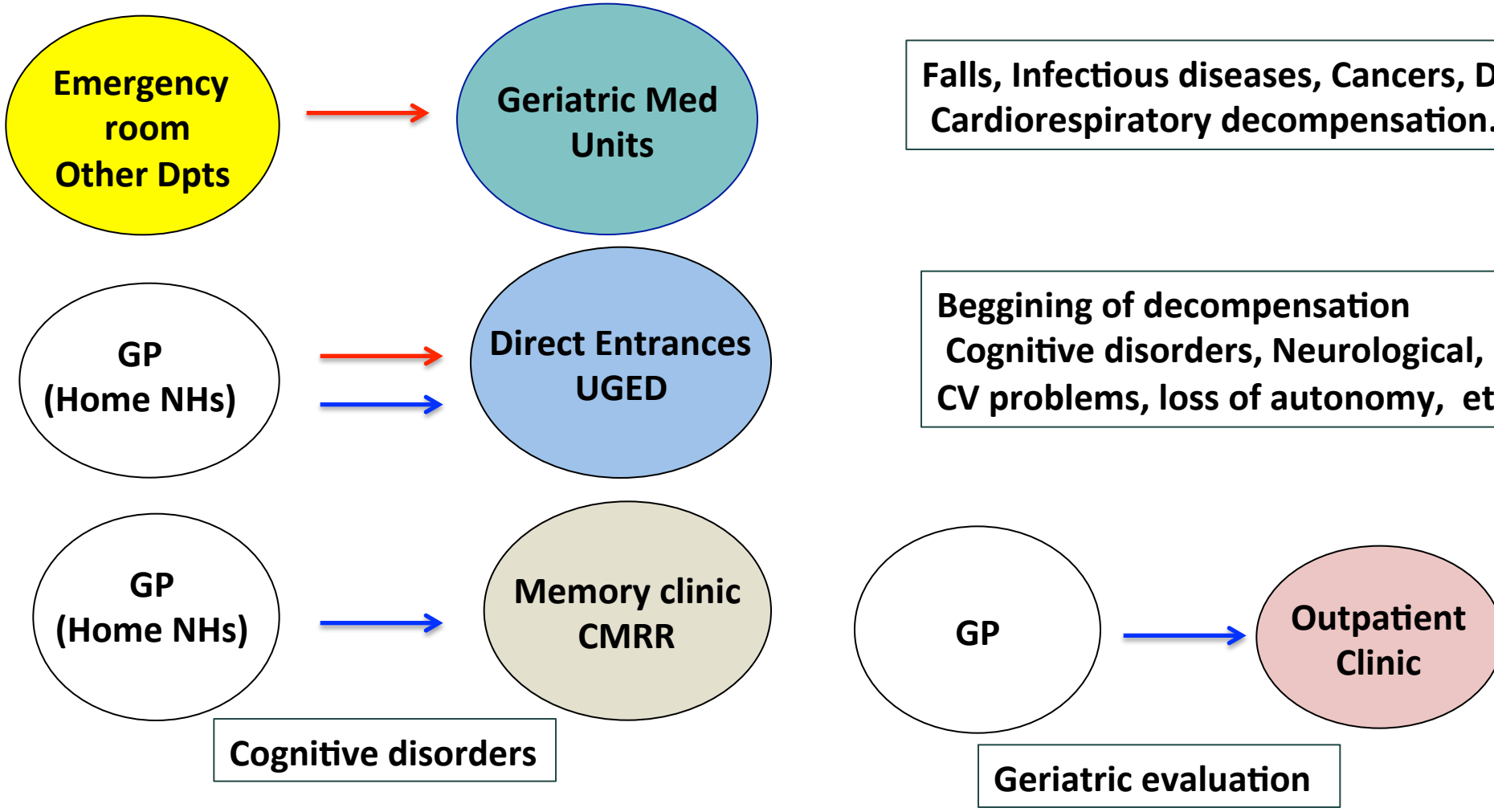
Where (Why) the patients are coming from?



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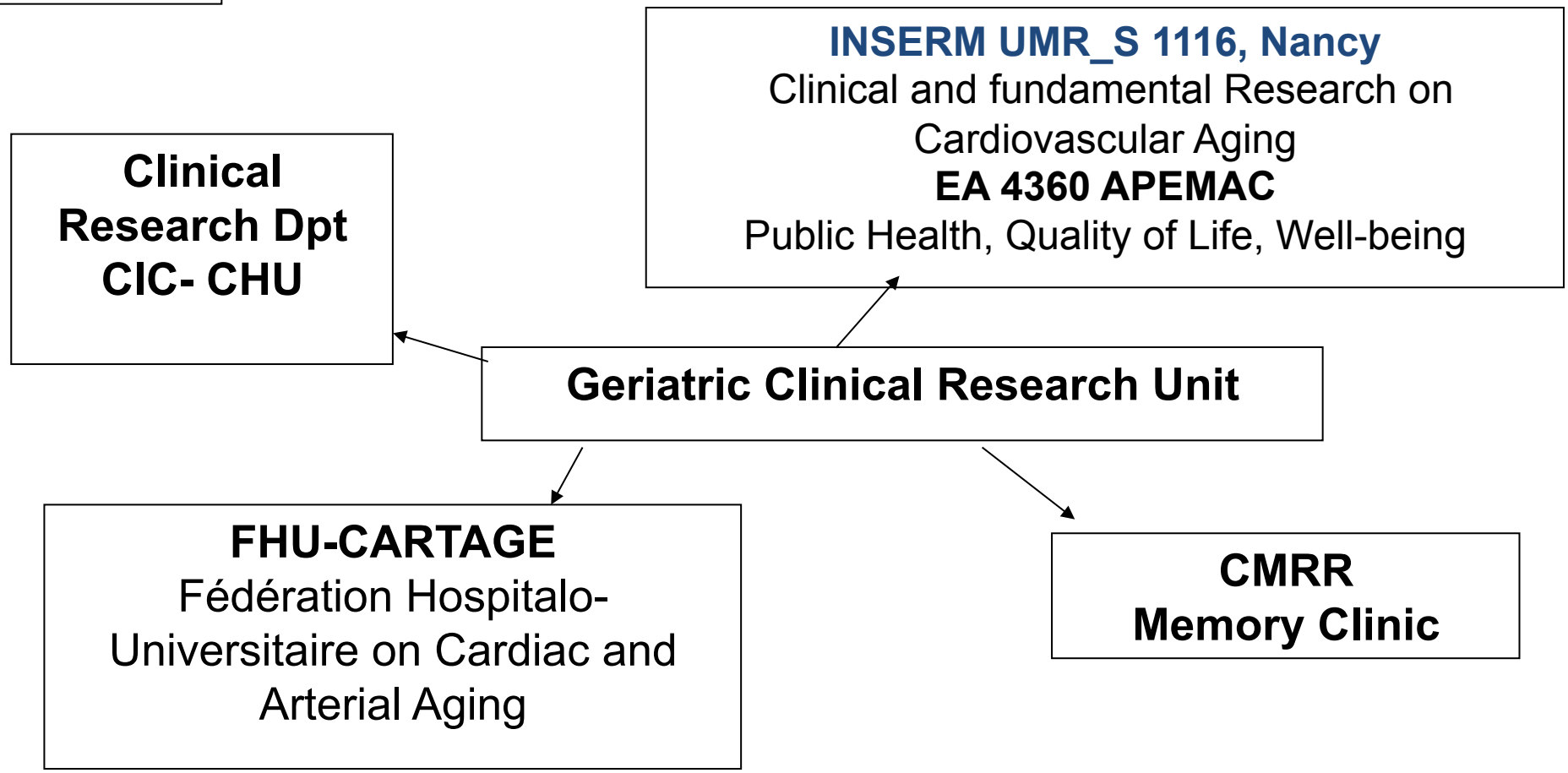
Organisation of the Research Unit



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Research Projects

- Interactions between arterial aging and frailty
- Management of hypertension in the very old, frail subjects
- Vascular contribution in cognitive decline in older adults
- Telomere dynamics and accelerated arterial aging.
- Acceptability of treatments in frail persons

Demographic, biological and clinical aspects of aging

Four questions

- At what age we get old?

- Longevity and centenarians. What is the future ?

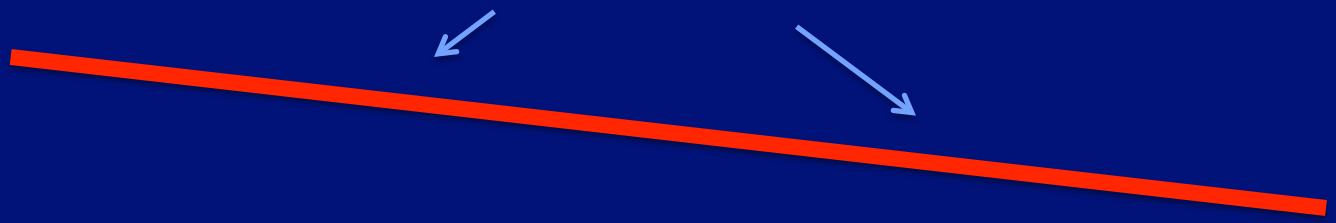
- Why do we age ?

- Can we slow down the aging process ?

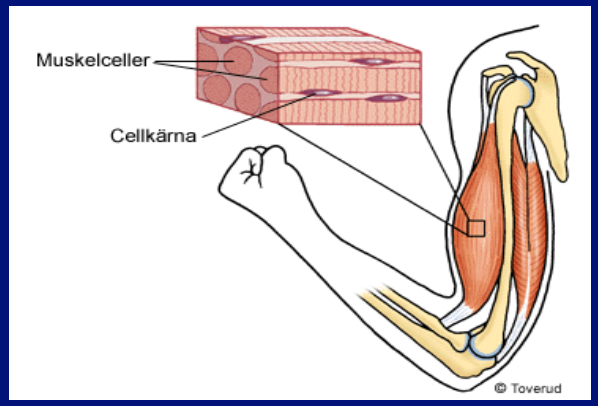
Old age

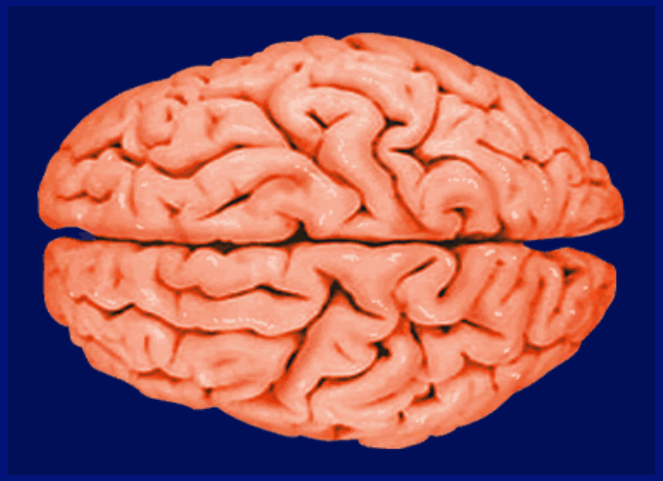
« …Is the last period of the life …. Characterized by a decrease in functional capacities

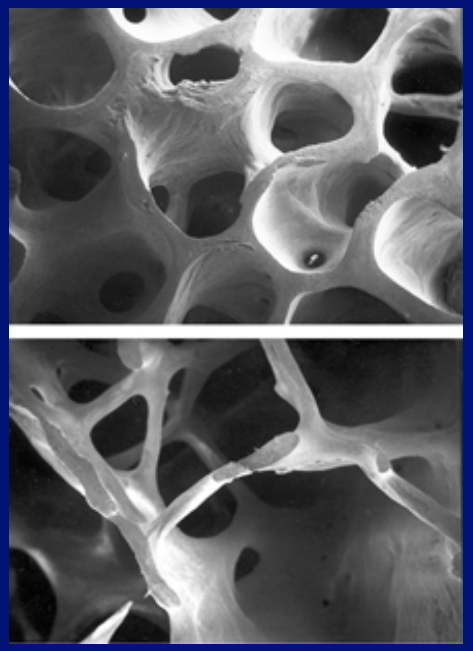
Where to put the cursor?

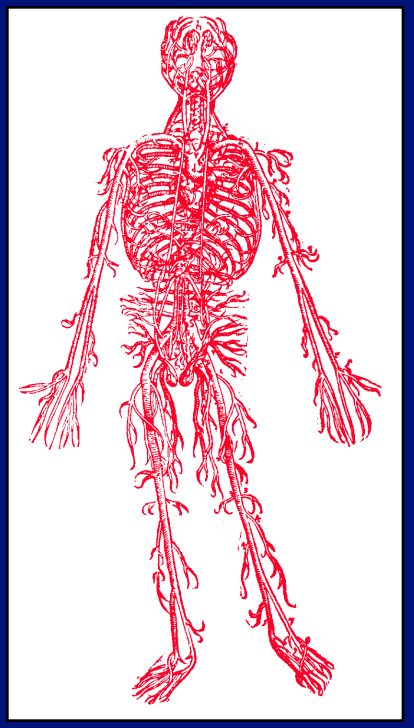


Functional capacities of muscles, bones, arteries, brain, skin…









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The aging process is very heterogeneous:

- From one cell to the other
- From one organ to the other
- From one function to the other
- From one individual to the other

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At what age we get old?
What is the best criterion?

- Age-related alterations: from birth
- Age-related diseases: >70-75 years
- Loss of autonomy: >75 yeas
- Increase in death rates: >80 years.

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Four questions

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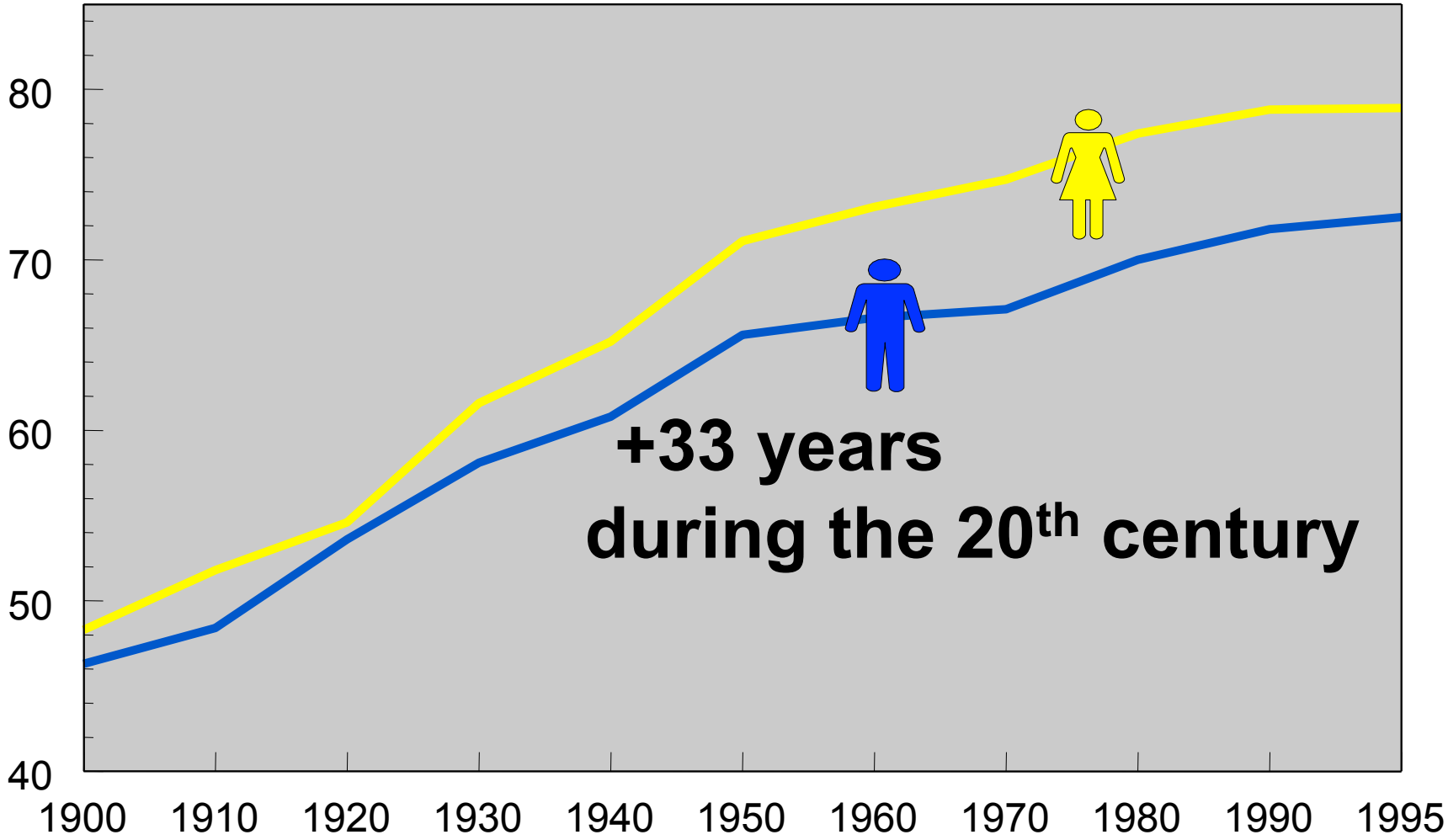
-Why do we age ?

- Can we slow down the aging process ?

Life expectancy at birth
(French men and women)



Source: National Center for Health Statistics

Evolution of the life expectancy at birth in men and women over the last century

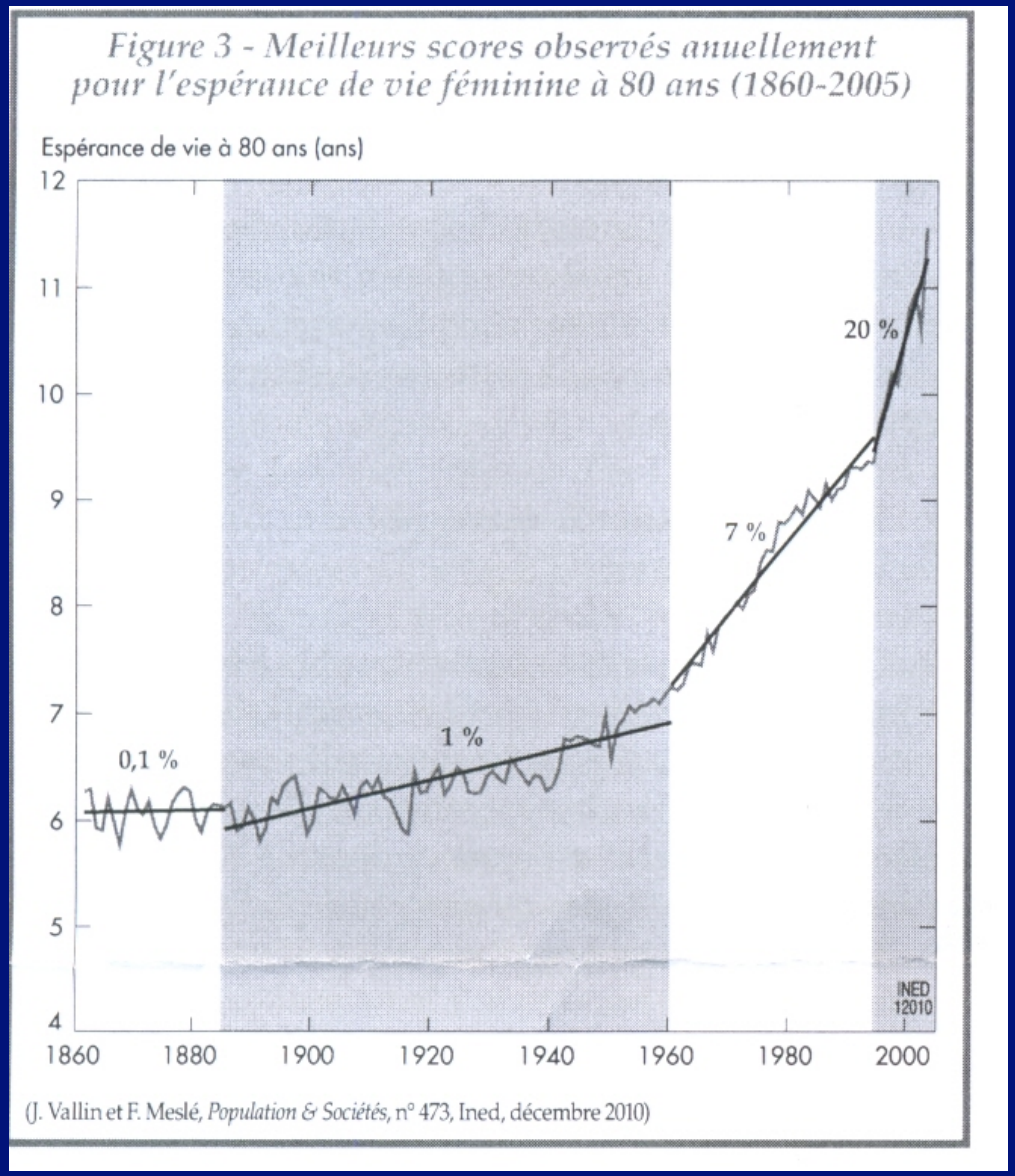
+33 years over a century is mainly due to:

50% to the decrease in infant mortality

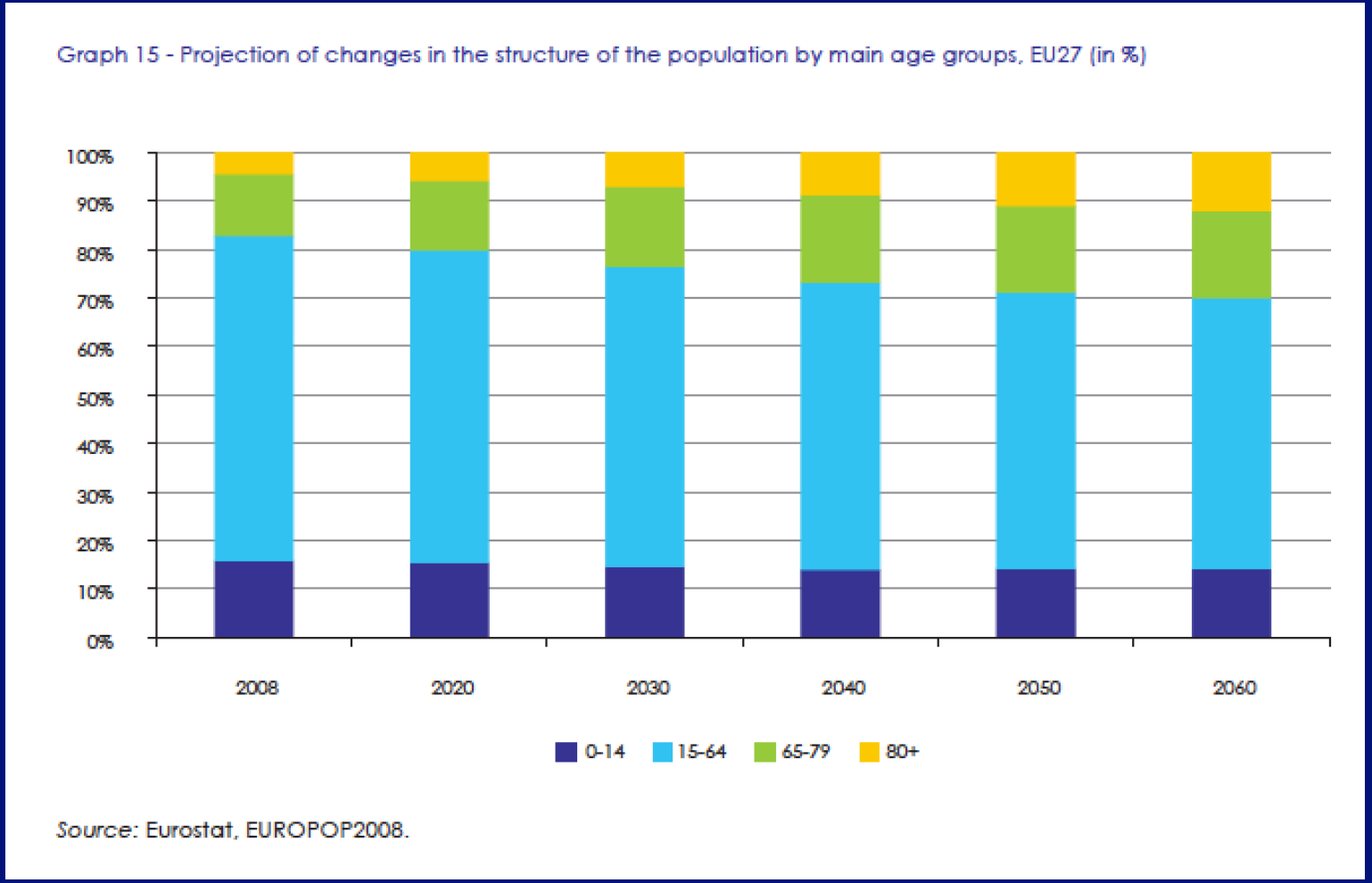
40% to the decrease in infection-related mortality

10% to the prevention of age-related diseases

Life expectancy at the age of 80 increased a lot these last years



Percentage of people over 80 years in Europe:
5% in 2015
10% in 2040

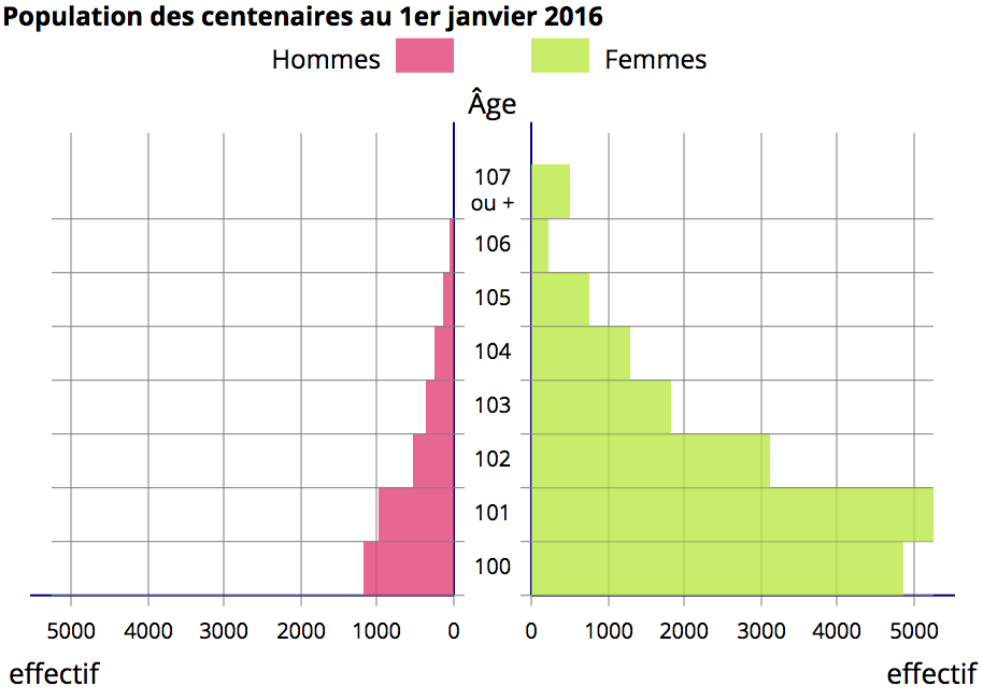


Is there a limite in the human maximal life expectancy?

The centenarians

2017: 21,000 Centenarians in France

Figure 1 – Population des centenaires au 1er janvier 2016



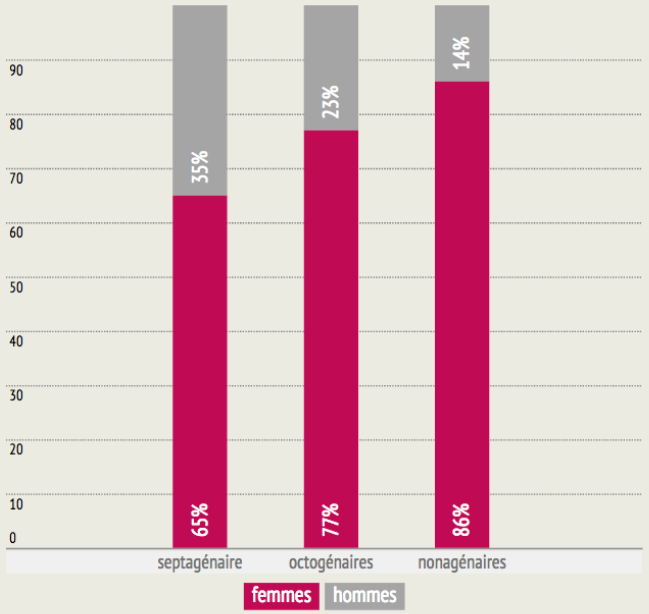
Lecture : au 1er janvier 2016, 4 882 femmes âgées de 100 ans vivent en France métropolitaine.
Note : les données au-delà de 106 ans sont indiquées à titre illustratif : elles sont très fragiles, étant donné le faible effectif.
Champ : personnes âgées de 100 ans ou plus, France y compris Mayotte.
Source : Insee, estimations de population et statistiques de l'état civil, 2016.

In France, 90% of the centenarians are women

Les femmes centenaires : plus nombreuses que les hommes

9 centenaires sur 10

sont des femmes. La proportion de femmes parmi les personnes âgées ne cesse d'augmenter comme en témoigne le graphique ci-dessous.



Au-delà de 110 ans, on entre dans la catégorie des "supercentenaires" qui, en France ne comporte que des femmes et dont la doyenne a 114 ans.

The « authentic » record(wo)man is the French Jeanne-Louise Calment

122 years
164 days

21 Février 1875 - 4 Août 1997

The 10 persons with the highest longevity since 1960 were all women

Rank	Name	Sex	Birth date	Death date	Age [**]	Country of death or residence
1	Jeanne Calment[1]	F	21 February 1875	4 August 1997	122 years, 164 days	France
2	Sarah Knauss[4]	F	24 September 1880	30 December 1999	119 years, 97 days	United States
3	Nabi Tajima[5]	F	4 August 1900	21 April 2018	117 years, 260 days	Japan
4	Lucy Hannah[6]	F	16 July 1875	21 March 1993	117 years, 248 days	United States
5	Marie-Louise Meilleur[7]	F	29 August 1880	16 April 1998	117 years, 230 days	Canada
6	Violet Brown[5]	F	10 March 1900	15 September 2017	117 years, 189 days	Jamaica
7	Emma Morano[5]	F	29 November 1899	15 April 2017	117 years, 137 days	Italy
8	Chiyo Miyako[8]	F	2 May 1901	22 July 2018	117 years, 81 days	Japan
9	Misao Okawa[5]	F	5 March 1898	1 April 2015	117 years, 27 days	Japan
10	María Capovilla[9]	F	14 September 1889	27 August 2006	116 years, 347 days	Ecuador

Kane Tanaka

Kane Tanaka at the age of 115.

Birth:	2 January 1903 Fukuoka, Fukuoka Pref., Japan
Age:	115 years, 293 days
Country:	JPN

Validated

The oldest person today (October 23, 2018) is Kane Tanaka (Japan)

She could beat the JL Calment record in June 15, 2025 (6 years and 200 days from now!!)

Kane Tanaka

Kane Tanaka at the age of 115.

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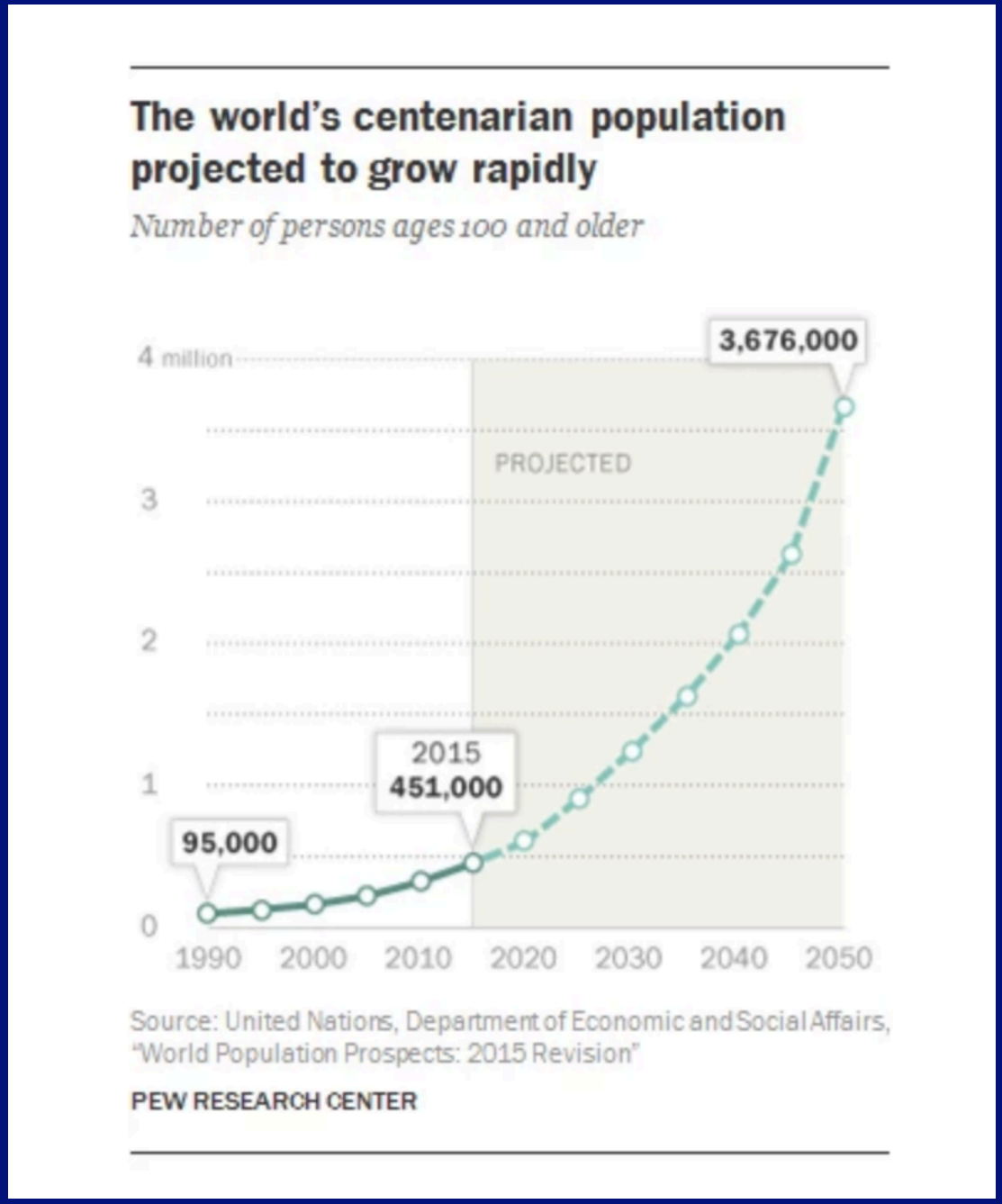
<0.5% of probability to reach it

In order to break the longevity record (e.g., survival to age 123 years), 262,200 people would have to be alive at age 105.

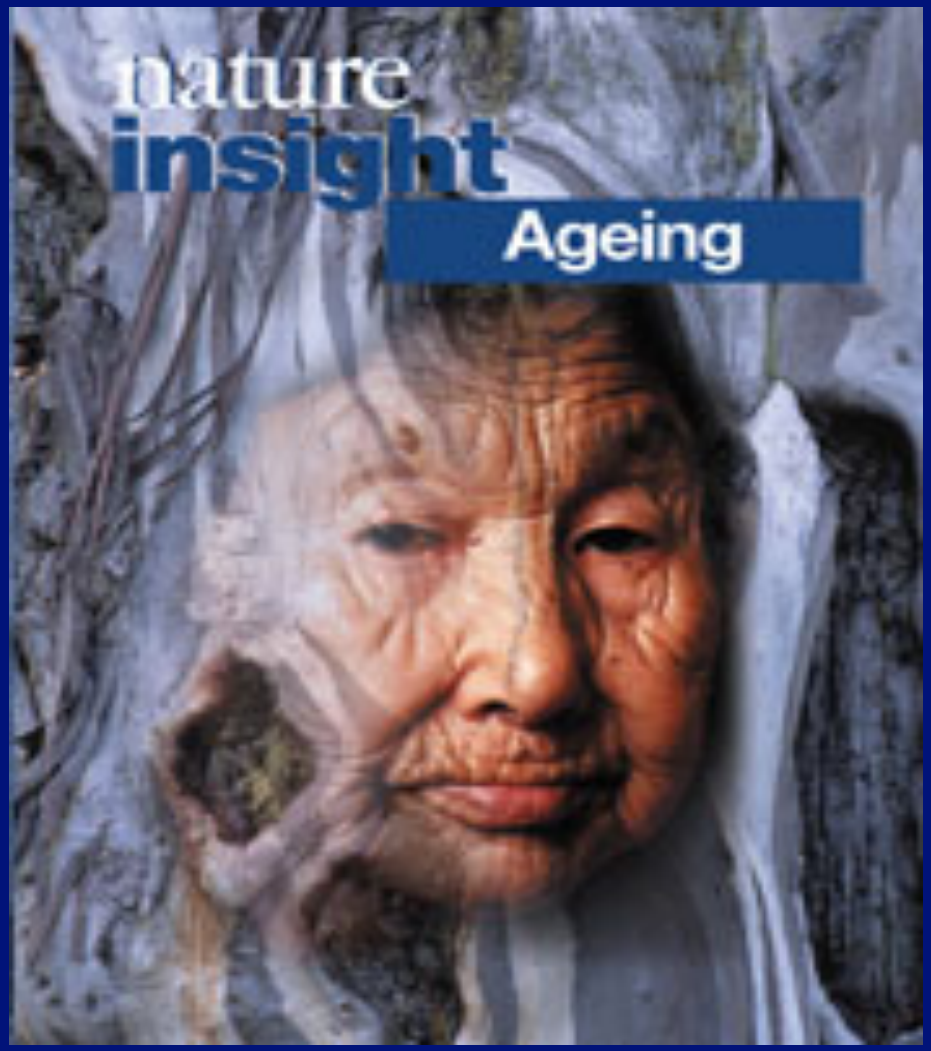
Olshansky SJ. JAMA. 2018 Oct 2;320(13):1323-1324.

Estimation in the world: in 2016
450,000 centenarians
45,000 (10%) reach age of 105 years



In 2050 there would be the necessary number of 105+ (>300,000) in order to break the record of JL Calment

JL Calment will be the record (wo)man of longevity for at least 28 years; probably more than 50 years

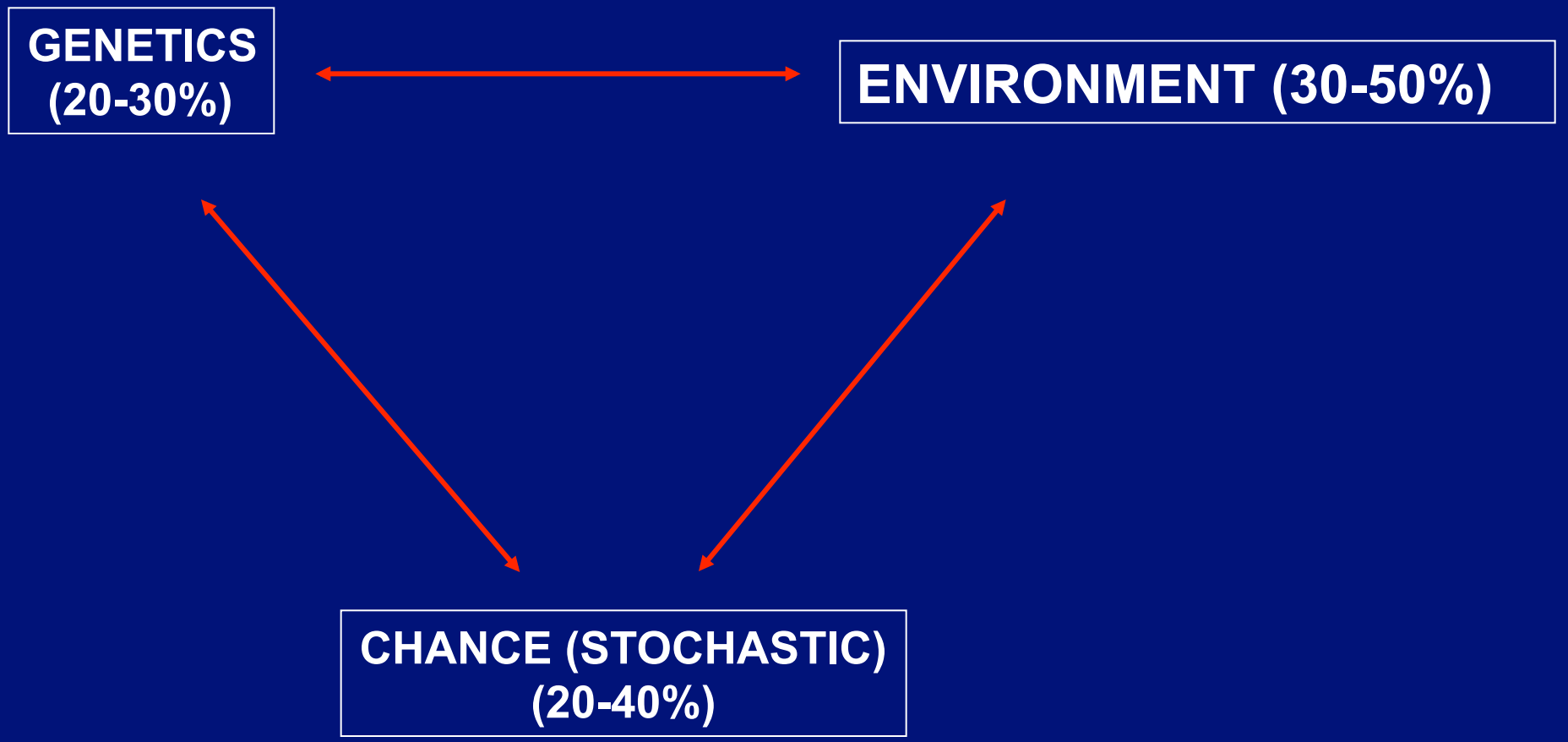


Who will live longer?

Who will age faster?

Can we increase our chances to live much longer?

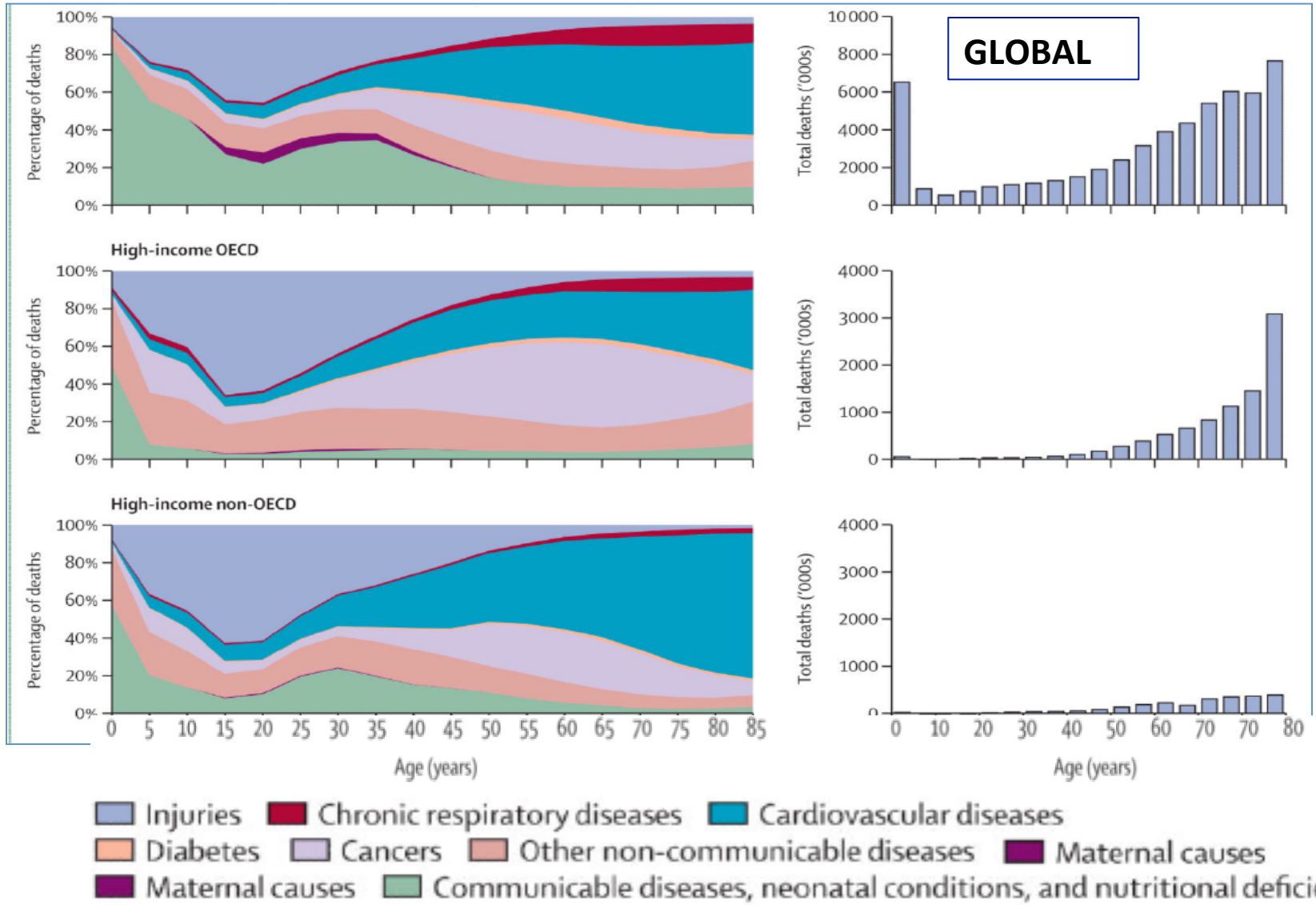
Who will live longer?
Who will age faster?



Mortality at different ages for countries of low, middle and high income in 2012

OECD=Organisation for Economic Co-operation and development

Beard J. et al: Lancet. 2016; 387: 2145–2154



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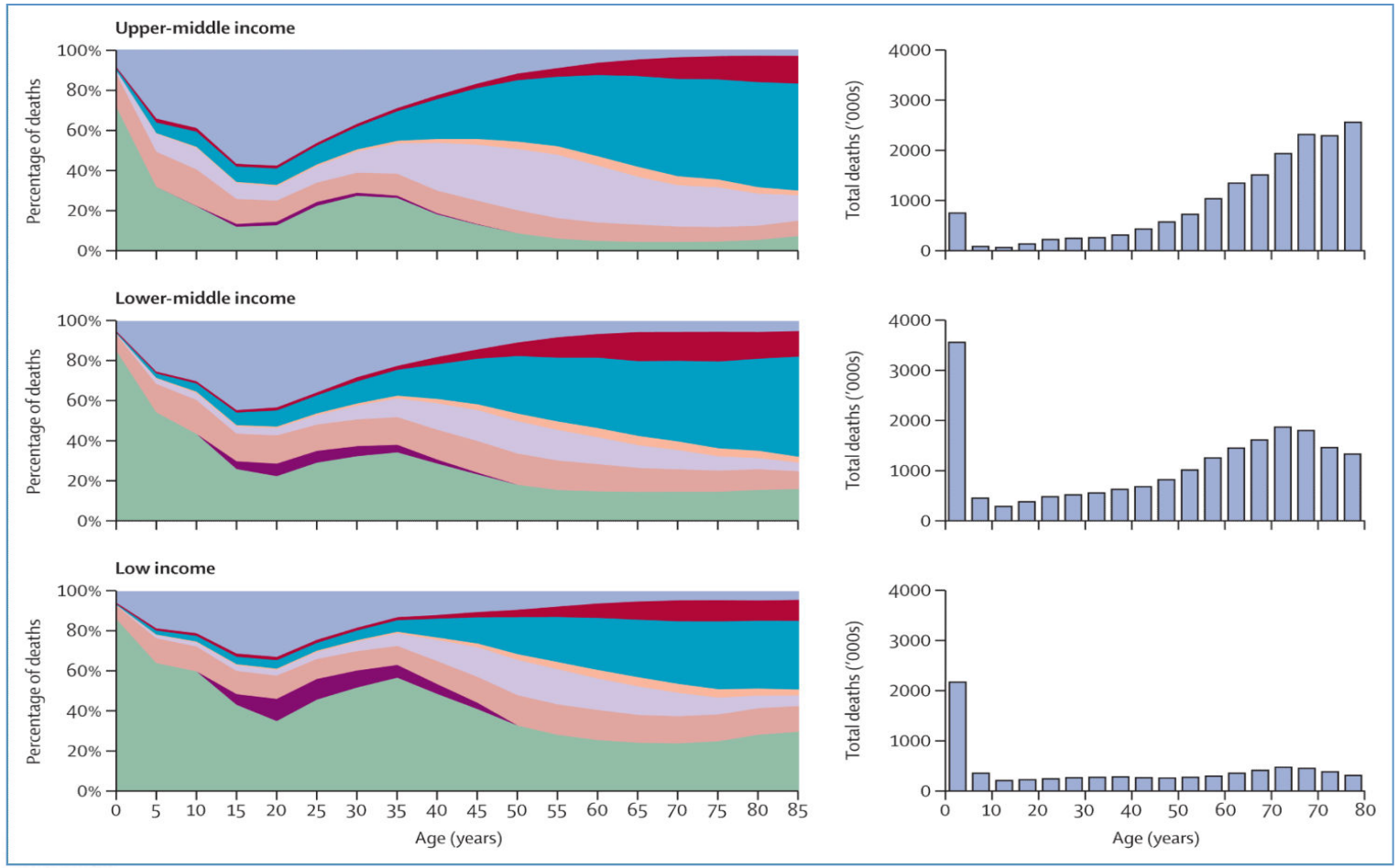


Environmental factors :

1- Fixed: Birthplace, socio economic parent status.

2- Hardly modifiable: Socio-economic status, wars, epidemics, polution.

3- Way of life: Physical activities, Nutrition, Tobacco, tobaco, diet, prevention of risks.

Four questions

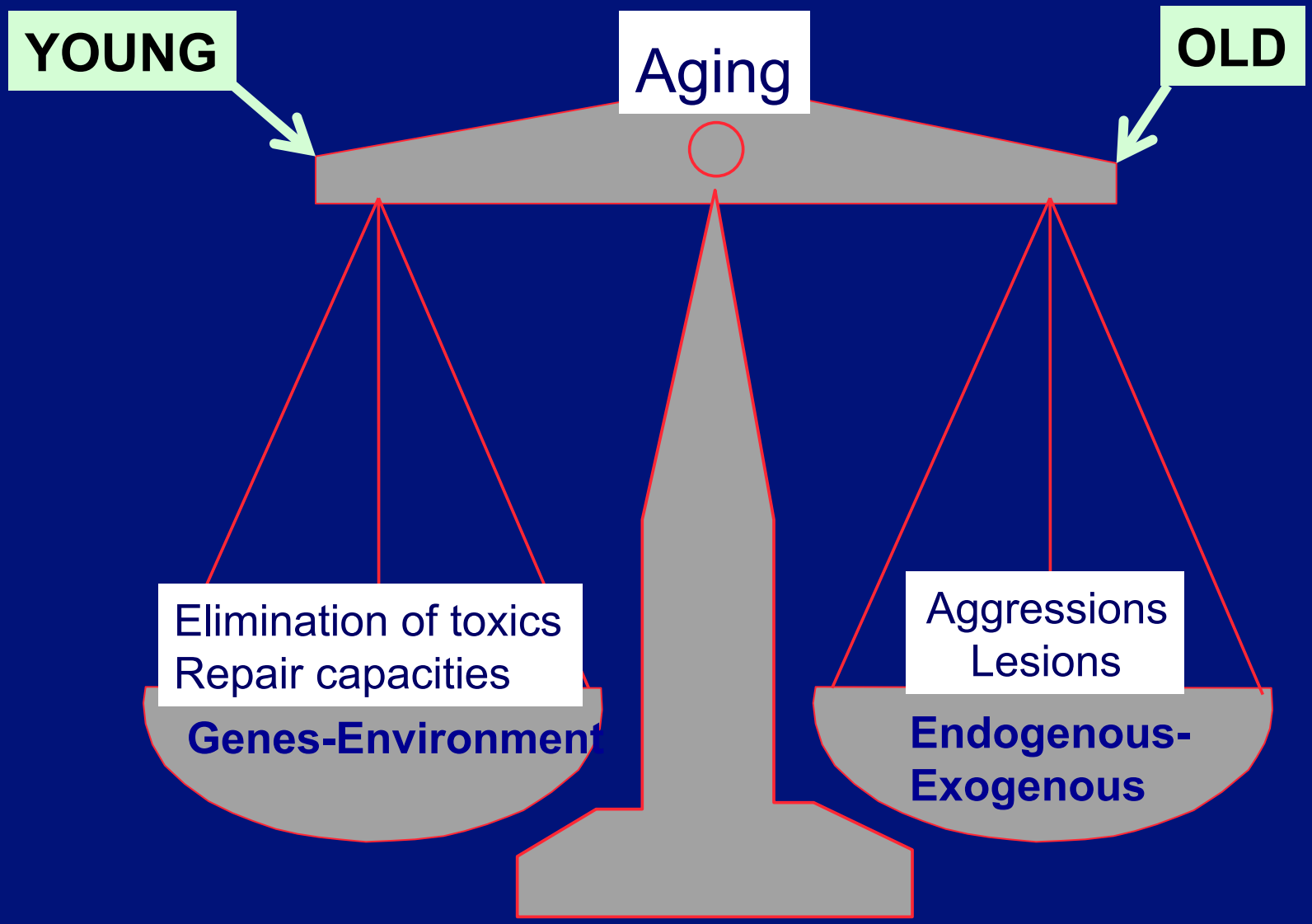
- At what age we get old?

- Longevity and centenarians. What is the future ?

- Why do we age ?

- Can we slow down the aging process ?

Mechanisms of aging



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The Hallmarks of Aging

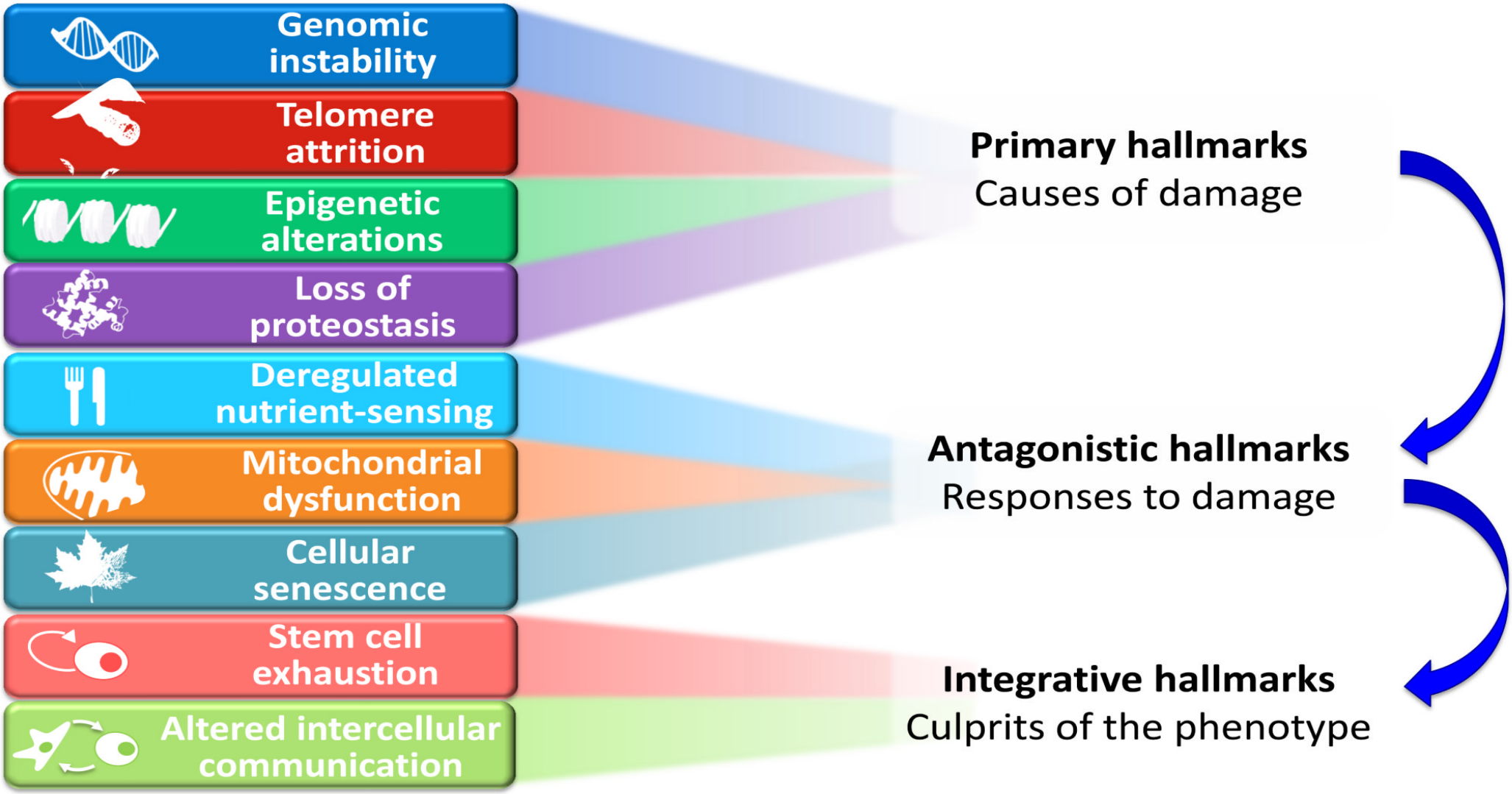
Cell. Author manuscript; available in PMC 2013 November 21.

Published in final edited form as:
Cell. 2013 June 6; 153(6): . doi:10.1016/j.cell.2013.05.039.

The Hallmarks of Aging

Carlos López-Otín[1,*], **Manuel Serrano**[2,*], **Linda Partridge**[3,4,*], **Maria A. Blasco**[5,*], and **Guido Kroemer**[6,7,8,9,10,*]

Functional Interconnections between the Hallmarks of Aging



Cell 2013

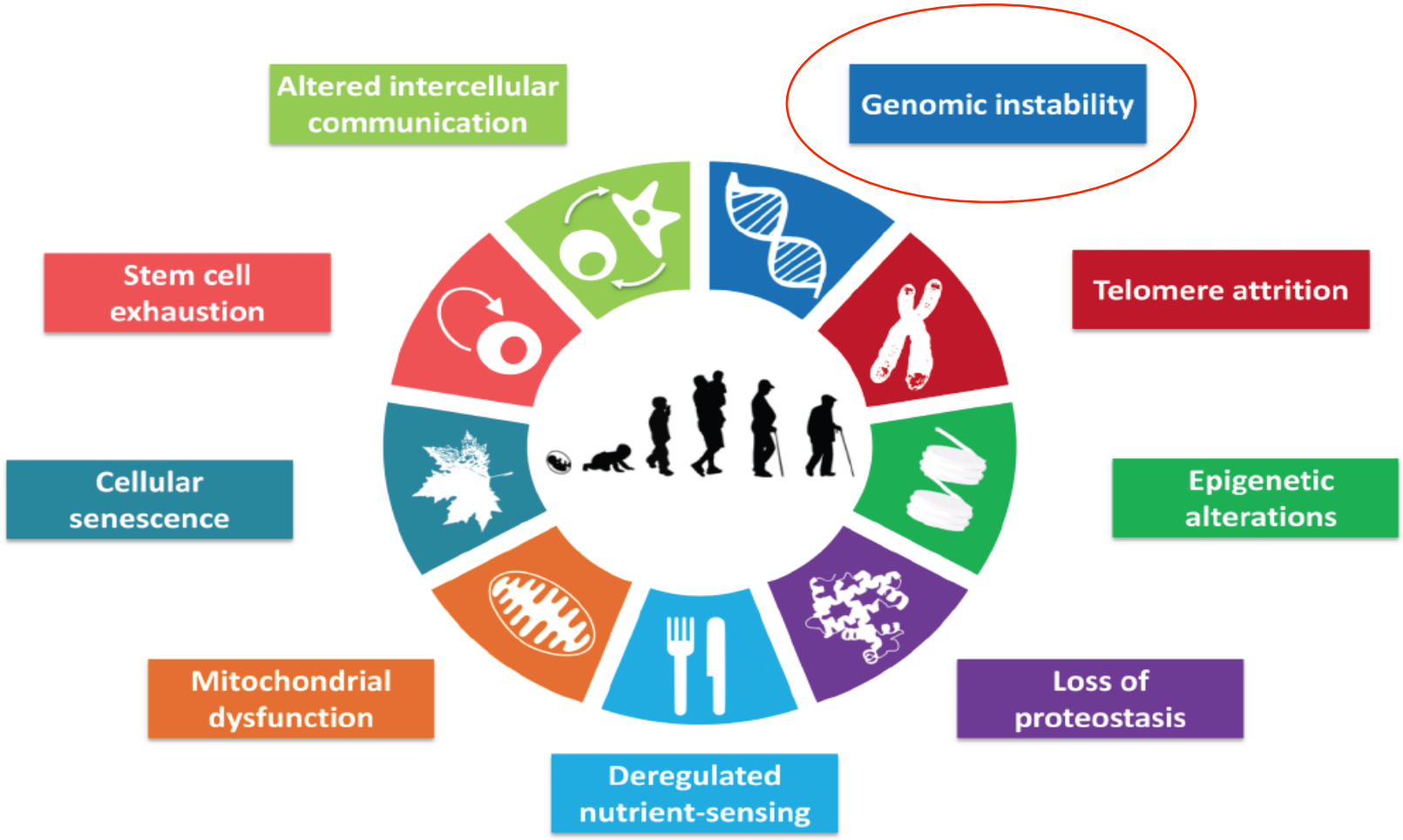
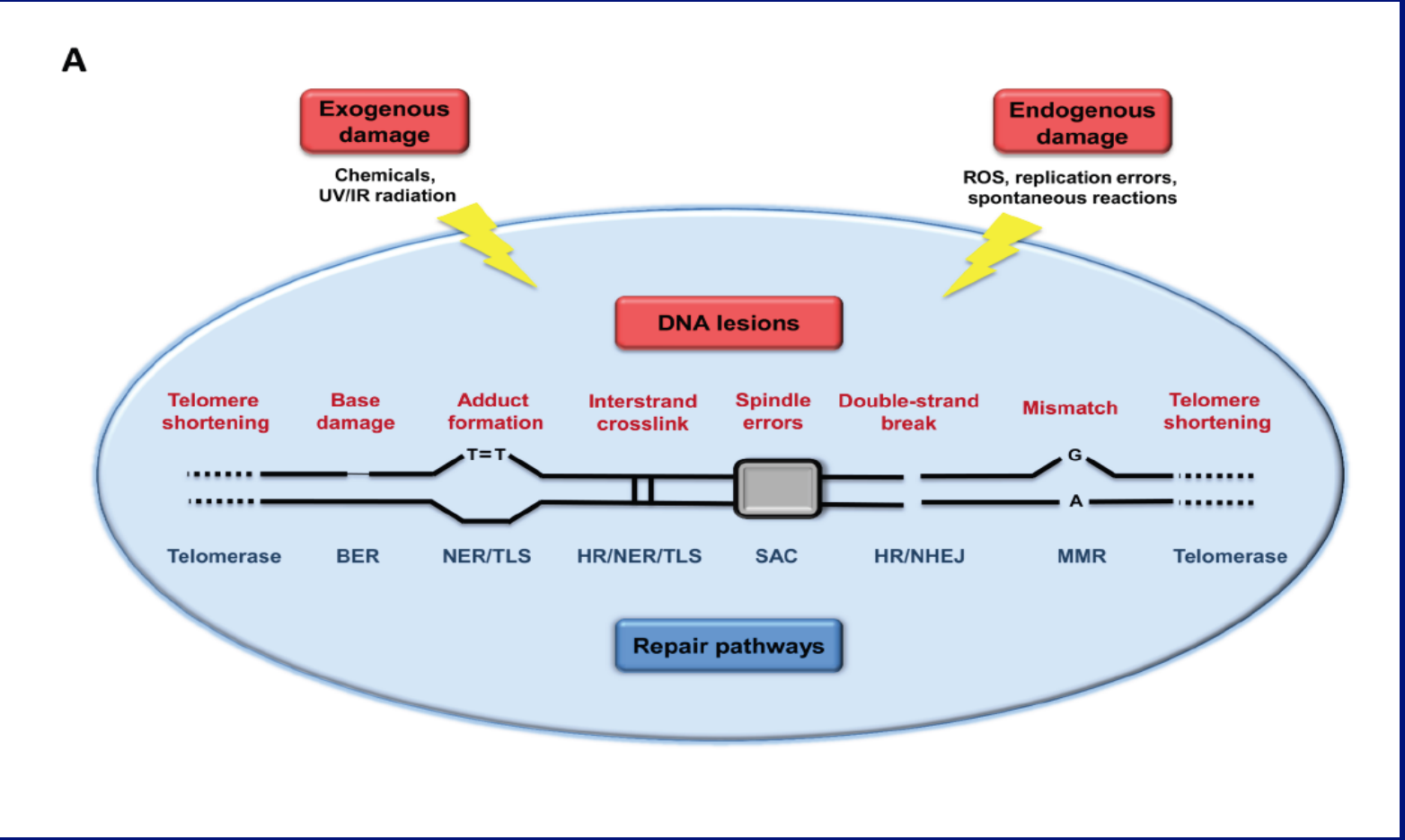


Figure 1. The Hallmarks of Aging

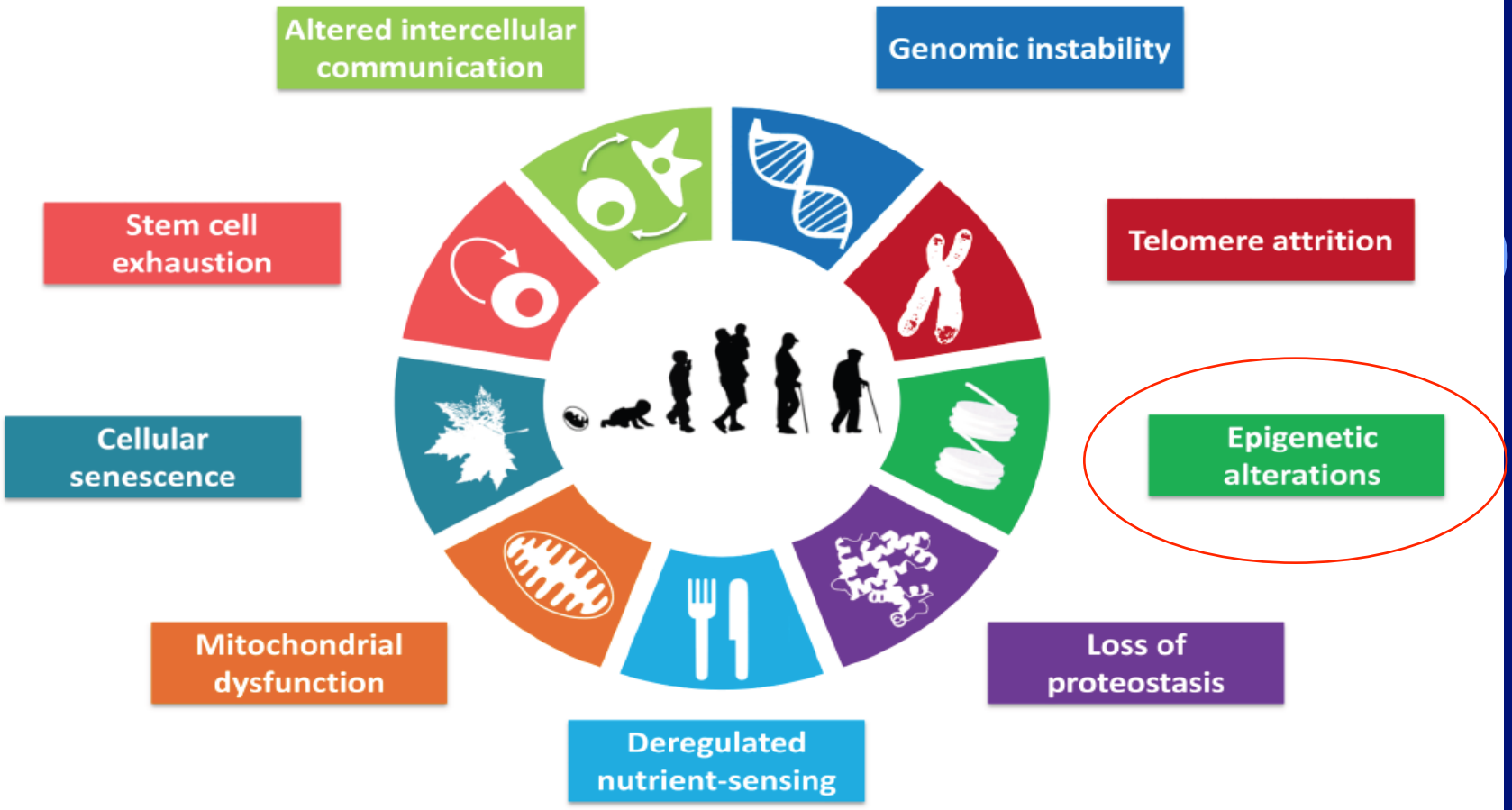
The scheme enumerates the nine hallmarks described in this review: genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient-sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication.

Cell 2013

Genomic instability: Endogenous and environmental factors leading to excessive production of free radicals are responsible for the accumulation of lesions on nuclear and mitochondrial DNA.



Cell 2013



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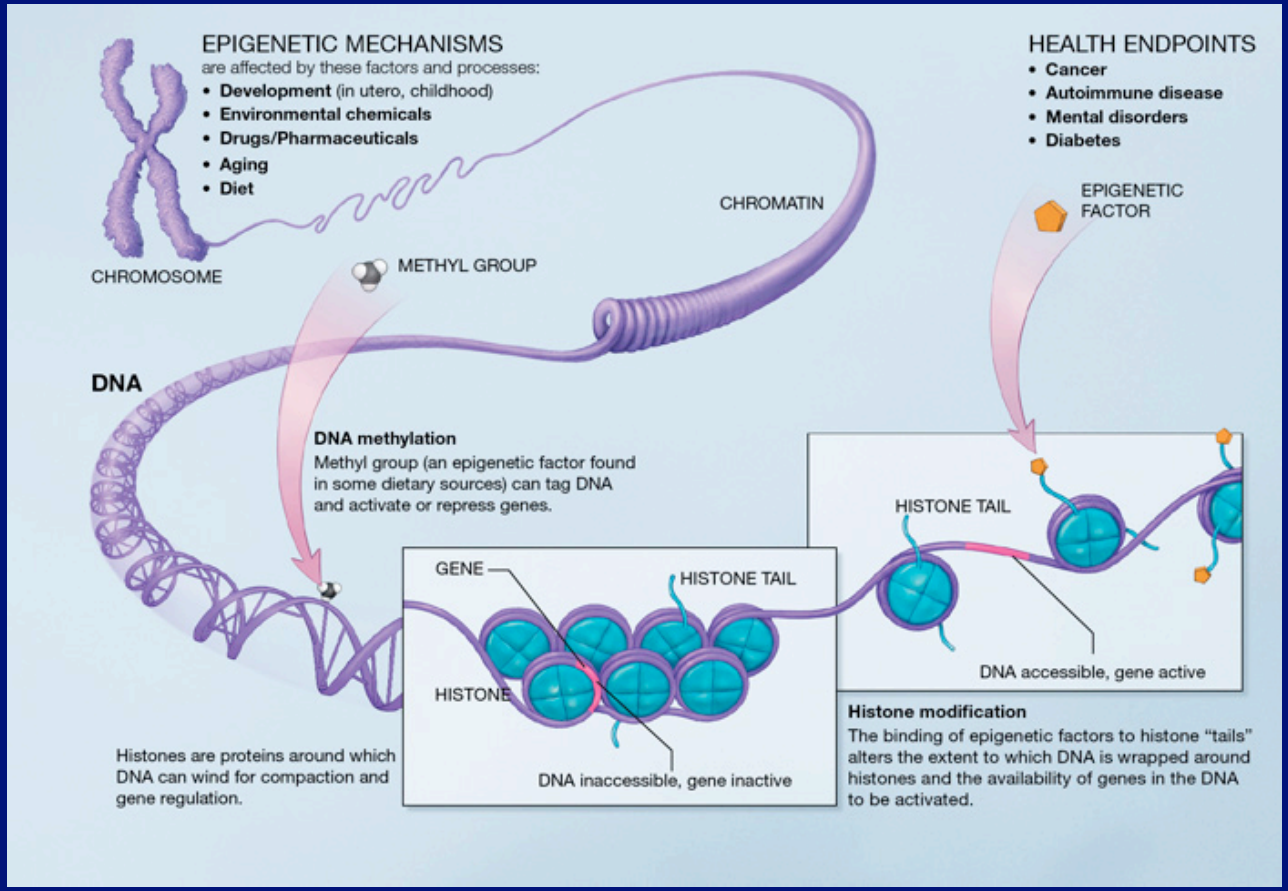
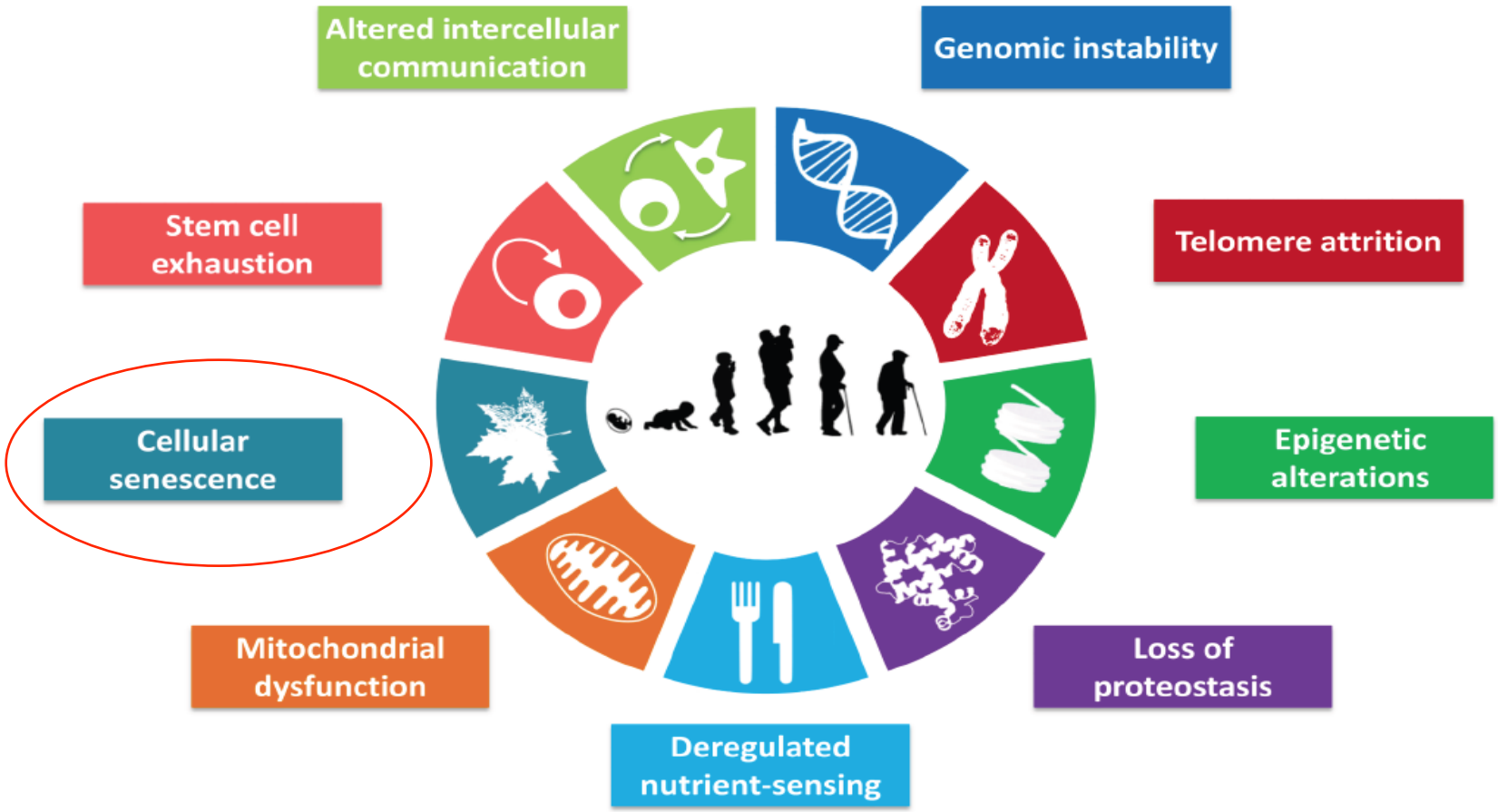
Cell 2013

Epigenetic alterations: play an important role in the pace of aging and longevity

DNA methylation; Remodelling of chromatin. Modifications of histones. Transcriptionnal modifications





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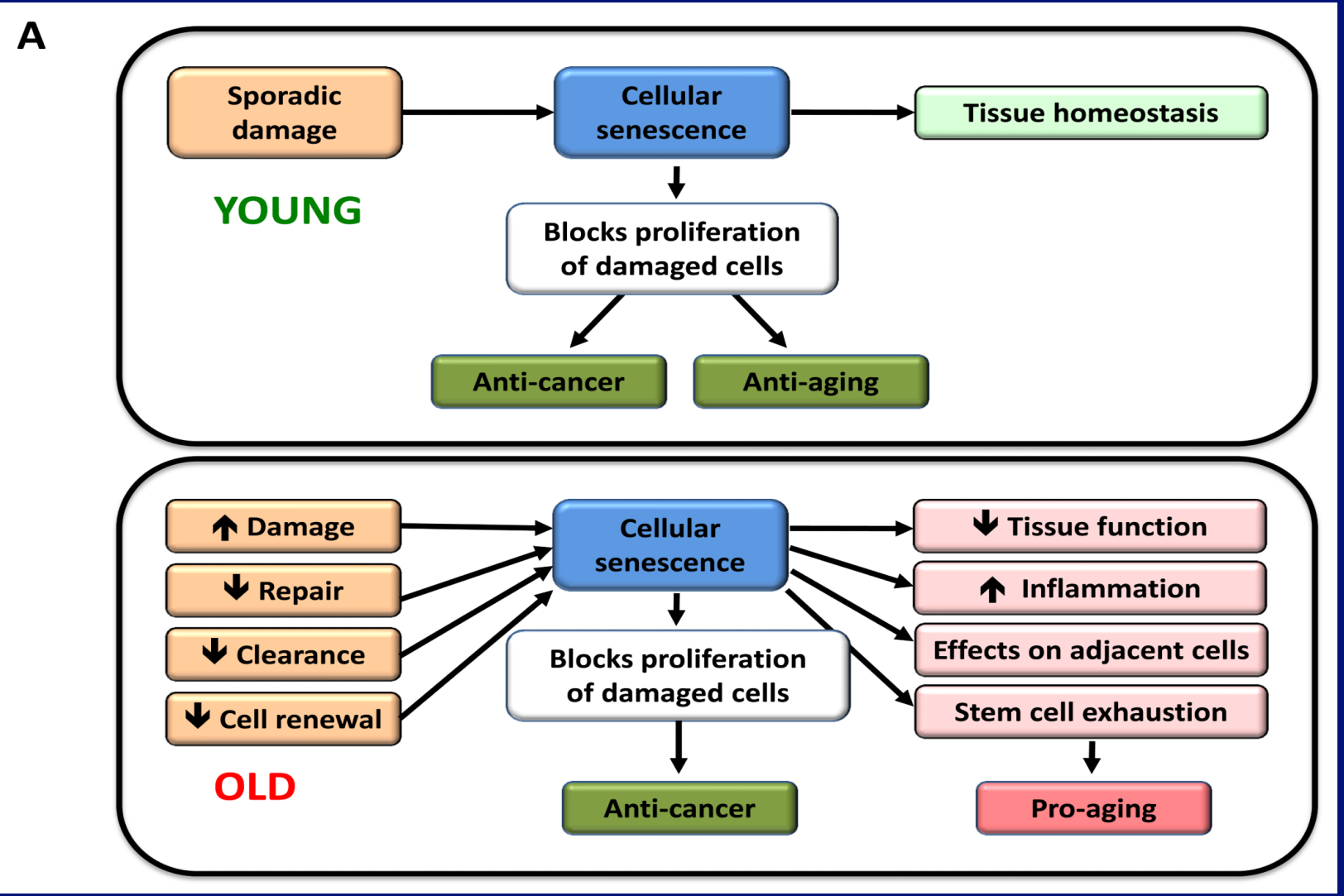
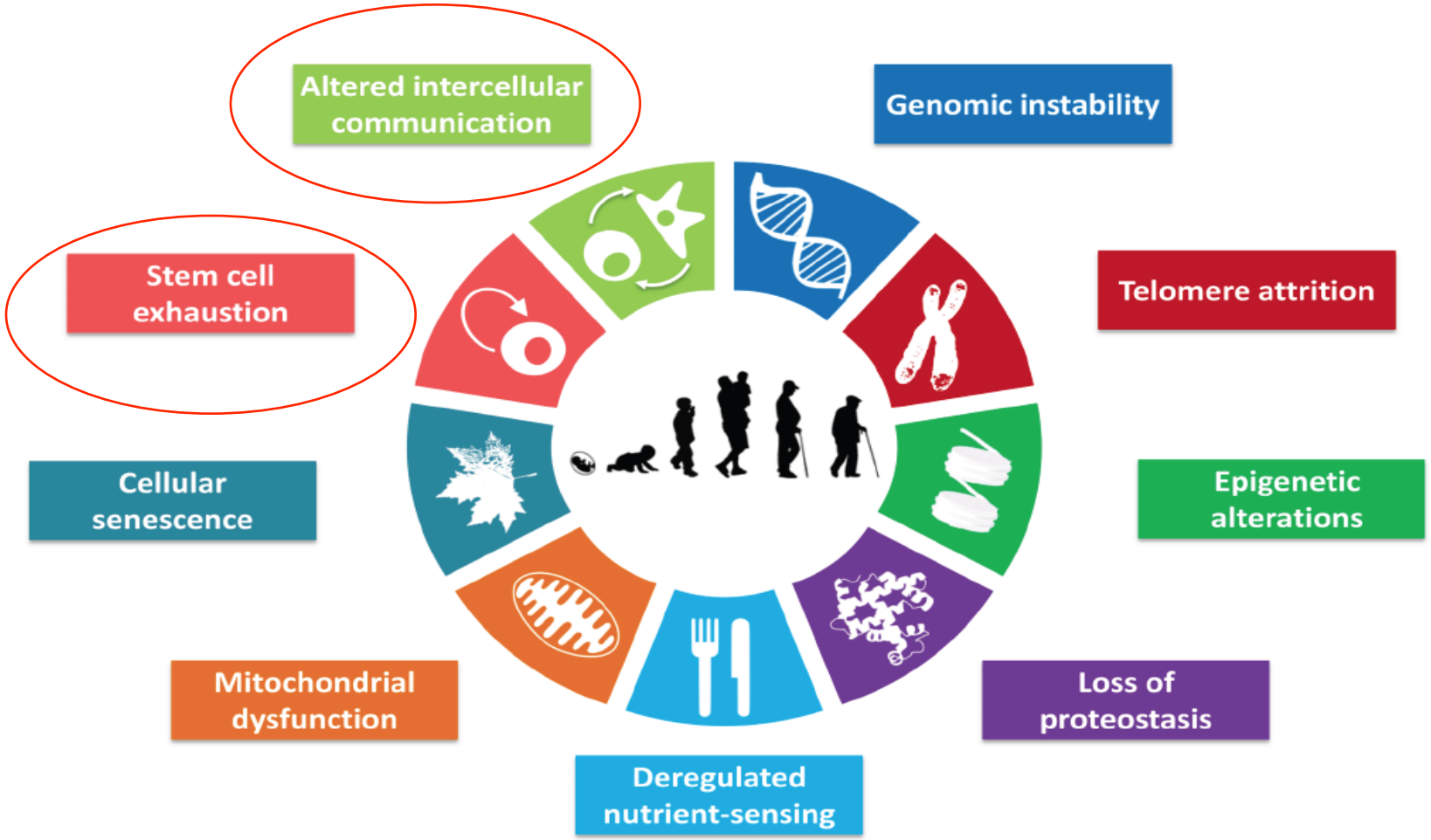
Cell 2013

Cellular senescence



Cell 2013



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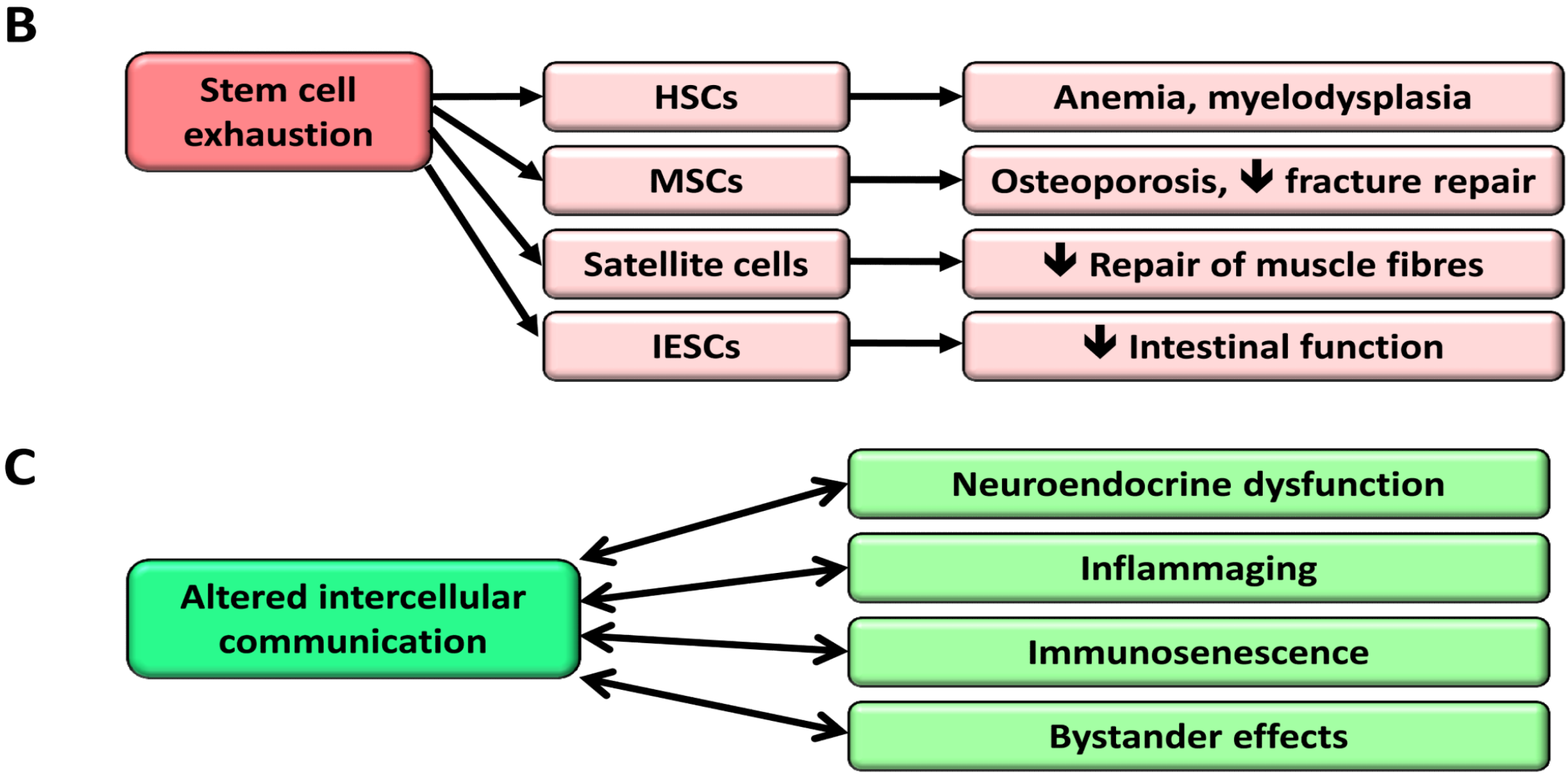
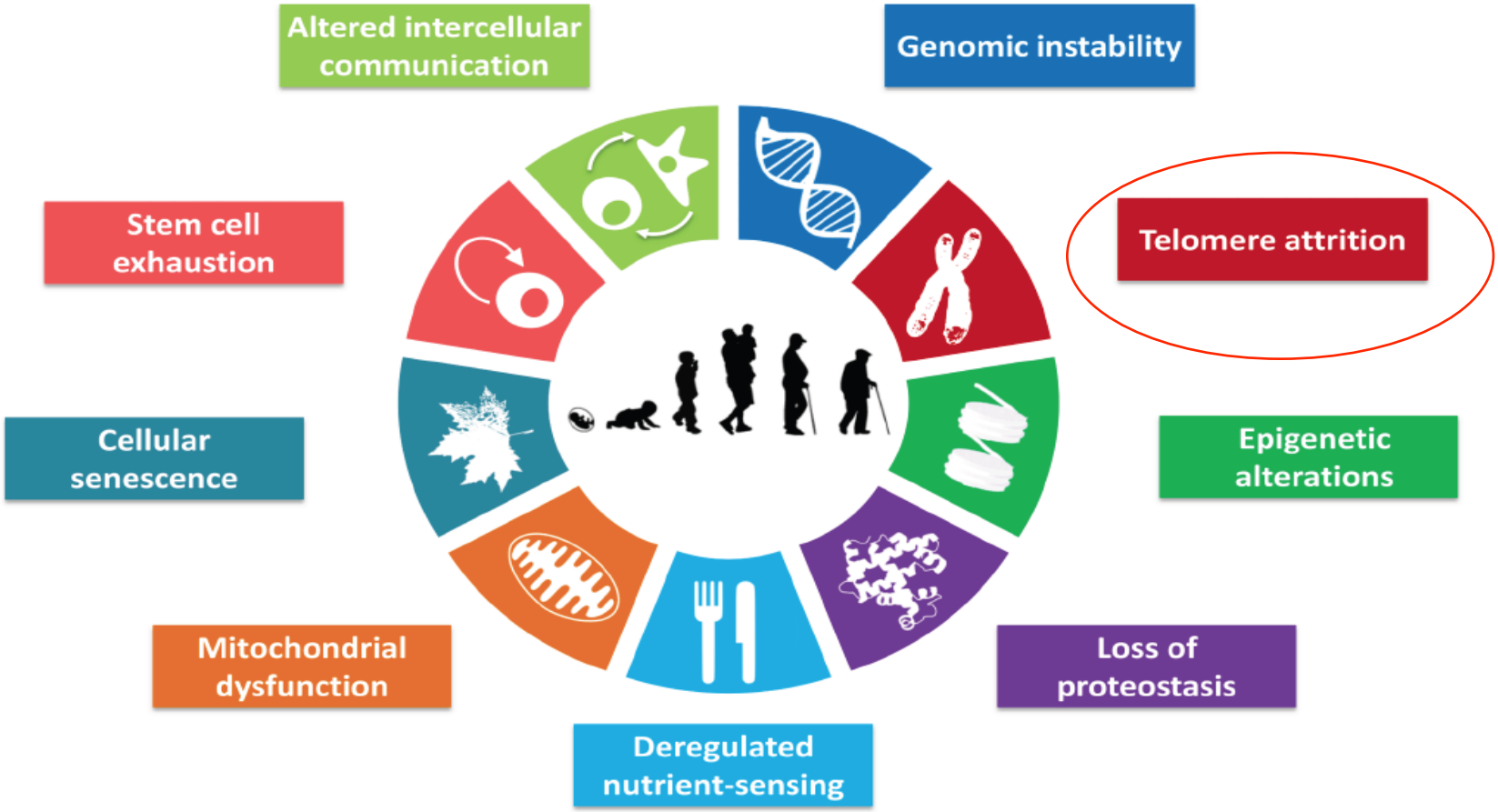
Cell 2013

Stem cell exhaustion and altered IC communication



C. Lopez-Otin, Cell 2013



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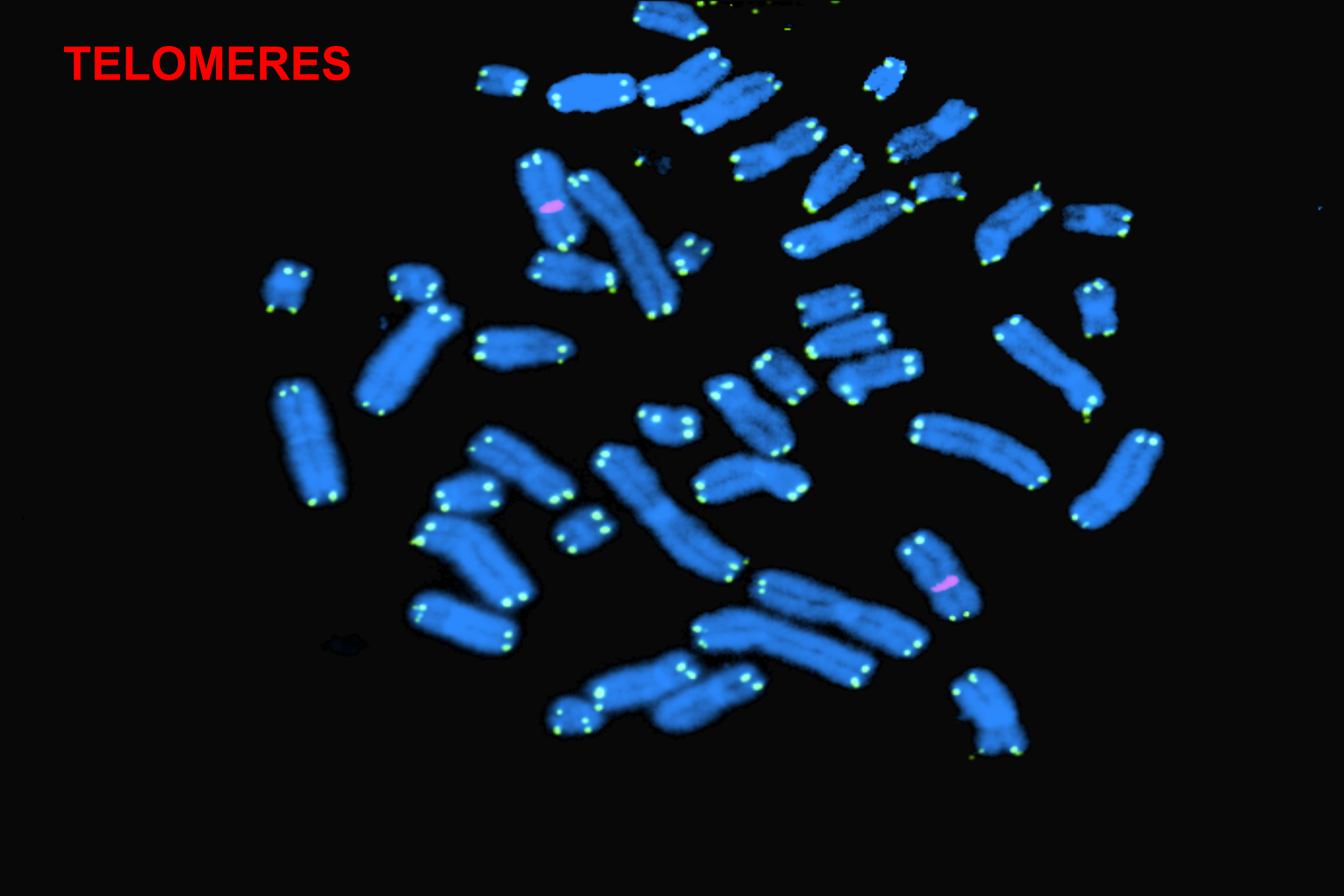
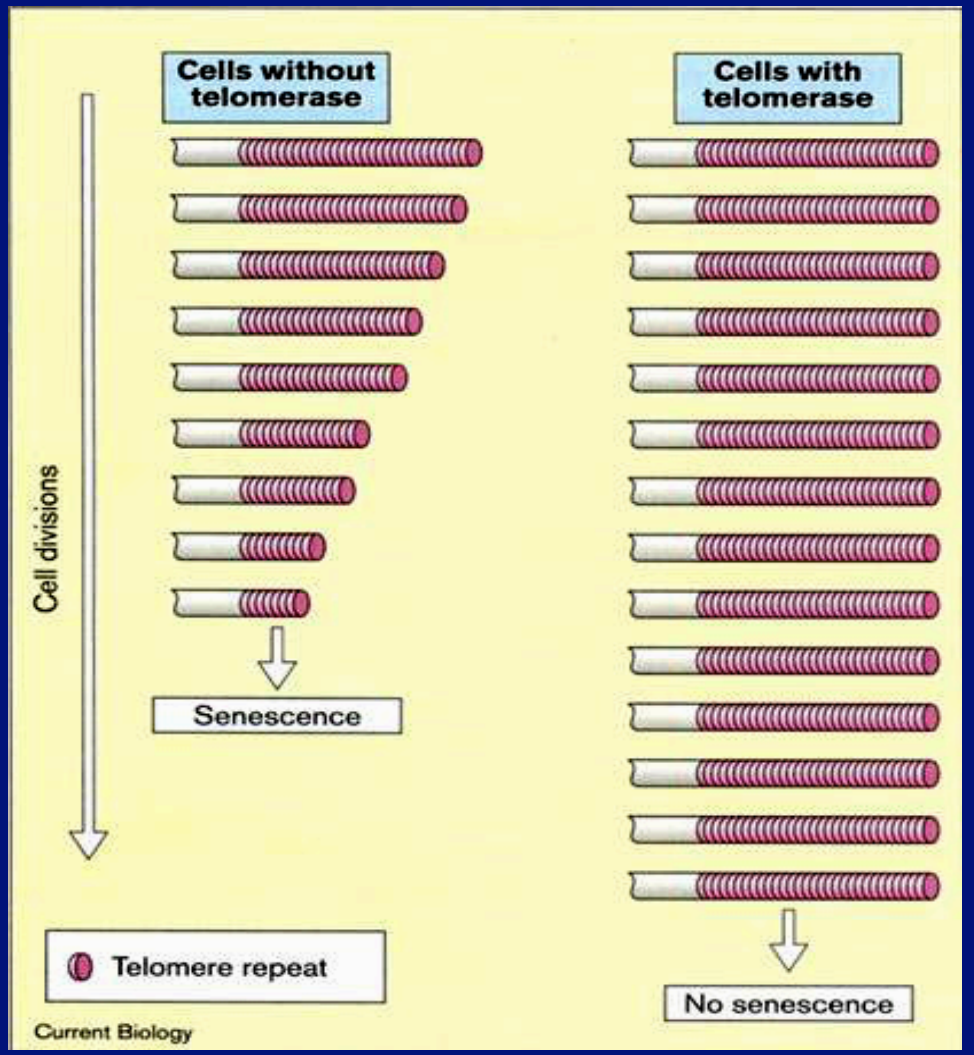
Cell 2013

TELOMERES

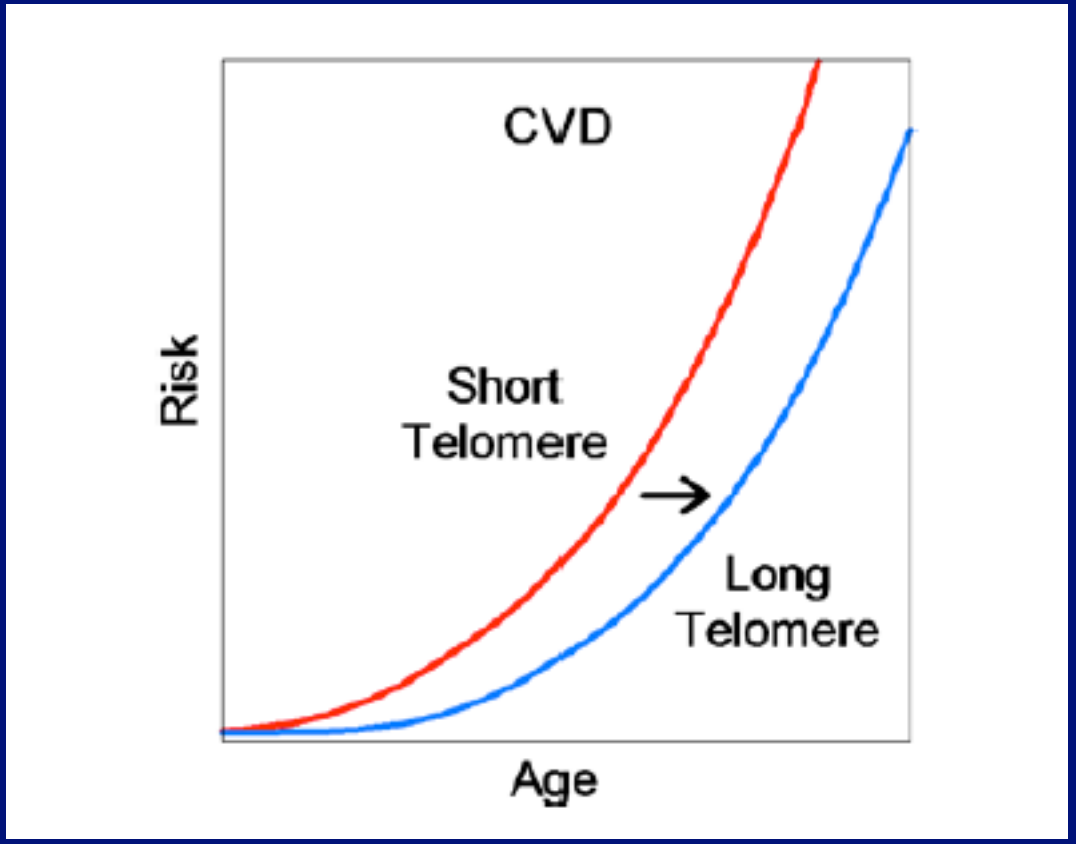


Presence of the enzyme telomerase can replace the telomere DNA lost during each cell division thus preventing cell senescence

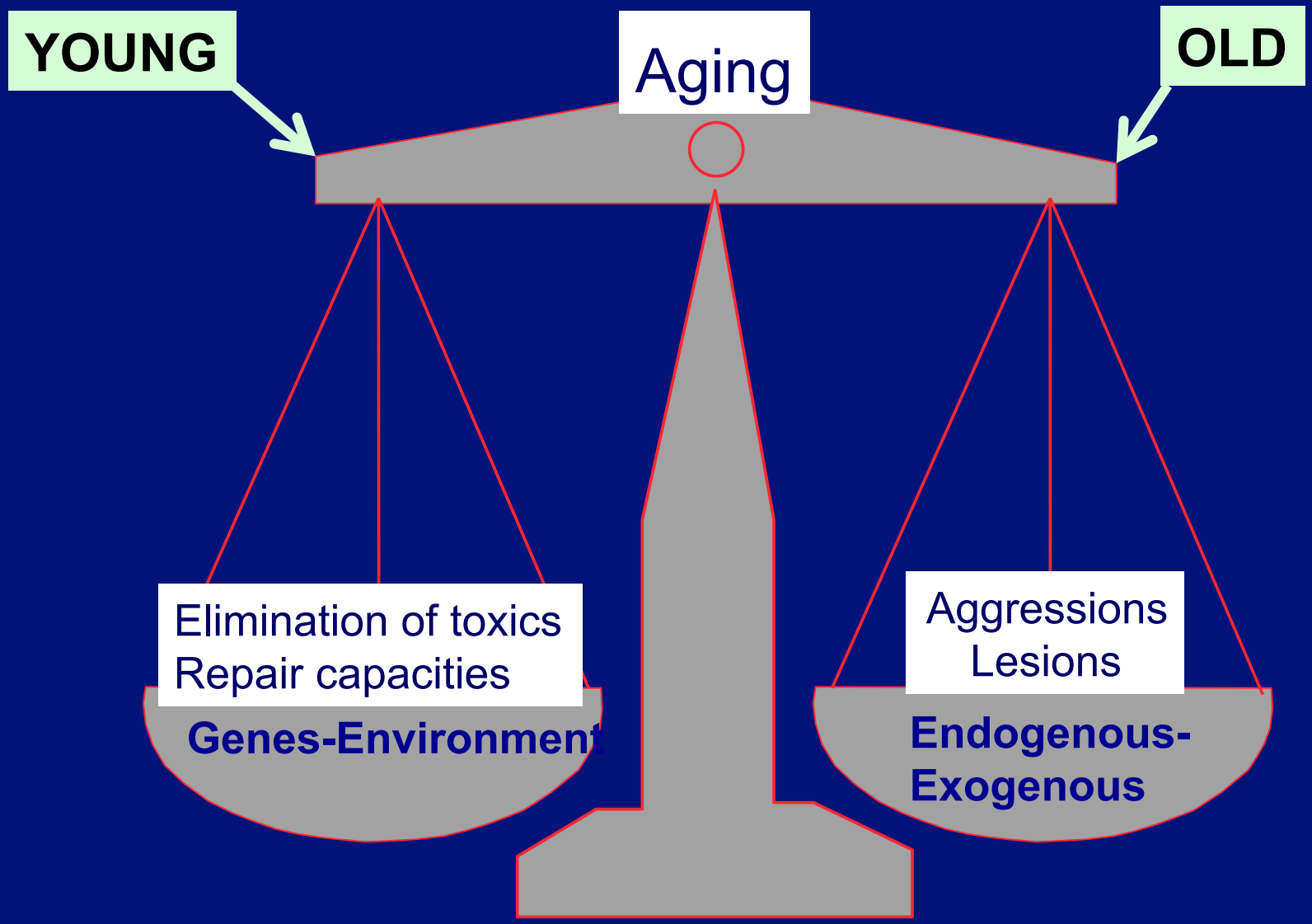
Greider and Blackburn, 1985, 1987, 1989



Long LTL is associated with a shift to an older age in cardiovascular disease risk.



S Hunt et al; Circ Cardiovasc Genet 2015;8:4-7



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From molecules and cells to the human aging process

-Loss of cells
-Deacrease of proliferative capacities
-Altered tissues
-Loss of functions
Degenerative diseases

Cell dysfunction
Mutations
Cancers

Functional Decline, Organic ailure,
Diseases, Death

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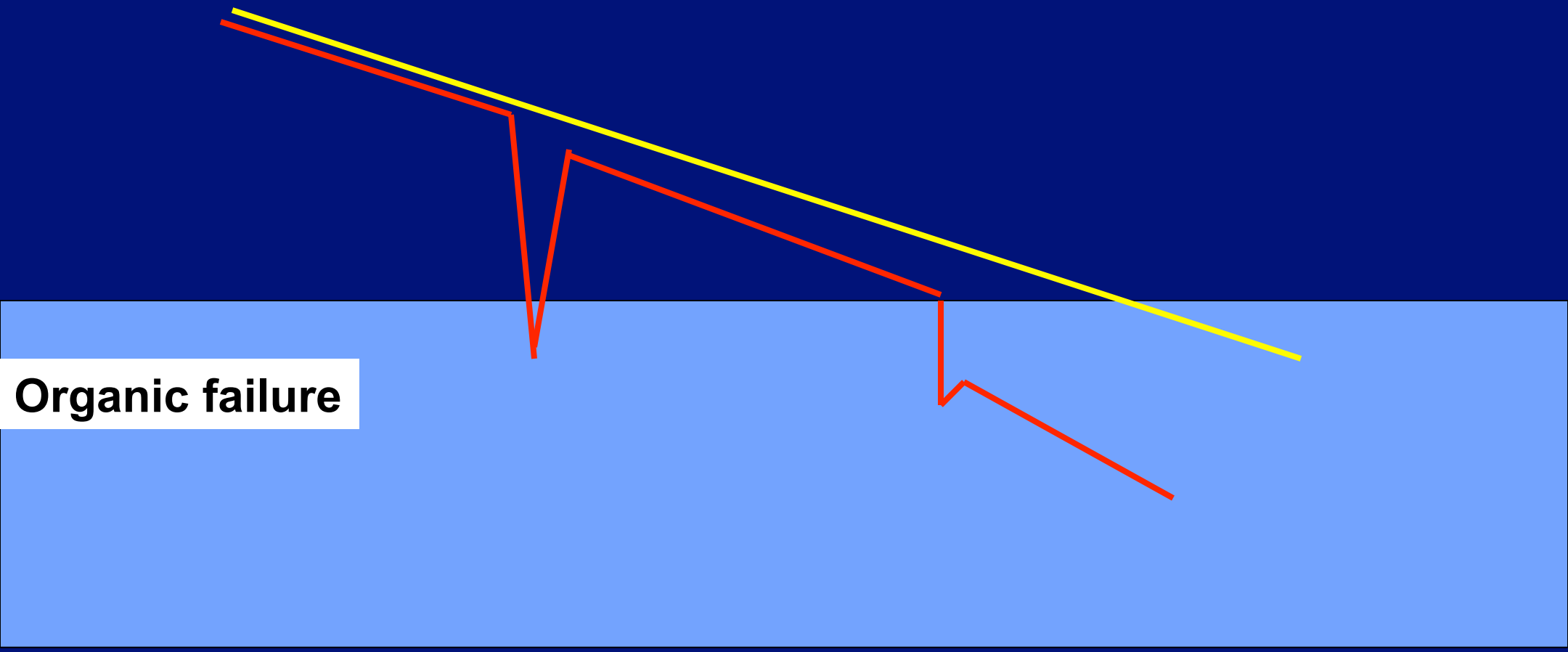
Ageing

Usual vs. Pathological



Four questions

- At what age we get old?

- Longevity and centenarians. What is the future ?

- Why do we age ?

- Can we slow down the aging process ?

Can we slow down the aging process

Can we prevent the age-related diseases?

Can we slow down the aging process?
Can we prevent the age-related diseases?

Genetic manipulations
Hormones
Antioxidants

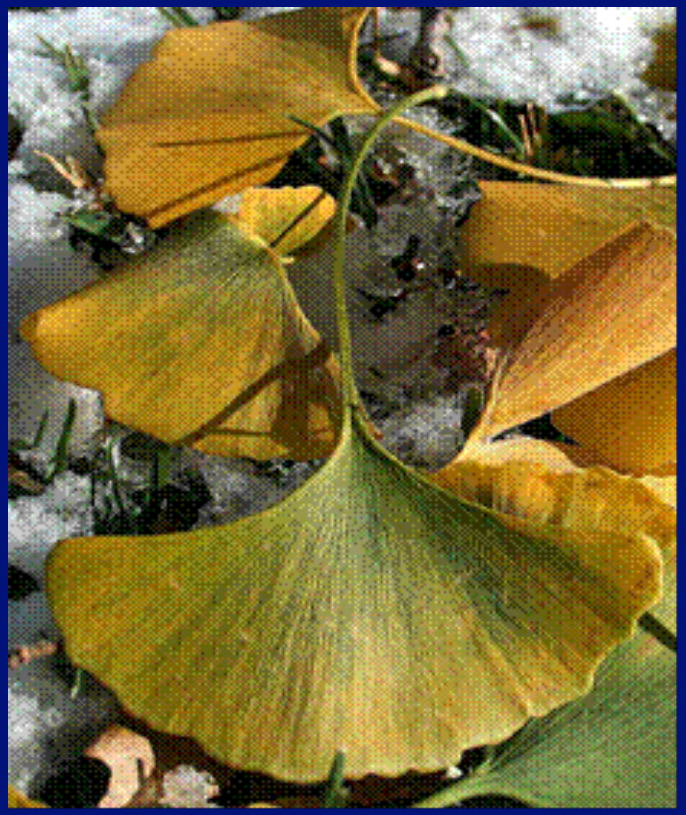
Preventive policies and medicine
Nutrition
Physical activities
Sociale action

Antioxidants

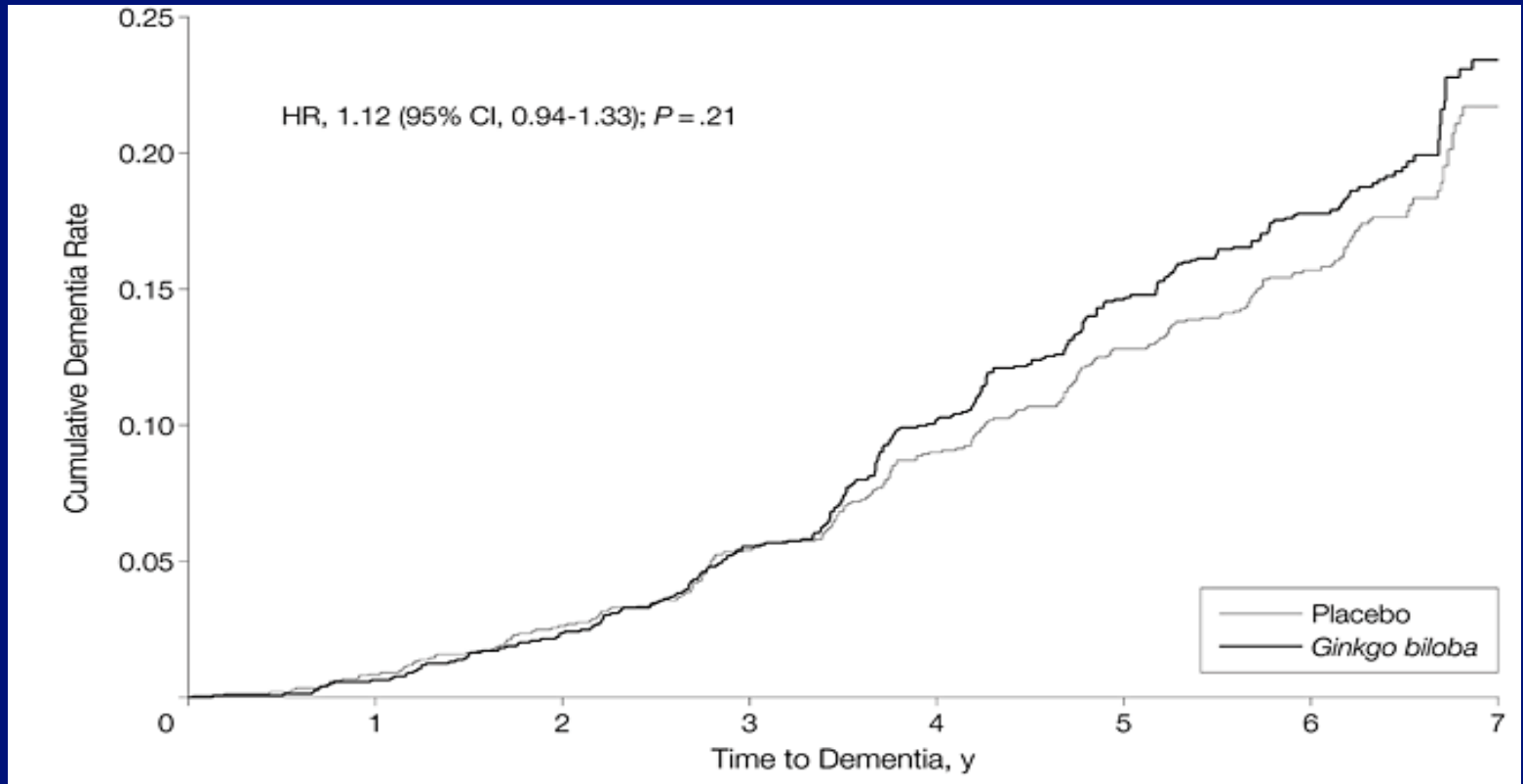
- Superoxide dismutase
- Alpha-lipoic acid
- Coenzyme Q10
- s-adenosyl-L-methionine
- Vitamin E
- Vitamin C
- Beta-carotene

Ginkgo Biloba

Ginkgo im Herbst



GEM Program
Main Result



No. at risk								
Placebo	1524	1485	1423	1342	1243	1148	792	81
G biloba	1545	1521	1458	1369	1254	1129	775	97

No. with incident dementia							
Placebo	13	26	40	50	51	36	30
G biloba	10	26	47	66	60	40	27

DeKosky, S. T. et al. JAMA 2008;300:2253-2262.

Ginkgo in cognitive decline: the European Study Guidage

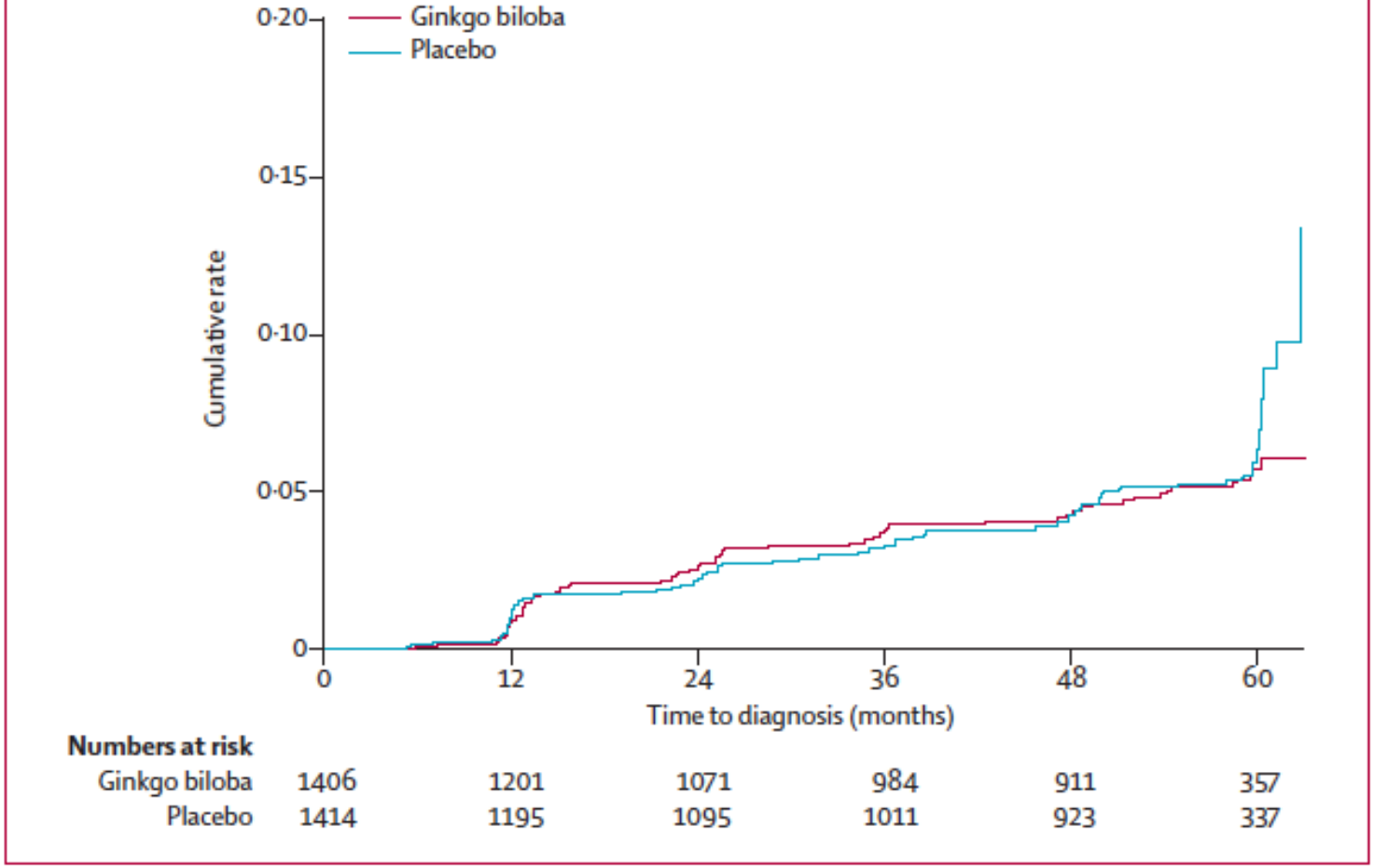


Figure 2: **Cumulative incidence of Alzheimer's disease**

Bruno Vellas et al, Lancet Neurology 2011

Conclusion:

No evidence of any benefit from anti-oxidants and vitamins

Excellents for those who sell them.

Can we slow down the aging process?
Can we prevent the age-related diseases?

Genetic manipulations
Hormones
Antioxidants

Preventive policies and medicine
Nutrition
Physical activities
Sociale implication

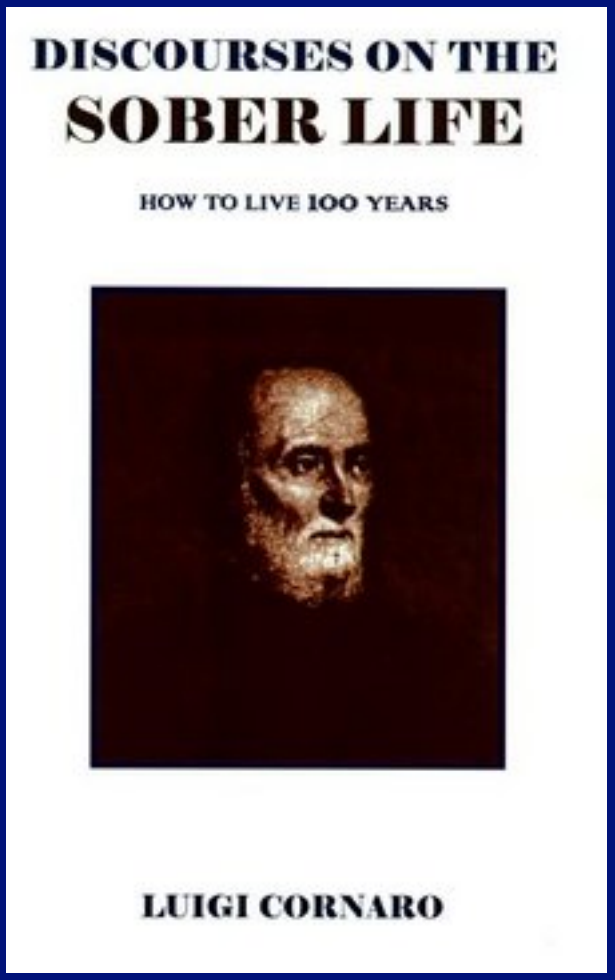

www.StrangeCosmos.com

"There is sufficient evidence to support the conclusion that unless broad scale public health measures are enacted to address the obesity epidemic, life expectancy in the United States could decline in the 21st century."

Olshansky et al., New England Journal of Medicine, 2005

Improve your diet

- Eat less
- Eat better



1467-1569

Luigi Cornaro

"The art of living long"
"The Sober life"

↓ Vital energy with aging

The solution : **Moderation**

Eating less

The secret ?

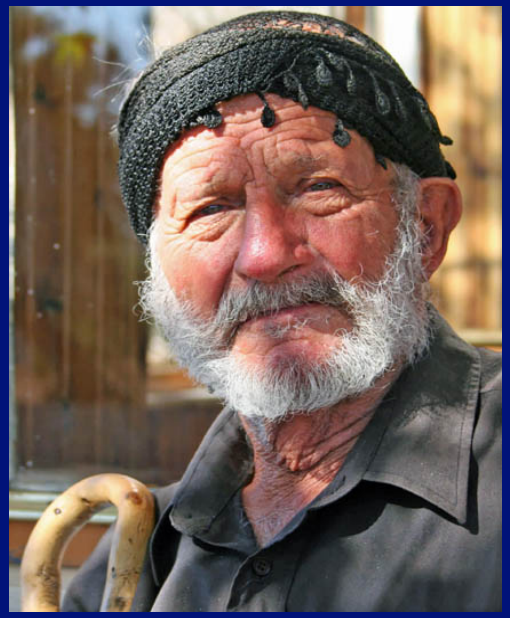
- Good genes (Father die at 94Mother at 86)
- Healthy lifestyle
- Olive oil, chocolate
- Bicycle until >100 years
- Good mood
- Strong character

- Good luck…

Jeanne Louise CALMENT
21 Février 1875 - 4 Août 1997

Fish Oils

Mediterranean-Cretian Diet



Does MedDiet work ?

Mediterranean Diet and Cardiodiabesity: A systematic Review

E. García-Fernández, L Rico-Cabanas N Rosgaard, R Estruch A Bach-Faig

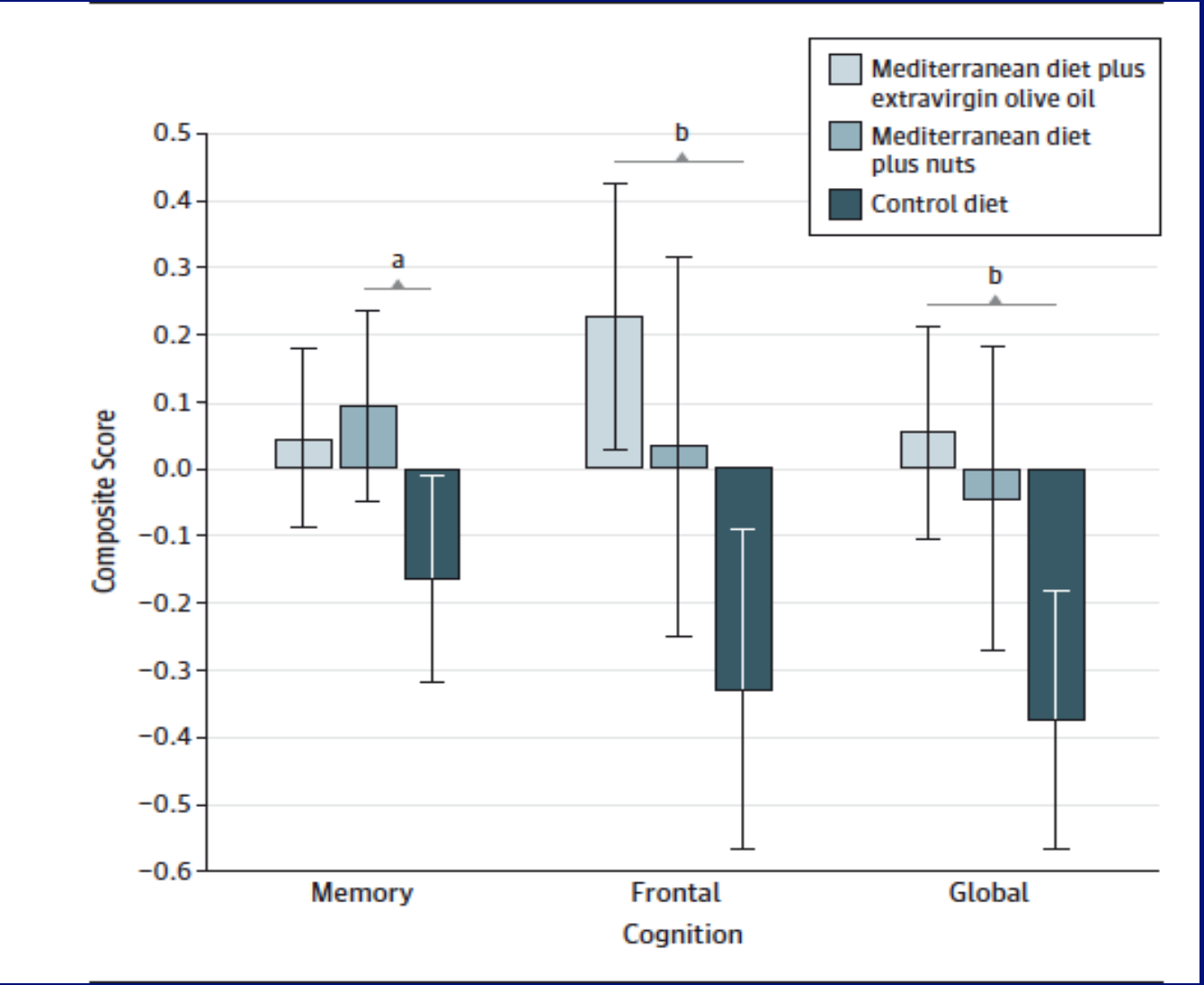
Nutrients, 2014; 6: 3474-3500

37 studies were reviewed:

- 14 related to obesity,
- 10 to CVD,
- 9 to MetS, and four to T2DM.

33 provided strong evidence on the association between adherence to a MedDiet and a reduced incidence of collective cardiodiabesity risk in epidemiological studies

Changes in Cognitive Function Measured With Composites by Intervention Group



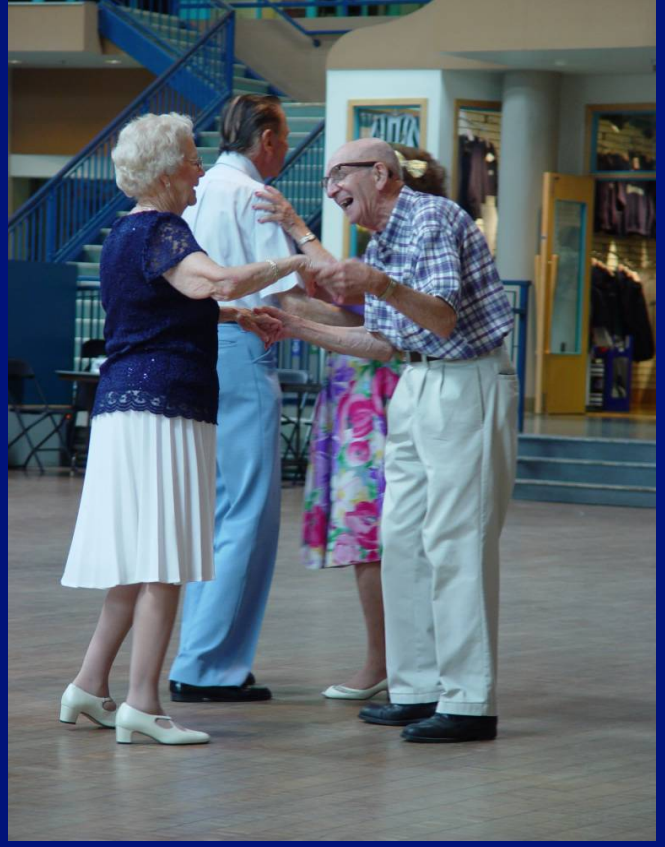
JAMA InternMed. 2015;175:1094-1103.

What about protection by alcohol?

White Wine, Red Wine, Vodka or Whisky ?

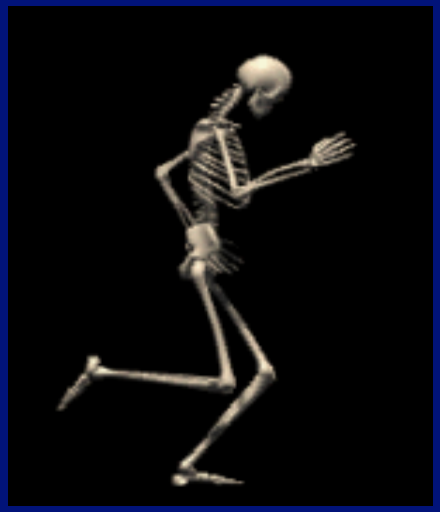
No more than 2-3 glaces per day.
After that level, risk increases with all alcoholic beverages

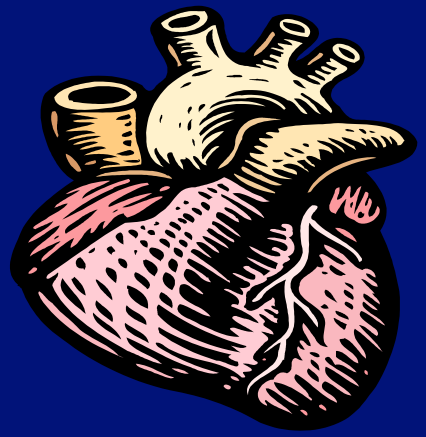
Drink water: One the best solutions to avoid several problems in older individuals



Physical Activities

Contribute to the bone, muscle, cardiovascular and metabolic health





Physical activities improve brain function and provide some protection against cognitive decline and dementias

Pr A. Benetos 2018

When to start?
When to stop?
Physical activities

Start at any age
Never stop, but adapt

Physical activity is the best way to reduce the pharmacological treatments in older individuals

SUCCESSFUL INFANCY ?

SUCCESSFUL ADOLESCENCE ?

SUCCESSFUL AGEING ?

Can we slow down Aging?
It is partially possible

1. Healthy diet with Mediterranean elements (any age), avoid obesity (younger++)
2. Exercise adapted to the functional status (any age)
3. No tobacco no drugs (younger+++)
4. Moderate alcohol consumption (younger+++)
5. Regular follow up of risk factors (younger+++)
6. Regular follow up functional status (older++)
7. Use correctly medication (any age)
8. Social role (older+++)
9. Family and social links (older+++)
10. Accept and adapt yourself to the aging process (older+++)

A. Benetos 2018

Aging biology and Geriatrics: What to do to improve things

Aging is not a disease that we can treat. It is a long process associating biological alterations, organic decline, chronic diseases, all that increasing the risk of incapacity, loss of autonomy and death.

Progress in the bio-medical and social fields contribute to the reduction of several age-related disease, can prevent frailty and its consequences and can slightly slow down the aging process.

A. Benetos 2018