

INTERVENCIONES PARA UN ENVEJECIMIENTO SALUDABLE

Jose Viña.

Facultad de Medicina.

Real Academia de M y CA

Valencia



Spanish Centenarian Study Group



REFLEXIONES DE UN GERONTOLOGO



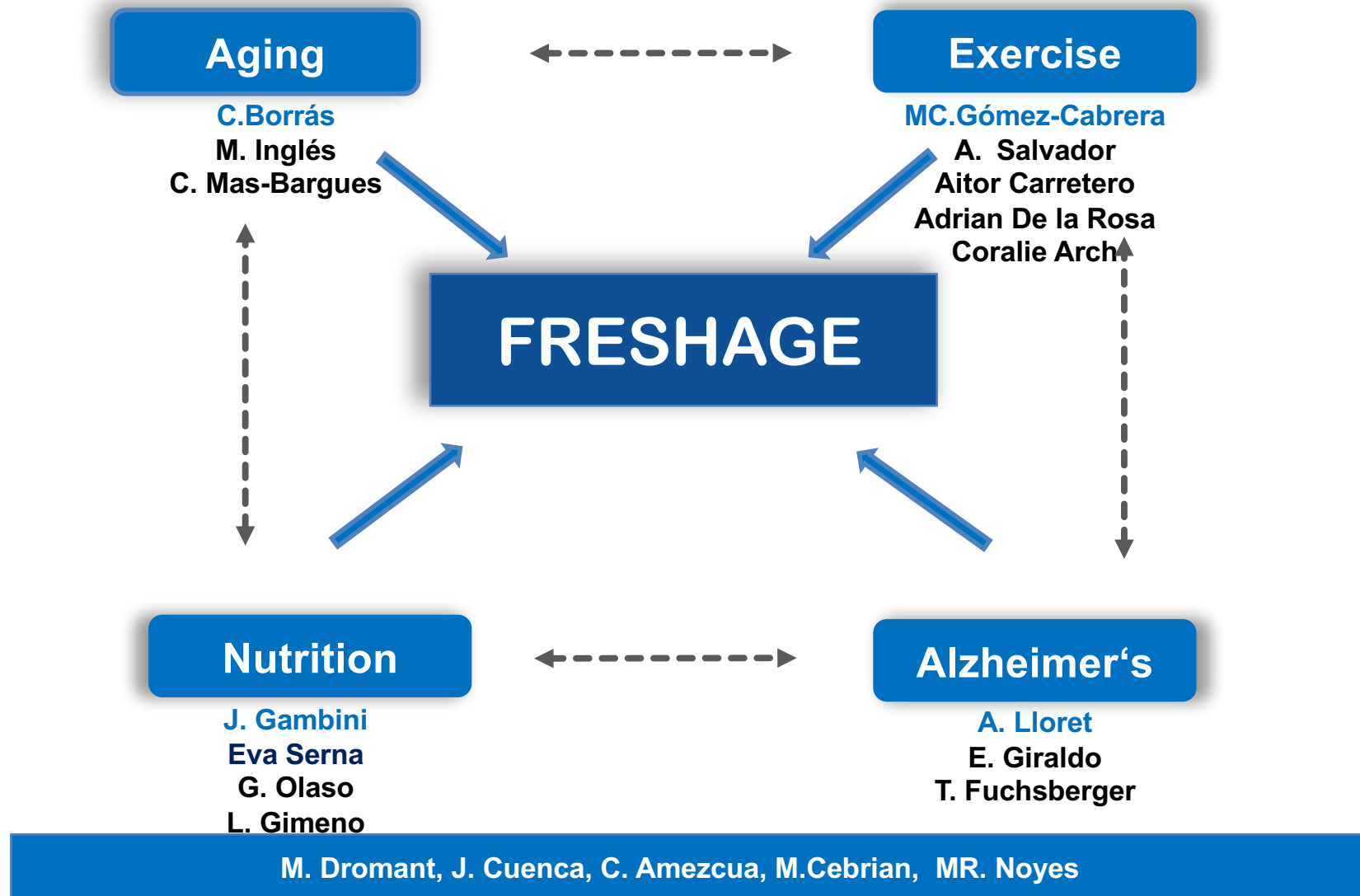
Jose Viña.
Facultad de Medicina.
Real Academia de M y CA
Valencia



Spanish Centenarian Study Group



**A TEAM IS A GROUP OF PERSONS OF DIFFERENT BACKGROUNDS
AND ABILITIES THAT ATTACK A COMMON PROBLEM.**



1988- 2018



INSTITUTO GERONTOLÓGICO de la COMUNIDAD VALENCIANA

Fundado en 1988

Entidad sin ánimo de lucro para fomentar la investigación en el envejecimiento

Instituto Gerontológico de la Comunidad Valenciana
Departamento de Fisiología, Facultad de Medicina,
Avda. Blasco Ibáñez 15
46010 VALENCIA

Tno. 96 386 4646 Fax 96 386 4642

Presidente
José Viña

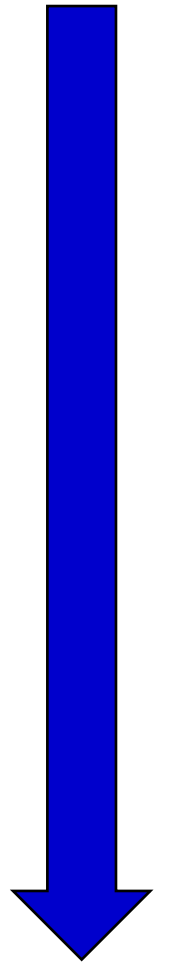
Secretario
Federico V.

Outline

 Aging is normal: Reflections of a gerontologist

 Interventions for healthy aging

 Epilogue: successful aging



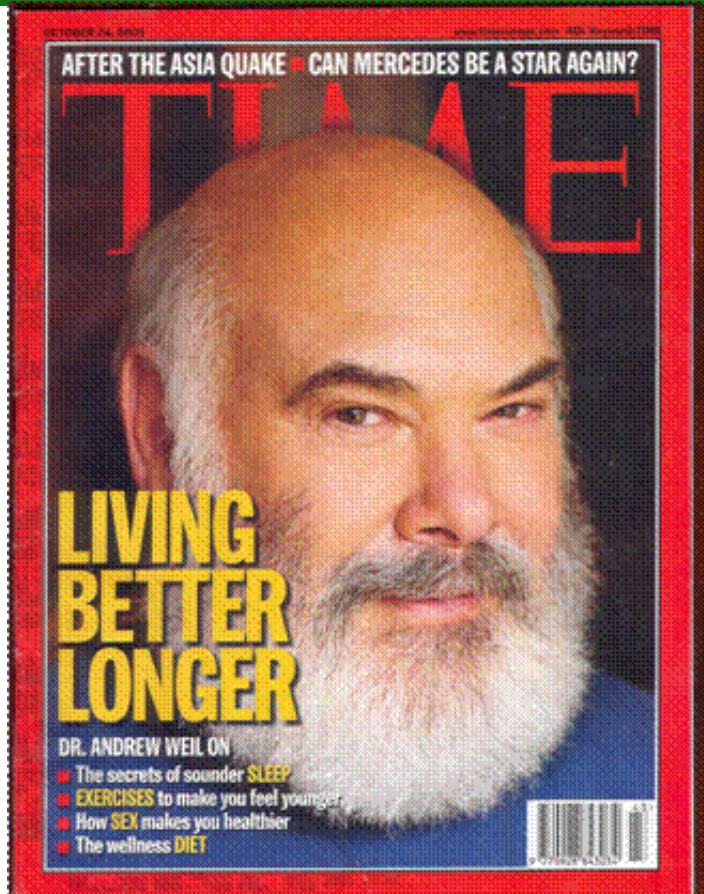
Outline

 Aging is normal: Reflections of a gerontologist

 Interventions for healthy aging

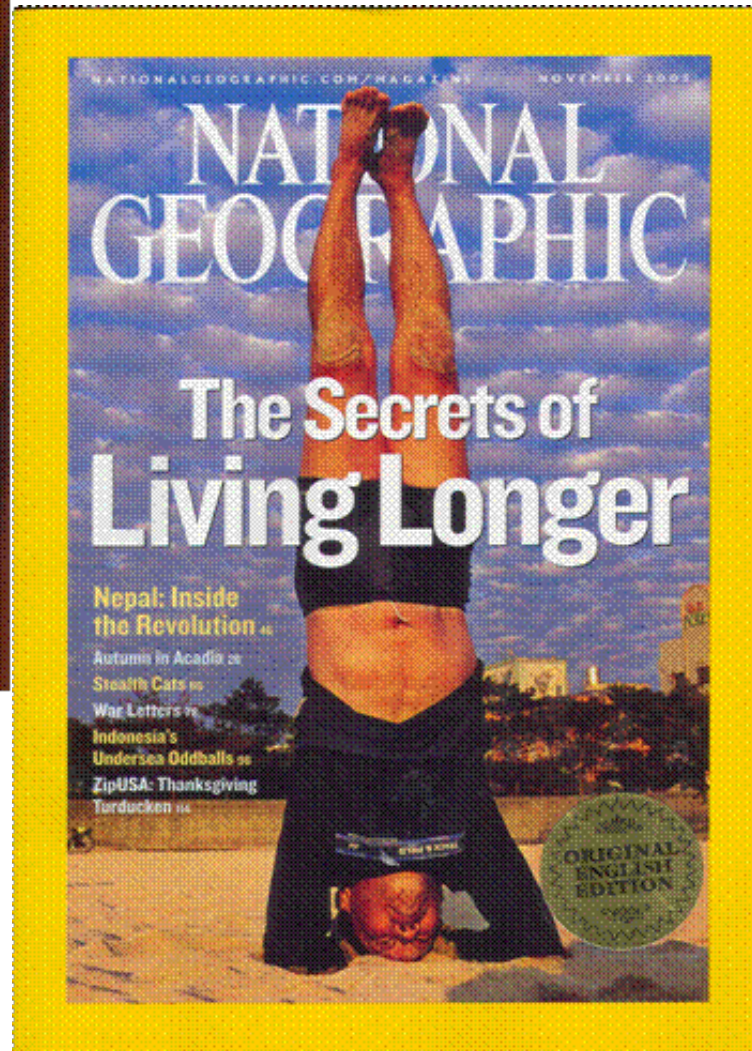
 Epilogue: successful aging

Social impact of aging studies

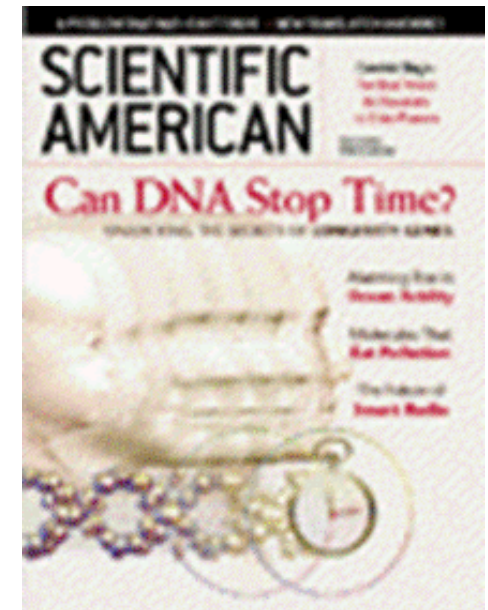


Time
October 2005

National Geographic
November 2005



Scientific American
March 2006

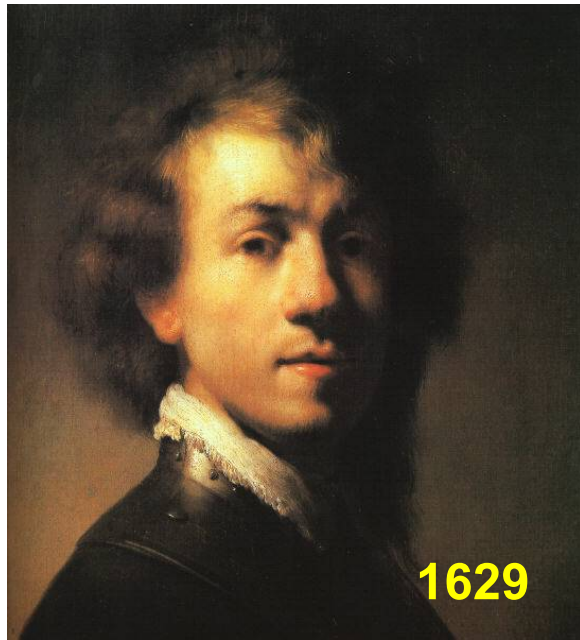


TIME: sept 10, 2013



Lo importante no es la posada sino el camino...

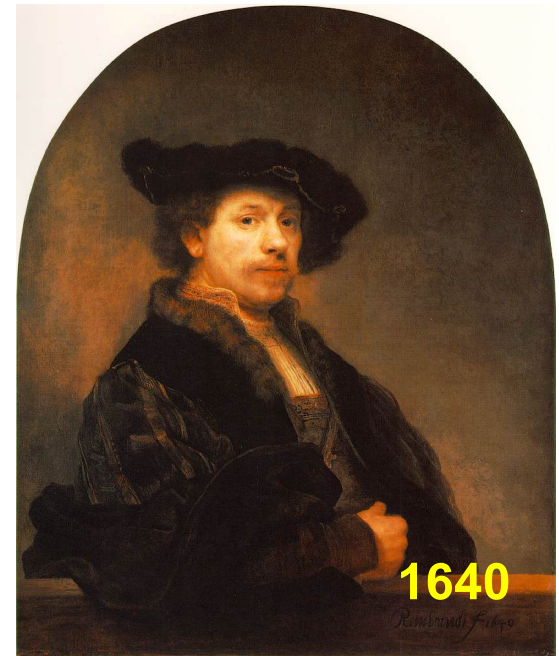




1629



1634



1640



1640

Rembrandt 1606-1669

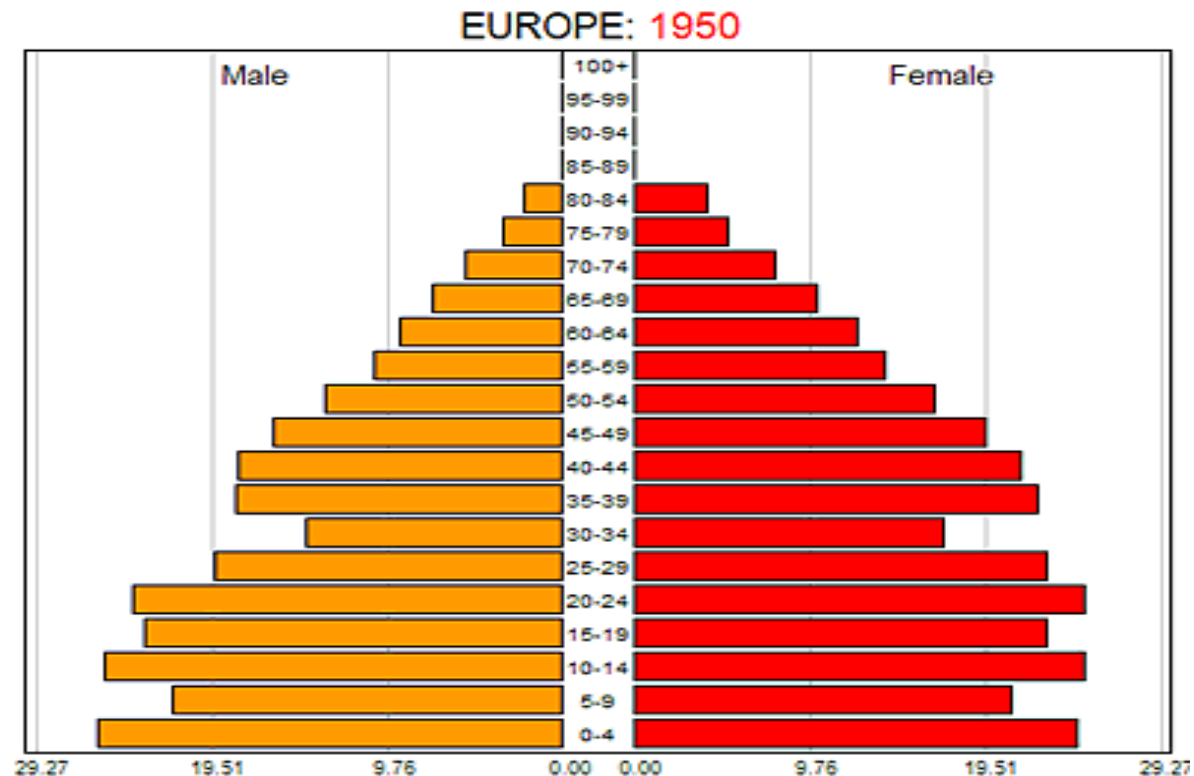


1661



1669

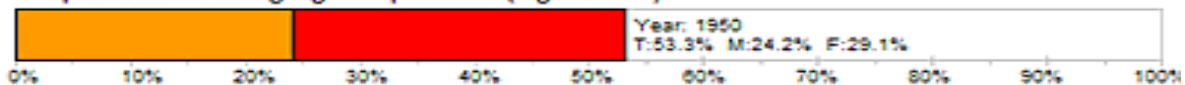
The ageing society



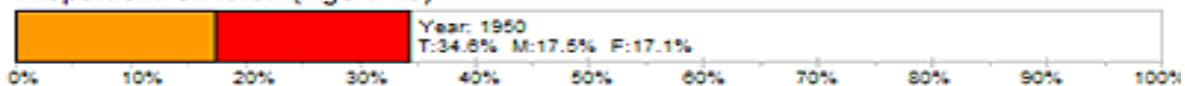
Proportion: Elderly (Age 60+)



Proportion: Working-age Population (Age 20-59)

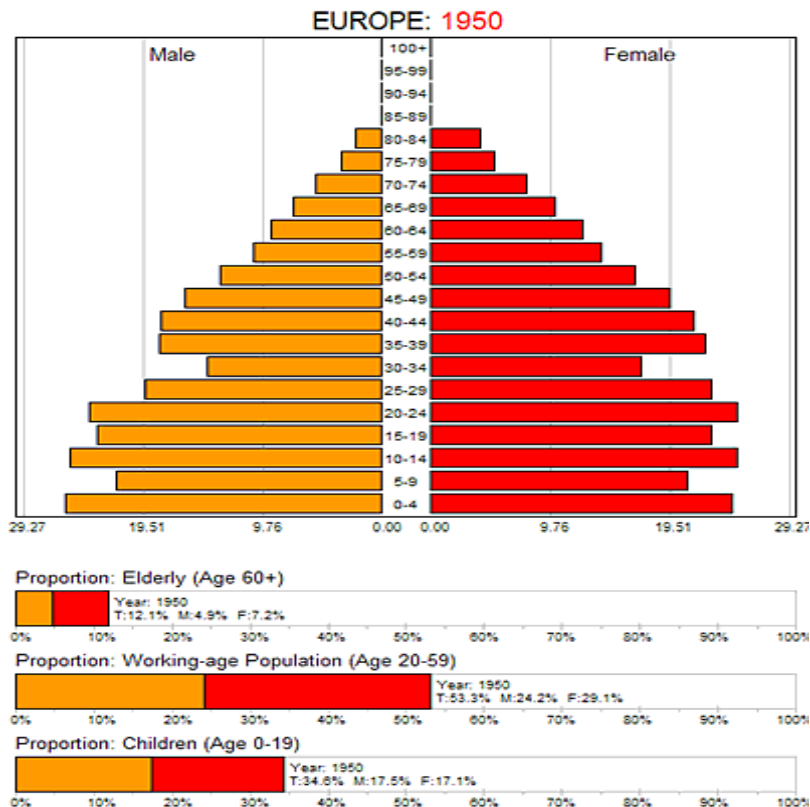


Proportion: Children (Age 0-19)



Challenges of the ageing society

Ageing
society



Chronic
conditions

Health
workforce
shortage

Financial
unsustainability

Health
inequalities

Courtesy of Ines G Sanchez

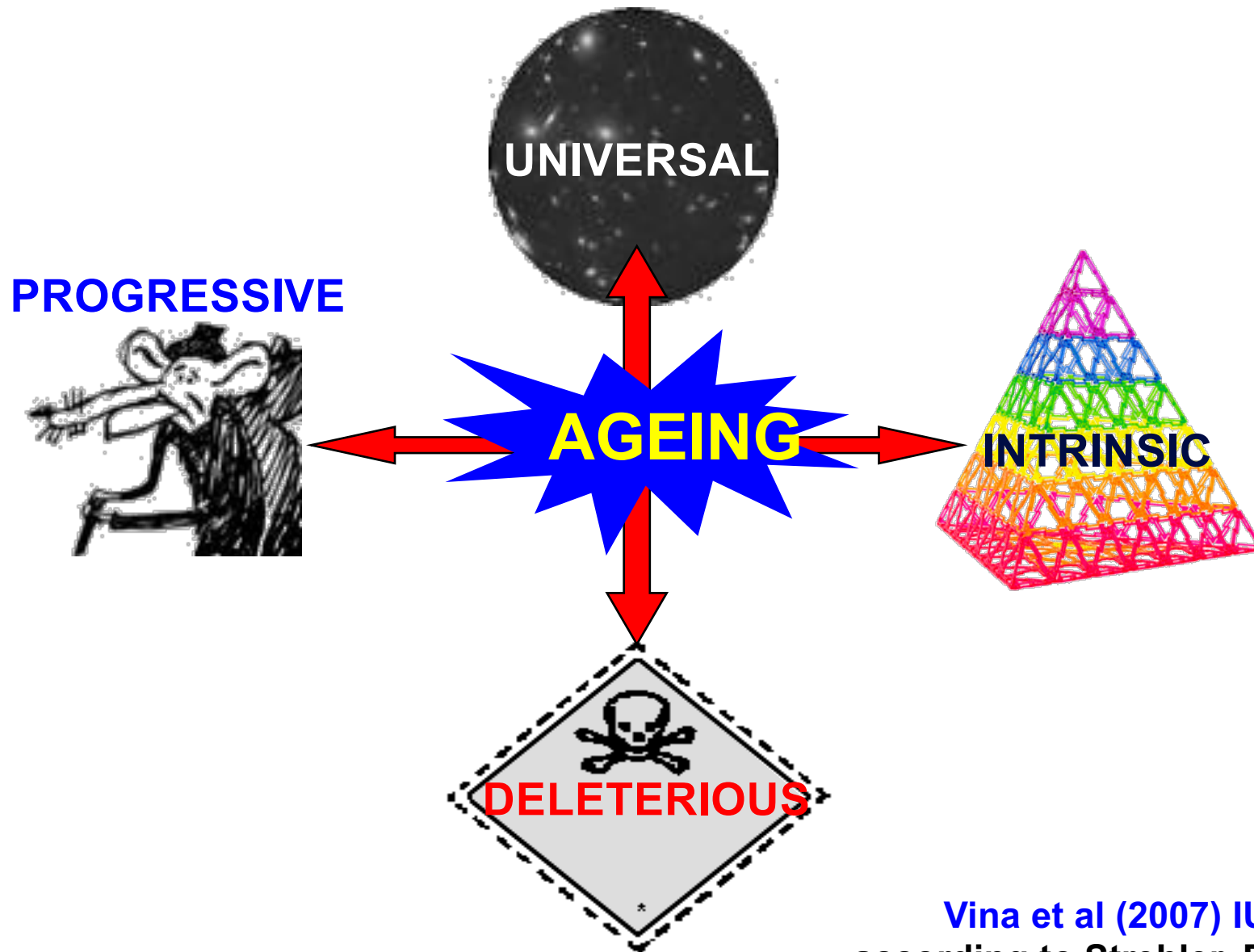
Aging as a problem: THAÏS



Renée Fleming

Ah ! tais-toi, voix
impitoyable, Voix que
me dis: **Thaïs, tu
vieilliras!** Un jour,
ainsi,
Thaïs ne serait plus
Thaïs! Non! Non! je
n'y puis croire

Characteristics of aging



Vina et al (2007) IUBMB Life,
according to Strehler, B. L. (1977)



Aging is not a disease: AGE ASSOCIATED CHANGES

**Biological Aging Is No Longer
an Unsolved Problem**
LEONARD HAYFLICK



**Ann. N.Y. Acad. Sci. 1100: 1–13 (2007). © 2007 New York Academy of Sciences.
doi: 10.1196/annals.1395.001**



Aging is not a disease: AGE ASSOCIATED CHANGES

- (1) occur in every multicellular animal that reaches a fixed size at reproductive maturity
- (2) cross virtually all species barriers
- (3) occur in all members of a species only after the age of reproductive maturation



Aging is not a disease: AGE ASSOCIATED CHANGES

(4) occur in all animals removed from the wild and protected by humans even when that species probably has not experienced aging for thousands or even millions of years

(5) occur in virtually all animate and inanimate matter

(6) have the same universal molecular etiology, that is, thermodynamic instability.

Unlike aging, there is no disease or pathology that shares these six qualities.



Outline

Prologue. Aging is normal: Reflections of a gerontologist

- ✓ Aging is not a disease
- ✓ **Our search for longevity genes**

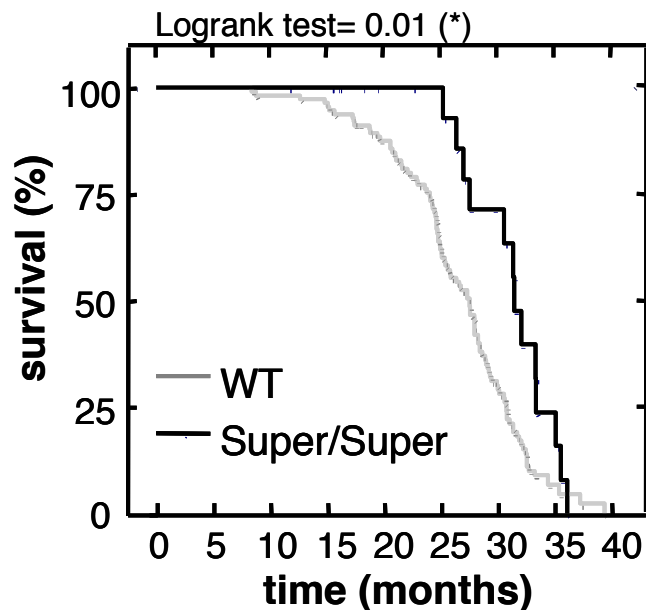
The search for longevity genes: p53



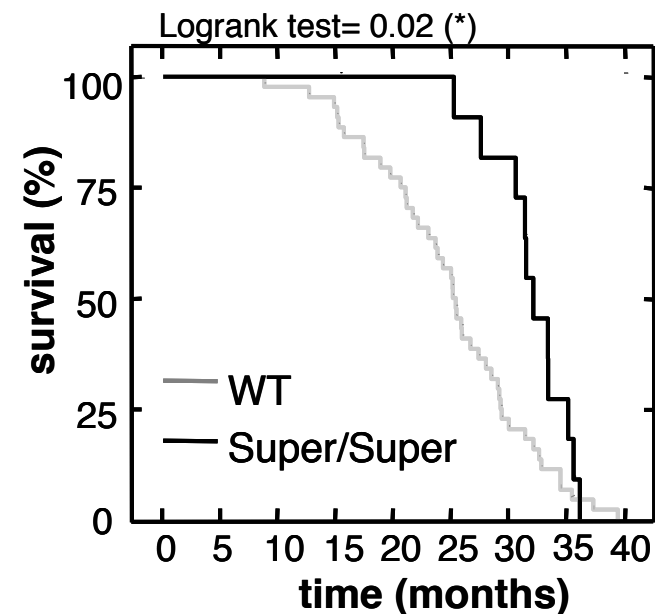
Delayed ageing through damage protection by the Arf/p53 pathway

Ander Matheu^{1*†}, Antonio Maraver^{1*}, Peter Klatt¹, Ignacio Flores², Isabel Garcia-Cao¹, Consuelo Borras^{3†}, Juana M. Flores⁴, Jose Viña³, Maria A. Blasco² & Manuel Serrano¹

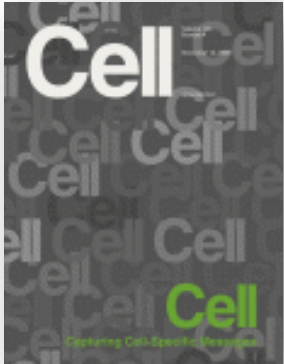
spontaneous survival curve



survival curve without tumors



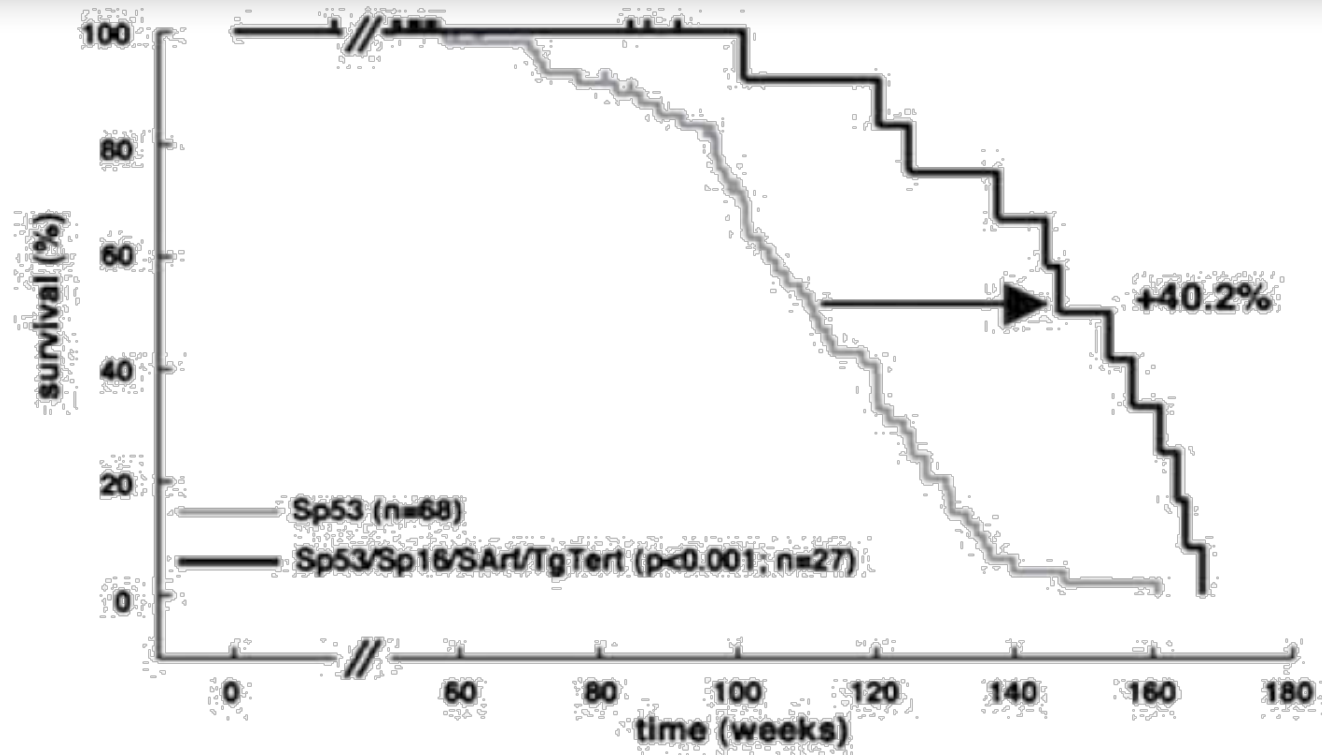
The search for longevity genes: telomerase



Telomerase Reverse Transcriptase Delays Aging in Cancer-Resistant Mice

Antonia Tomás-Loba,^{1,5} Ignacio Flores,^{1,5} Pablo J. Fernández-Marcos,² María L. Cayuela,^{1,6} Antonio Maraver,² Agueda Tejera,¹ Consuelo Borrás,³ Ander Matheu,² Peter Klatt,^{1,2} Juana M. Flores,⁴ José Viña,³ Manuel Serrano,² and María A. Blasco^{1,*}

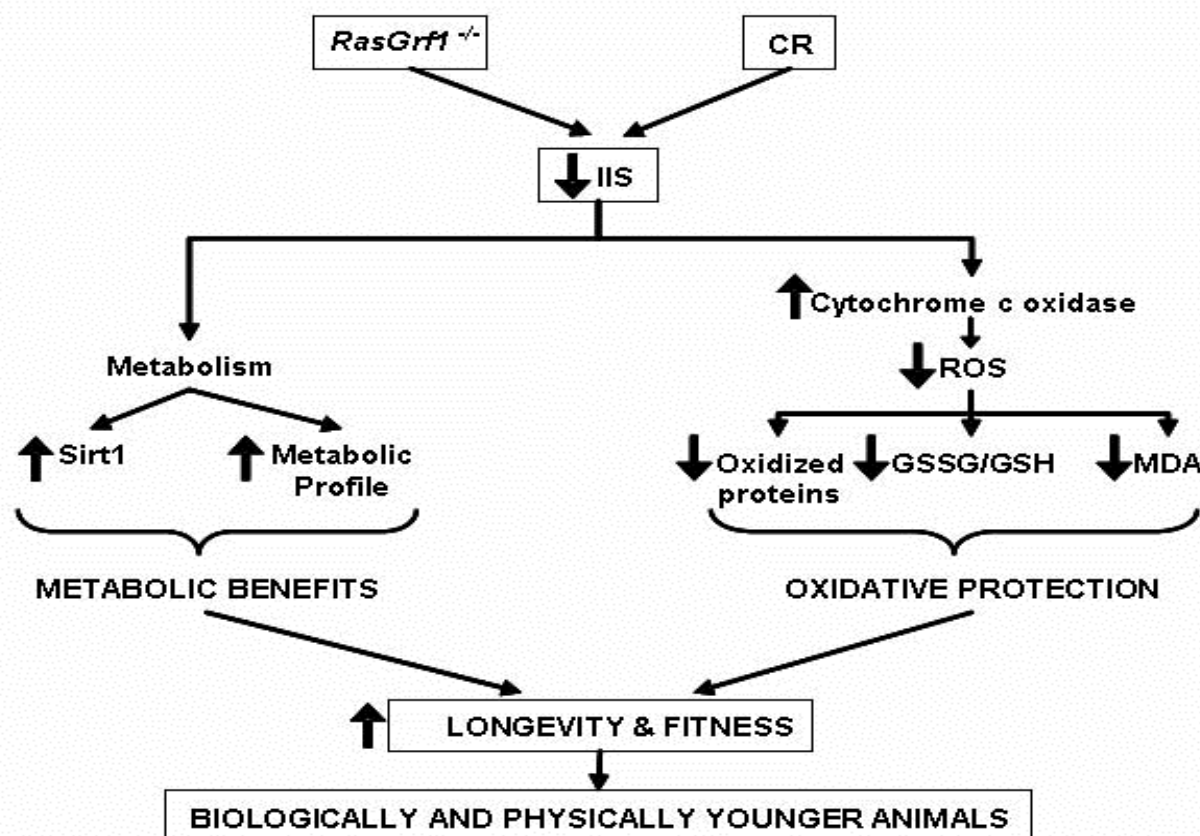
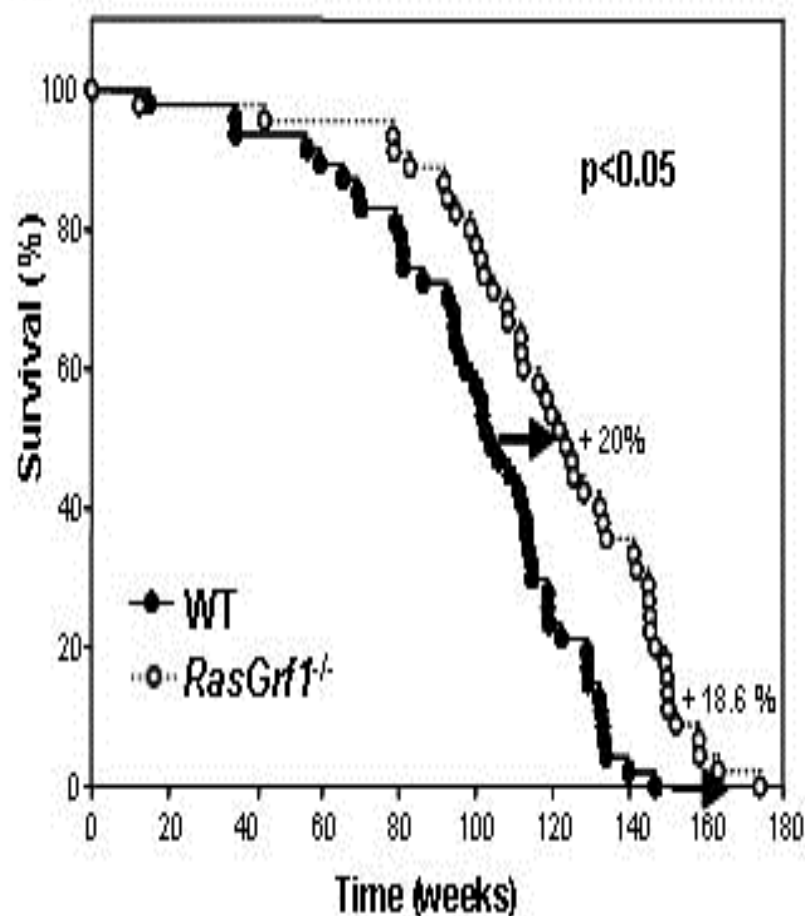
Sp53
vs
Sp53/Sp16/SArf/TgTert



RasGrf1 deficiency delays aging in mice

Consuelo Borrás¹, Daniel Monleón², Raul López-Grueso¹, Juan Gambini¹, Leonardo Orlando³, Federico V. Pallardó¹, Eugenio Santos⁴, José Viña^{1,*} and Jaime Font de Mora^{3,*}

The search for longevity genes: Ras



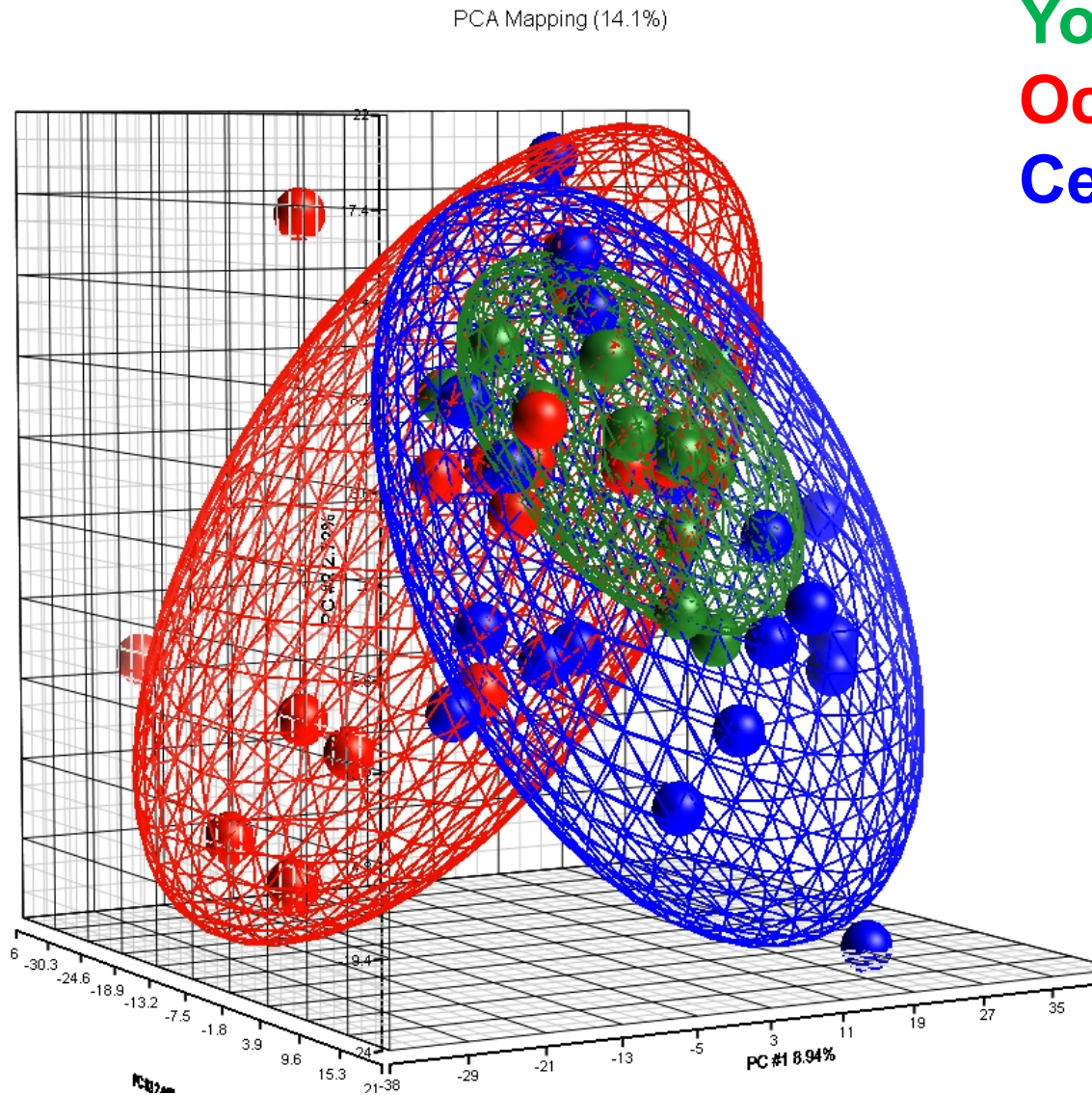
100's: Health span approaches life span



miRNAs in centenarians

Young
Octogenarian
Centenarian

**miRNAs are similar
in young and
centenarians!!!!**



Functional transcriptomic analysis

Centenarians, but not octogenarians, up-regulate the expression of microRNAs

Eva Serna¹, Juan Gambini², Consuelo Borras², Kheira Mohammed², Angel Belenguer³, Paula Sanchis³,
Juan A. Avellana³, Leocadio Rodriguez- Mañas⁴ & Jose Viña²

SCIENTIFIC REPORTS SREP-12-02982-T.3d 3/12/12 13:37:19

www.nature.com/scientificreports

www.nature.com/scientificreports



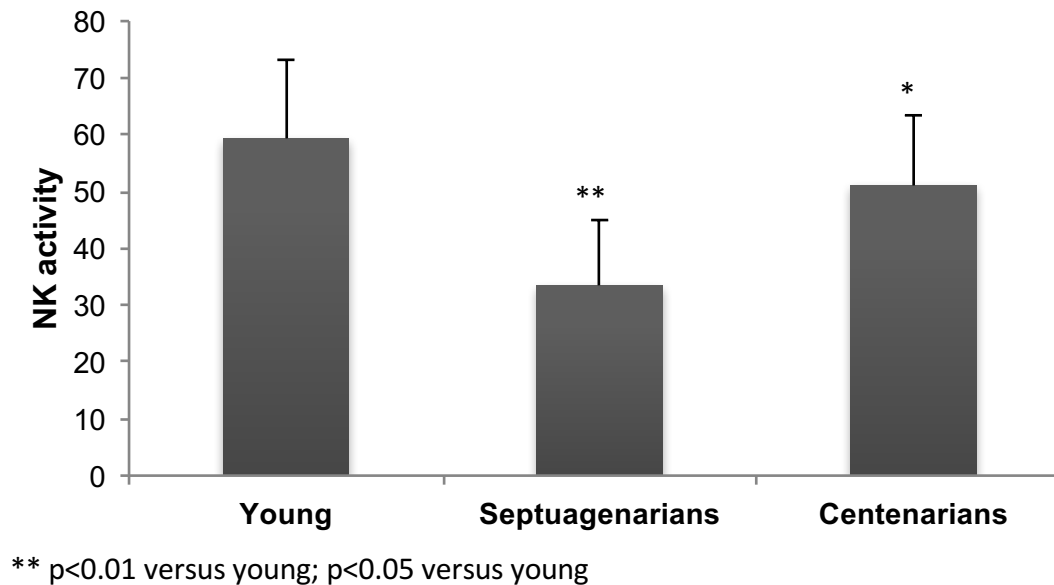
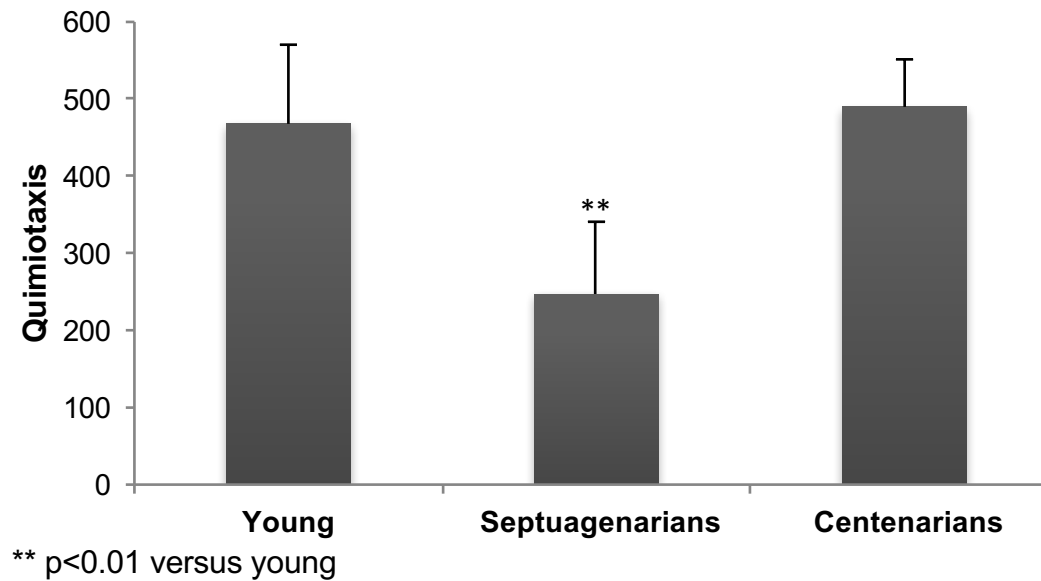
Age-Trajectories of Metabolomic Biomarkers



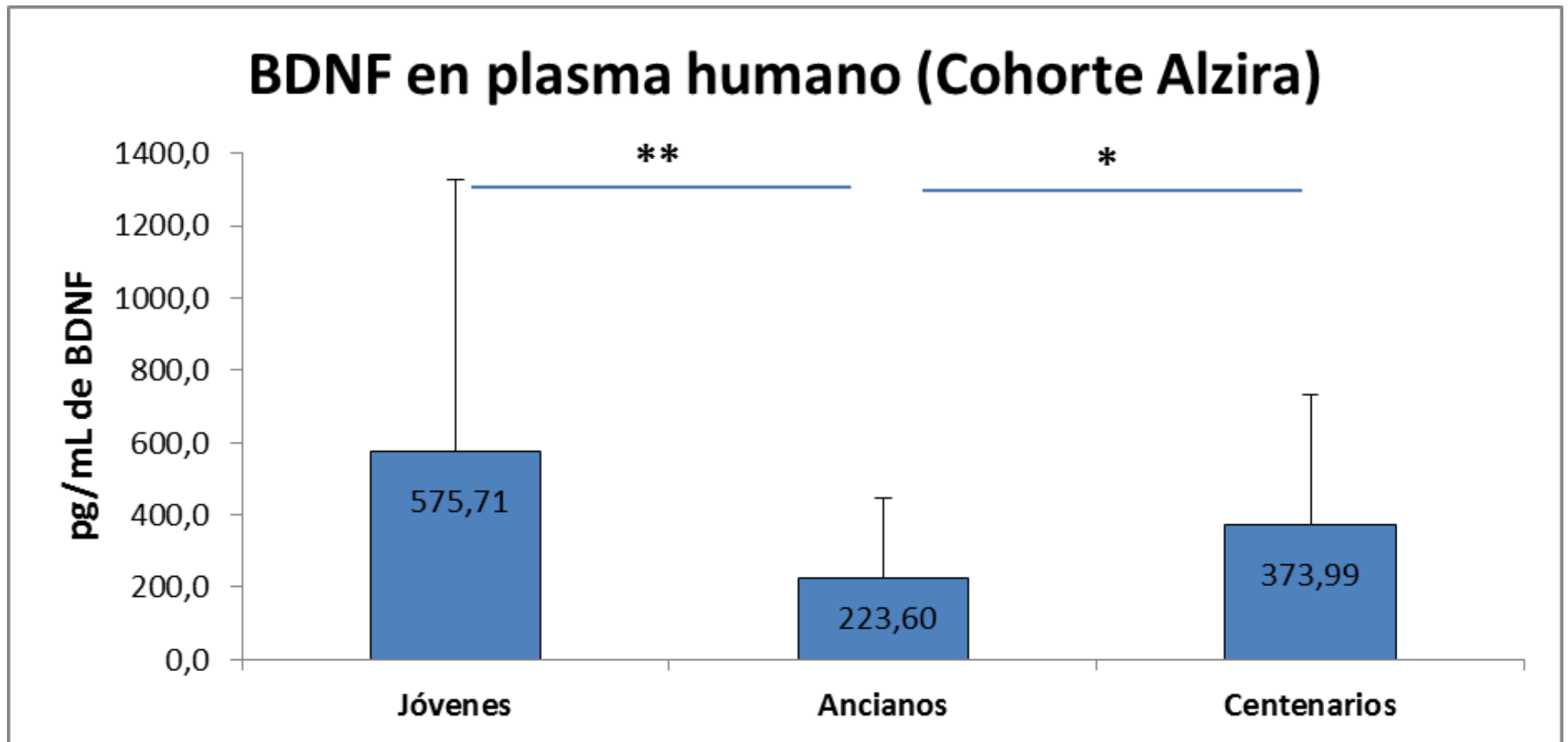
A G E

Courtesy of Claudio Franceschi

Lymphocyte function is preserved in centenarians



Centenarians have high plasma BDNF levels



Lessons to be learnt from centenarians

- Centenarians exhibit extreme longevity and a remarkable compression of morbidity.
- Their health span approximates their life span.
- They have an outstanding capacity to maintain homeostatic mechanisms

Outline

 Aging is normal: Reflections of a gerontologist

 Interventions for healthy aging

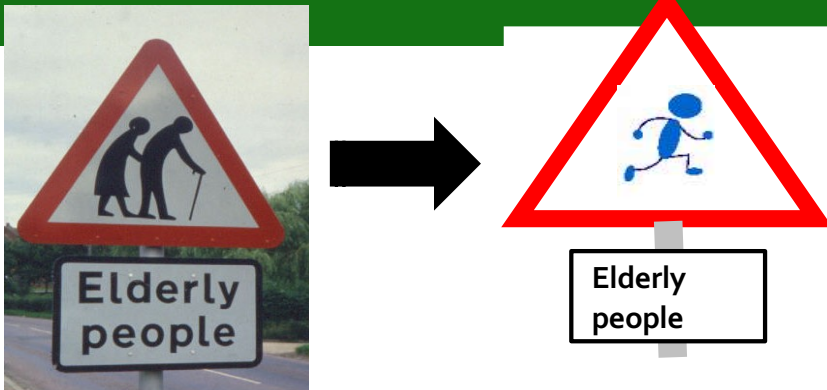
 Epilogue: successful aging

INTERVENTIONS FOR A SUCCESSFUL AGING

Aims:

-  Adapt to changes that are going to occur
-  Compress morbidity
-  Prevent frailty and dependency
-  Feel that you are useful.

HEALTH SPAN AND LIFESPAN



**LIFESPAN IS INCREASING
SIGNIFICANTLY**

**HEALTH SPAN IS NOT
IMPROVING**

Increases in life span have led to more age associated diseases

**Osteoporosis
Alzheimer
Degeneración macular
Problemas de audición
Accidentes cerebrovasculares**



THE PROCESS OF AGING



IT IS NEVER TOO LATE....



AGING CAN BE MODULATED

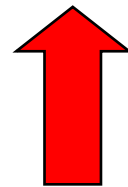


 **Moderate exercise**

 **Four helpings of fruit**

 **Two wine glasses**

 **Do not smoke**



Increases life

14 years

Khaw et al Plos
Med (2008)

AGING CAN BE MODULATED



 **Moderate exercise**

 **Four helpings of fruit**

 **Two wine glasses**

 **Do not smoke**



Increases life

14 years

Khaw et al Plos
Med (2008)

AGING CAN BE MODULATED



 **Moderate exercise**

 **Four helpings of fruit**

 **Two wine glasses**

 **Do not smoke**



Increases life

14 years

Khaw et al Plos
Med (2008)

NUTRITIONAL INTERVENTION



Bent Objects



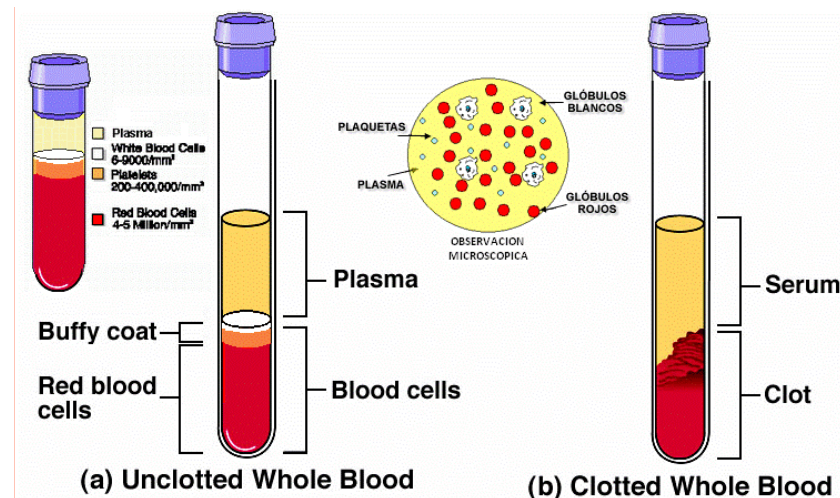
THE VALENCIA NUN STUDY



**Effect of moderate wine
consumption on longevity
gene expression in humans**

Effect of wine (moderate) on gene expression in catholic nuns

**Blood sampling:
Before the study**



**Blood sampling :
after 14 days of
wine**

Gene

Pathway

AKT1, CDKN2A, FOXO3, IRS1, FRAP1

Insulin

TERF1, TERF2, TERT

Telomerase

SESN2, CAT, SOD2, P53

Oxidative stress

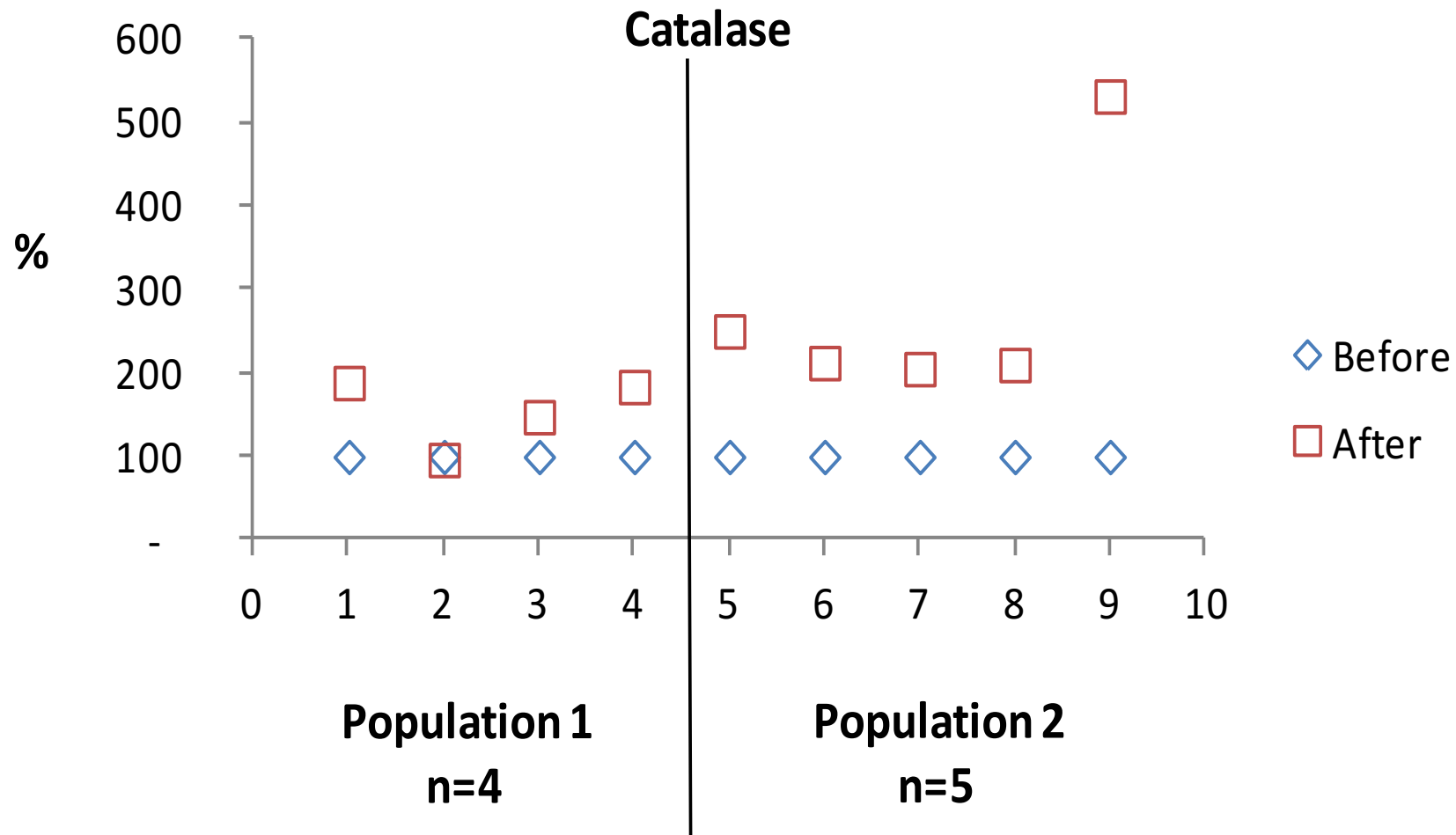
SIRT1

Caloric restriction

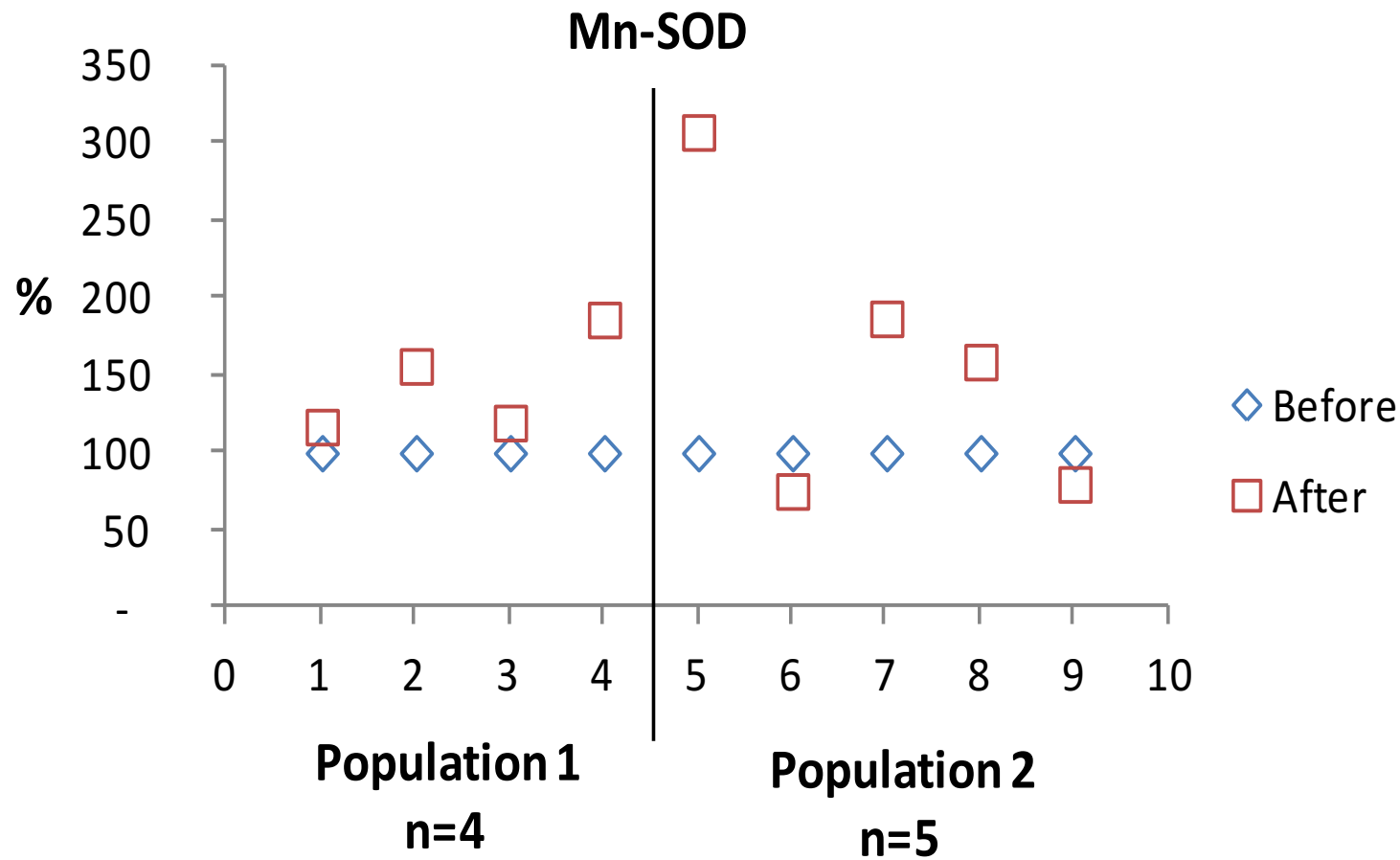
IL1A

Inflammation

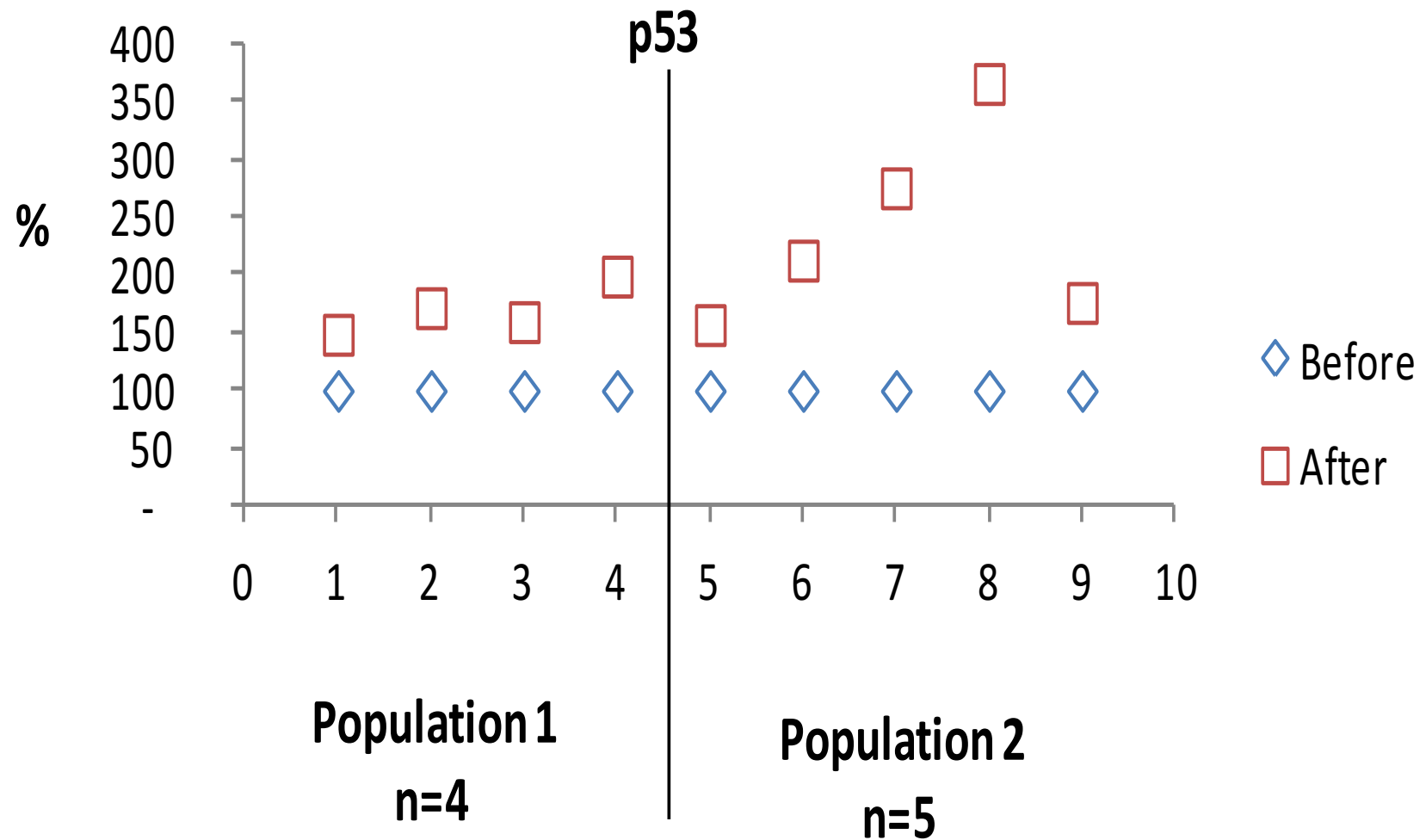
Red wine increases catalase expression



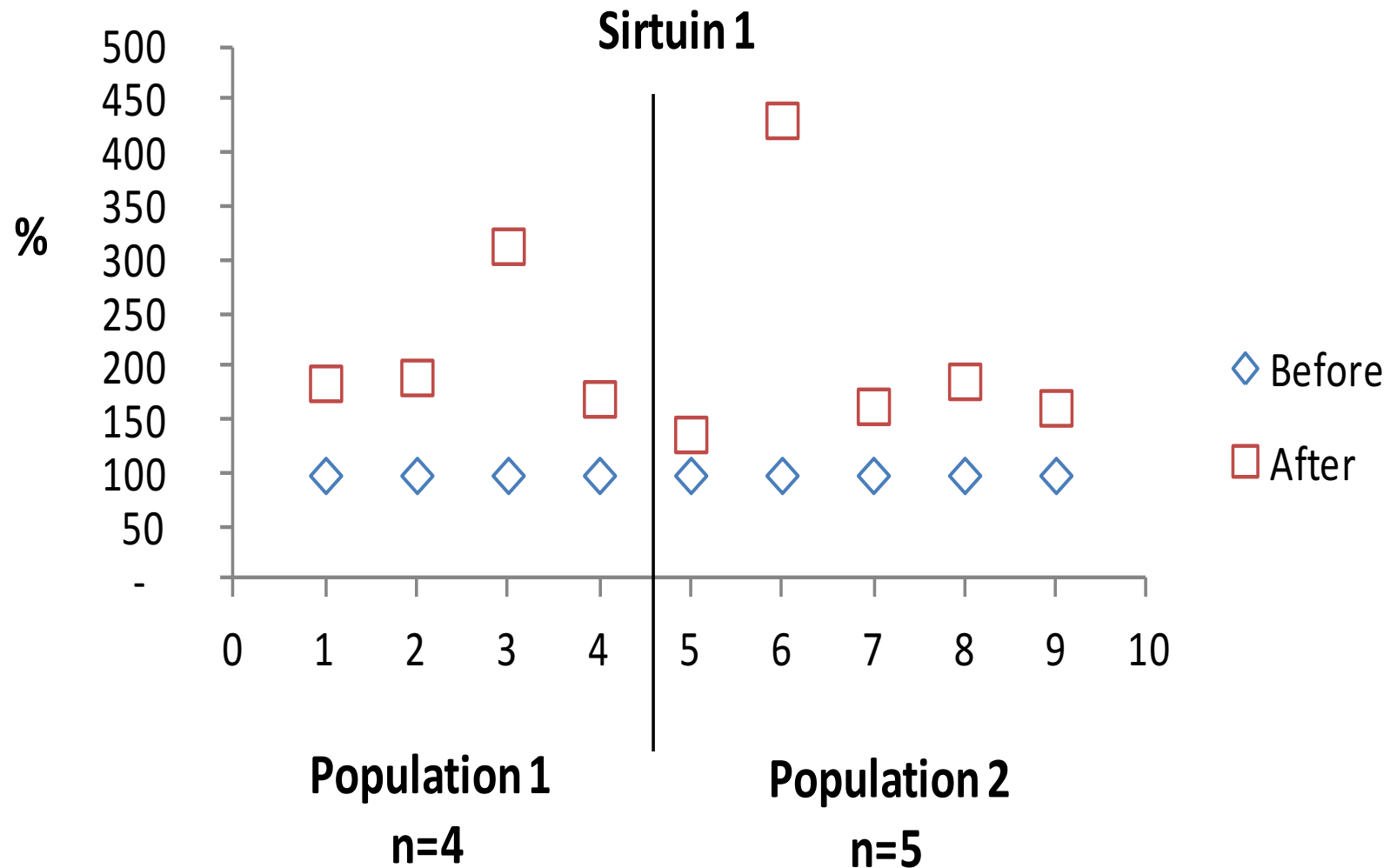
Red wine increases Mn-SOD expression



Red wine increases p53 expression



Red wine increases sirtuin expression



PHYSIOLOGICAL INTERVENTION: EXERCISE



EXERCISE ACTS AS A DRUG

BJP

British Journal of
Pharmacology

REVIEW

Exercise acts as a drug; the pharmacological benefits of exercise

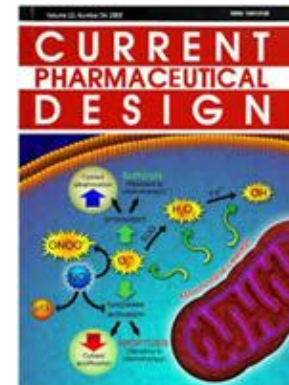
J Vina, F Sanchis-Gomar, V Martinez-Bello and MC Gomez-Cabrera



Current Pharmaceutical Design, 2014, 20, 000-000

Pharmacological Properties of Physical Exercise in the Elderly

Jose Viña*, Consuelo Borras, Fabian Sanchis-Gomar, Vladimir E Martinez-Bello, Gloria Olaso-Gonzalez, Juan Gambini, Marta Ingles¹ and Mari Carmen Gomez-Cabrera



Freshage

Age and **Exercise** Research Group

EXERCISE IS A TREATMENT FOR FRAILTY

Free Radical Biology and Medicine ■ (■■■■) ■■■–■■■



ELSEVIER

Contents lists available at ScienceDirect

Free Radical Biology and Medicine

journal homepage: www.elsevier.com/locate/freeradbiomed



Exercise training as a drug to treat age associated frailty

Jose Viña^{a,b,c,d}, Andrea Salvador-Pascual^{a,b,c,d}, Francisco Jose Tarazona-Santabalbina^{b,c},
Leocadio Rodriguez-Mañas^d, Mari Carmen Gomez-Cabrera^{a,b,c,d,*}

^a Department of Physiology, University of Valencia, Investigación Hospital Clínico Universitario/INCLIVA, Spain

^b Hospital Universitario de la Ribera, Alzira, Valencia, Spain

^c School of Nursing, Catholic University of Valencia San Vicente Mártir, Spain

^d Servicio de Geriátría, Hospital Universitario de Getafe, Red Temática de Investigación Cooperativa en Envejecimiento y Fragilidad (RETICEF), Instituto de Salud Carlos III, Spain

Freshage

Age and Exercise Research Group

EXERCISE IS A SUPPLEMENT FOR HEALTHY AGEING

The Journal of
Physiology

[Explore this journal >](#)

Topical Review

Exercise: the lifelong supplement for healthy ageing and slowing down the onset of frailty

Jose Viña , Leocadio Rodriguez-Mañas, Andrea Salvador-Pascual, Francisco José Tarazona-Santabalbina, Mari Carmen Gomez-Cabrera

First published: 14 April 2016 [Full publication history](#)

DOI: 10.1113/JP270536 [View/save citation](#)

Cited by: 0 articles [Check for new citations](#)

Freshage

Age and [Exercise](#) Research Group

EXERCISE ACTS AS A DRUG (BJP, 2012)

- ***Exercise is beneficial for your health***
- ***The dosing of exercise***
- ***Exhaustive exercise and longevity***
- ***Systemic adaptations to exercise***
- ***Exercise, a psychoactive drug***

Lifespan vs healthspan

COMMENTARY

(Reprinted) JAMA, February 13, 2008—Vol 299, No. 6 689

Medical Challenges of Improving the Quality of a Longer Life

En la medida que la expectativa de vida aumenta también lo hacen las enfermedades asociadas al envejecimiento

(Osteoporosis, Alzheimer's, Stroke, Macular degeneration Hearing problems)

Healthspan: Parte de la vida durante la cual somos capaces de mantener la autonomía, la independencia, productividad y el bienestar



Editorial

 Ageing well: a global priority

THE LANCET

Sadly, as the authors of a letter in the April 7 issue of *The Lancet* note, population ageing is often framed in negative terms. Older people are viewed as a burden to society and resources. This negativity is also true at the individual level. Past a certain age, many people bemoan another birthday or a grey hair. But ageing is something that should be celebrated. Older people contribute to society in many ways—through their experiences and

Longevidad, fragilidad y discapacidad



Journal of Gerontology: MEDICAL SCIENCES
Cite journal as: J Gerontol A Biol Sci Med Sci. 2013 January;68(1):62-67
doi:10.1093/geron/ghl119

© The Author 2012. Published by Oxford University Press on behalf of The Gerontological Society of America.
All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.
Advance Access publication April 16, 2012

Searching for an Operational Definition of Frailty: A Delphi Method Based Consensus Statement. The Frailty Operative Definition-Consensus Conference Project

Leocadio Rodríguez-Mañas,¹ Catherine Féart,^{2,3} Giovanni Mann,⁴ Jose Viña,⁵ Somnath Chatterji,⁶
Wojtek Chodsko-Zajko,⁷ Magali Gonzalez-Colaço Harmand,¹ Howard Bergman,⁸ Laure Carcaillon,^{1,9}
Caroline Nicholson,⁴ Angelo Scuteri,¹⁰ Alan Sinclair,¹¹ Martha Pelaez,¹² Tischa Van der Cammen,¹³
François Beland,¹⁴ Jerome Bickenbach,¹⁵ Paul Delamarche,¹⁶ Luigi Ferrucci,¹⁷ Linda P. Fried,¹⁸
Luis Miguel Gutiérrez-Robledo,¹⁹ Kenneth Rockwood,²⁰ Fernando Rodríguez Artalejo,²¹ Gaetano Serviddio,²²
and Enrique Vega²³; on behalf of the FOD-CC group (Appendix 1)

**Síndrome geriátrico para el que no hay una
definición consensuada**

Síndrome caracterizado por un aumento de la
vulnerabilidad a las agresiones externas,
como resultado de una alteración de las reservas
fisiológicas de múltiples sistemas, lo cual origina
**dificultades para mantener la
homeostasis**

(Fried, L.P. et al. 2001)

- **Masa magra**
- **Fuerza**
- **Resistencia**
- **Equilibrio**
- **Velocidad de la marcha**
- **Actividad**



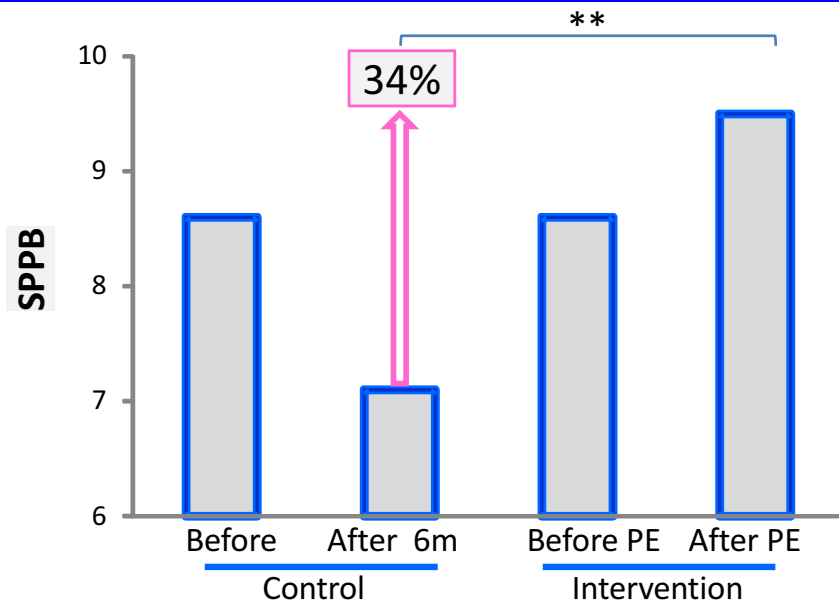
THE “PROGRAMA MEJORA” INTERVENTION TO PREVENT FRAILTY

**AIM: TO DETERMINE THE EFFECT OF CONTROLLED
PHYSICAL EXERCISE ON FRAILTY**

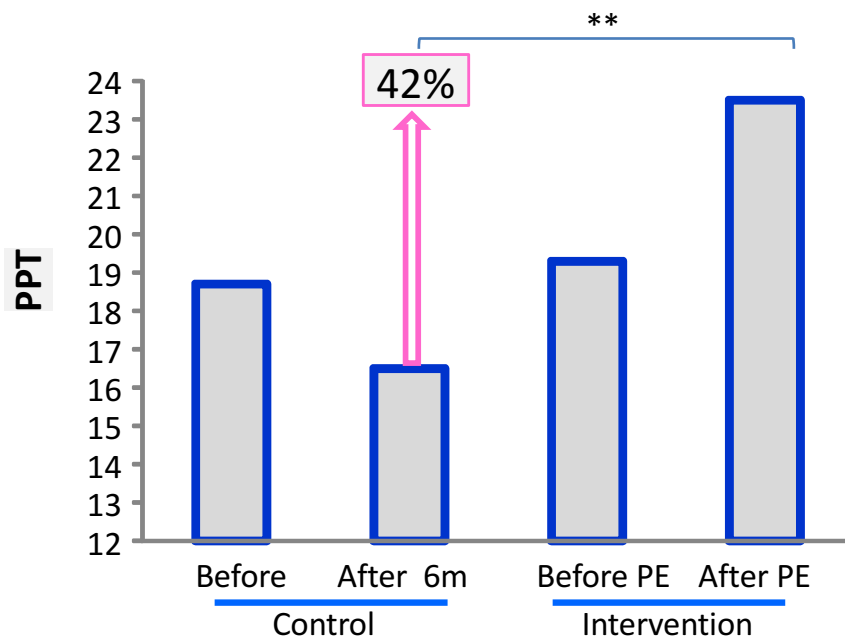
FRANCISCO TARAZONA (Alzira, Valencia)

MARICARMEN GOMEZ CABRERA

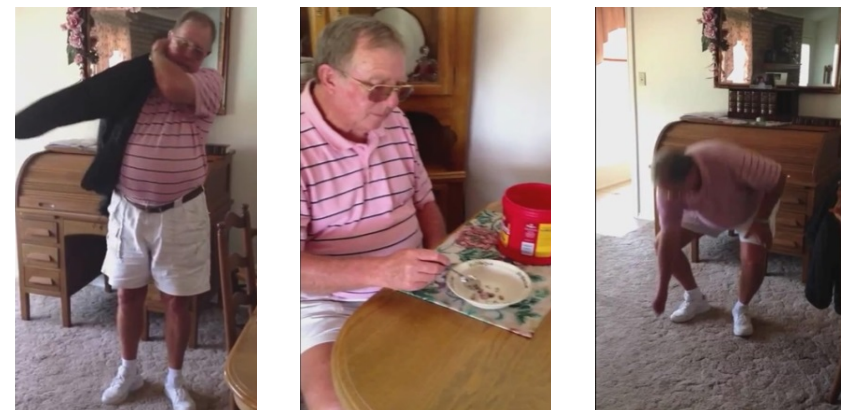
ANDREA SALVADOR

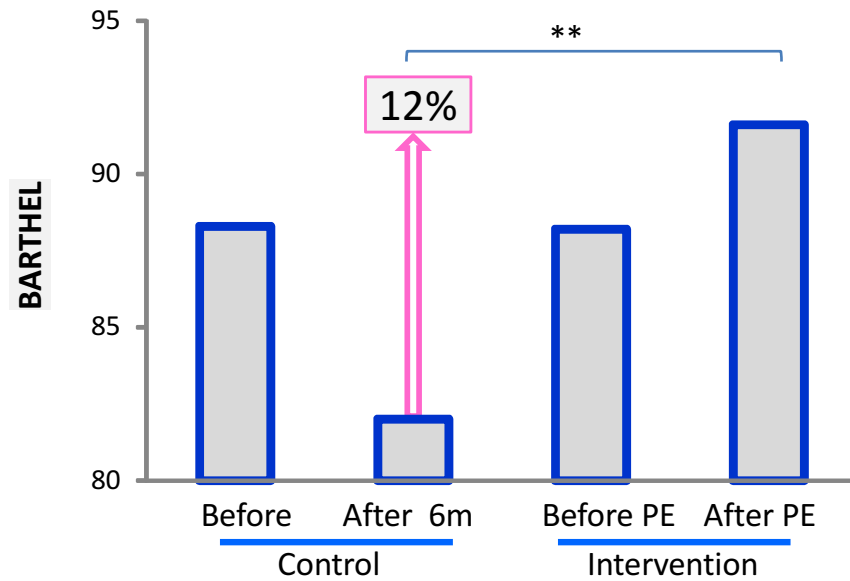


SPPB: Short Physical Performance Test



PPT: Physical Performance Test

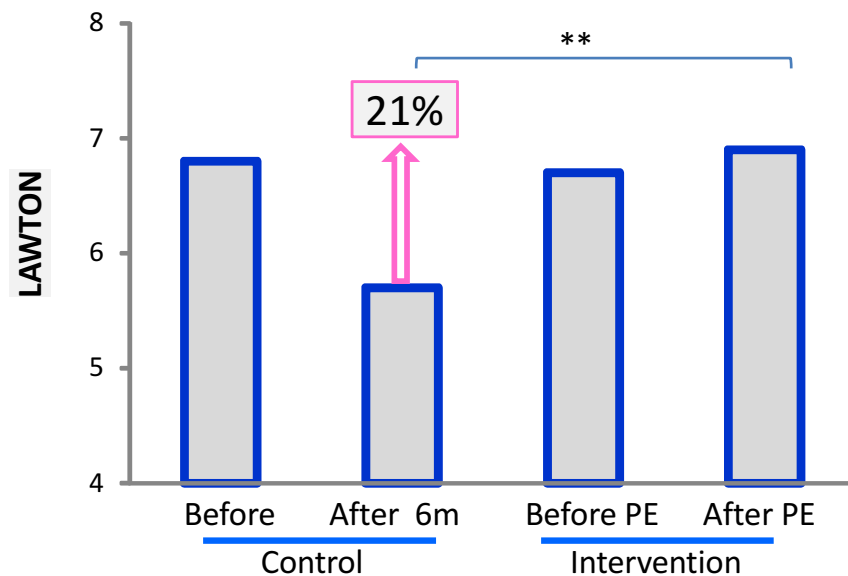




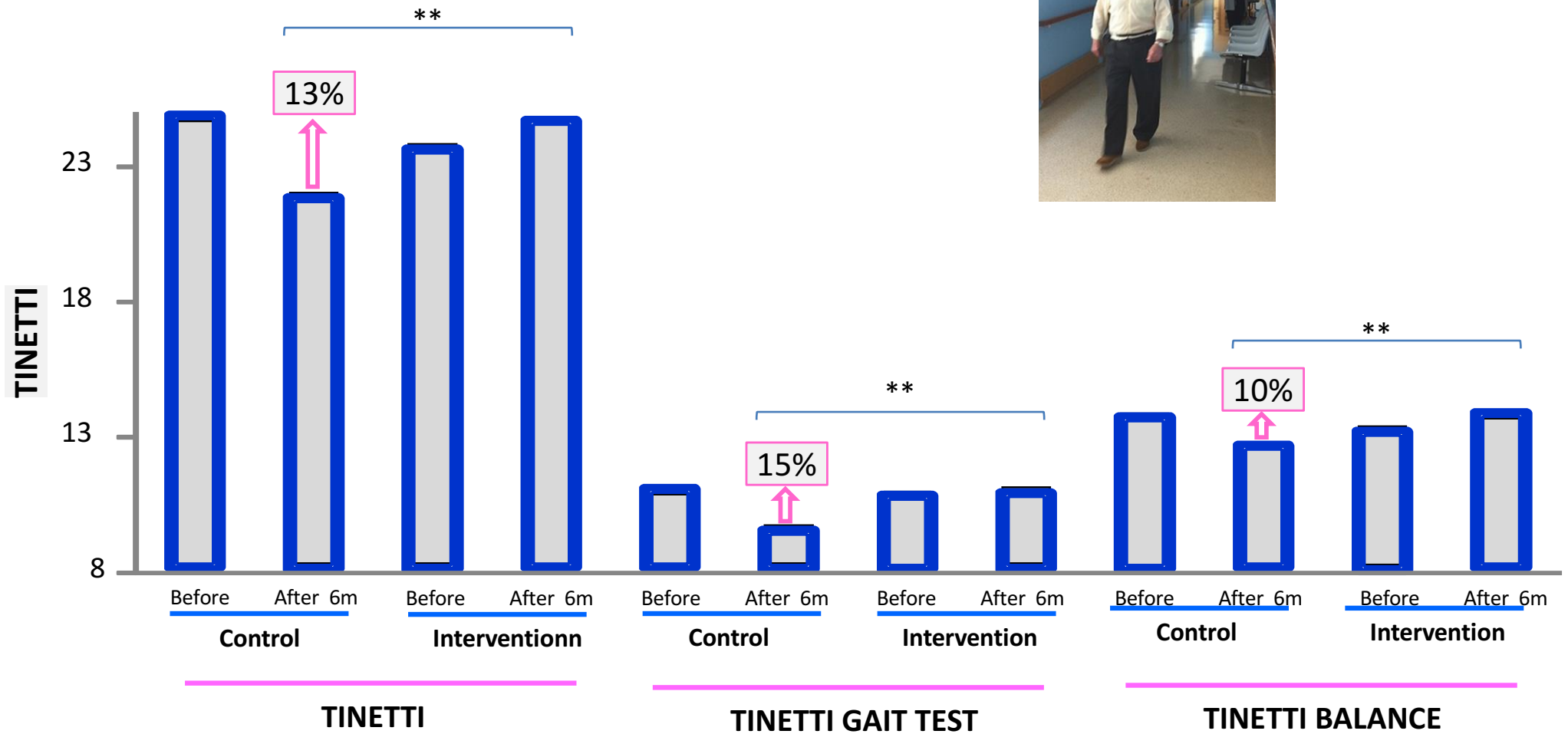
BARTHEL: Activities of daily living

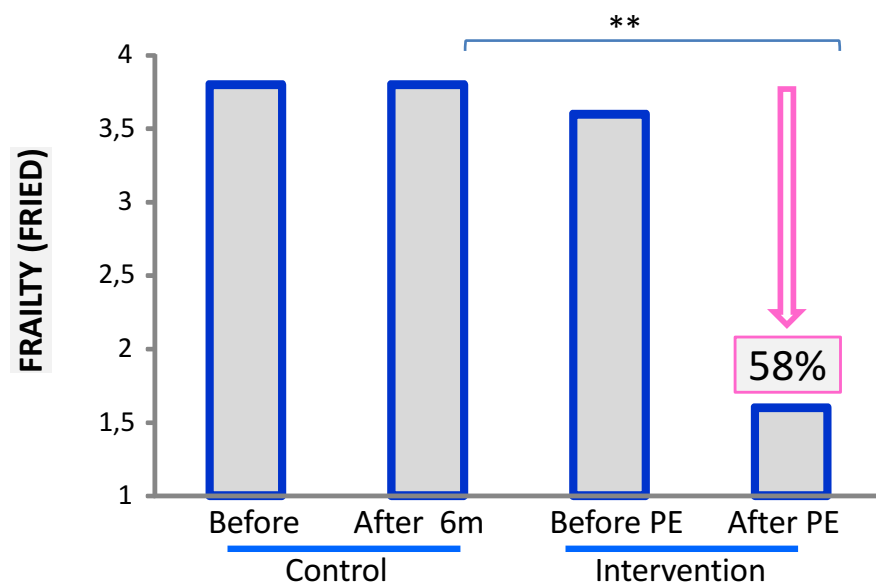


LAWTON: Instrumental activities of daily living

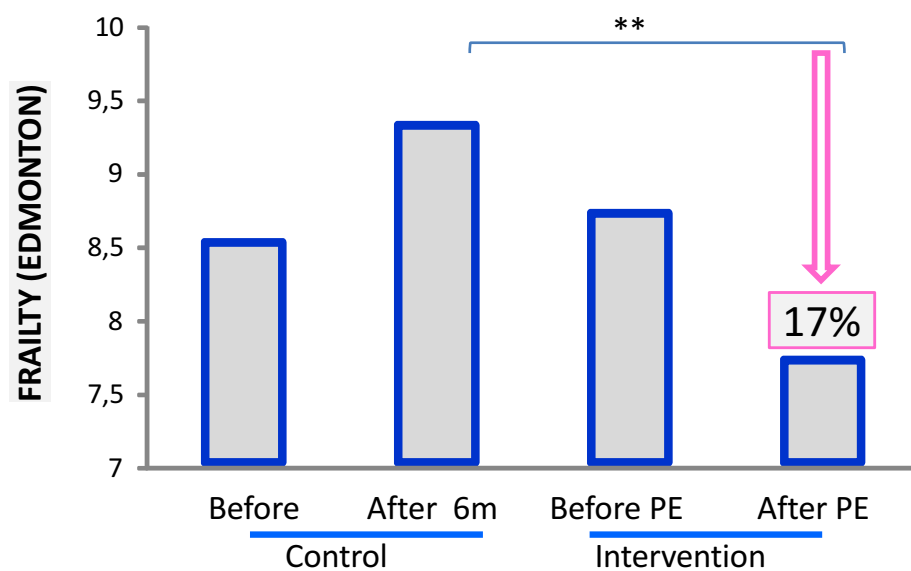


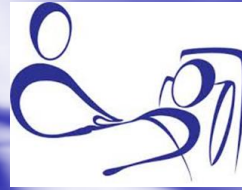
TINETTI: Gait and Balance



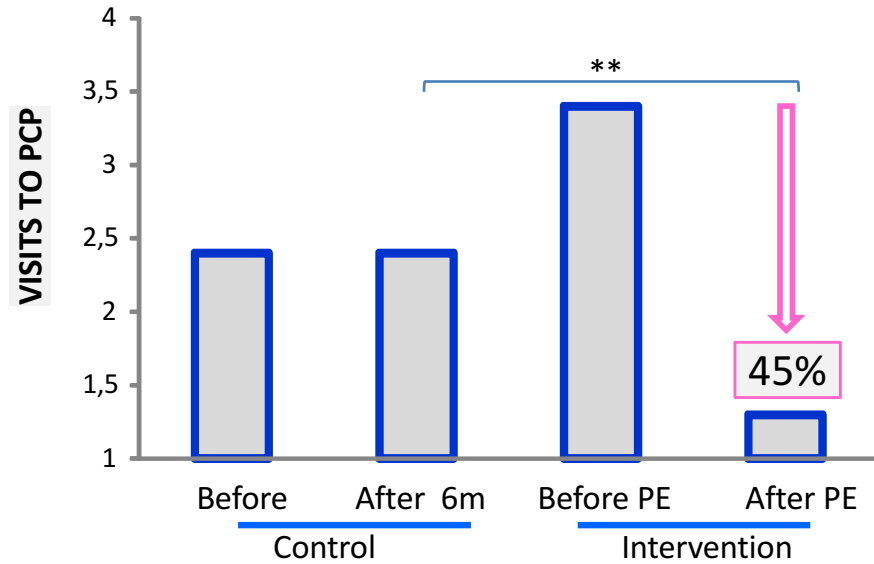


NNT= 3.2 (95% CI 2.0-4.5).

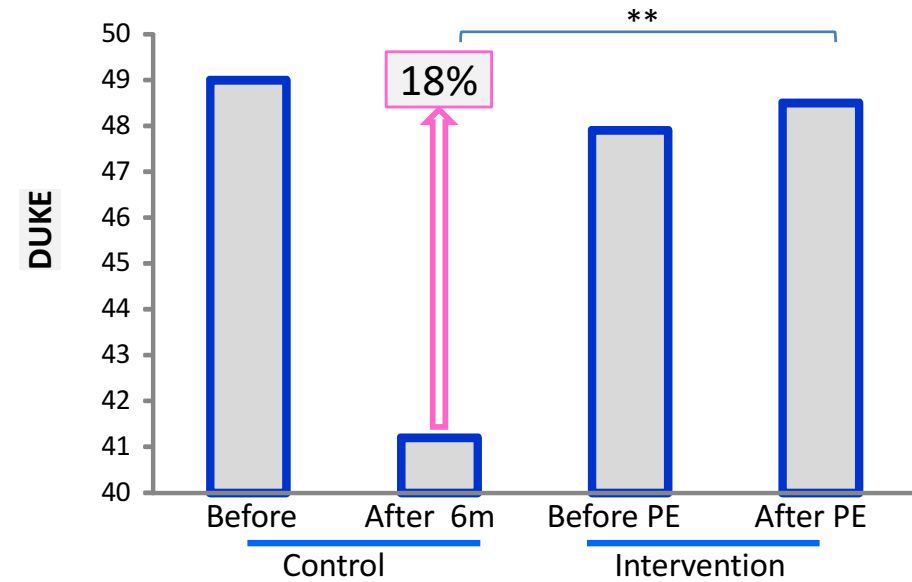




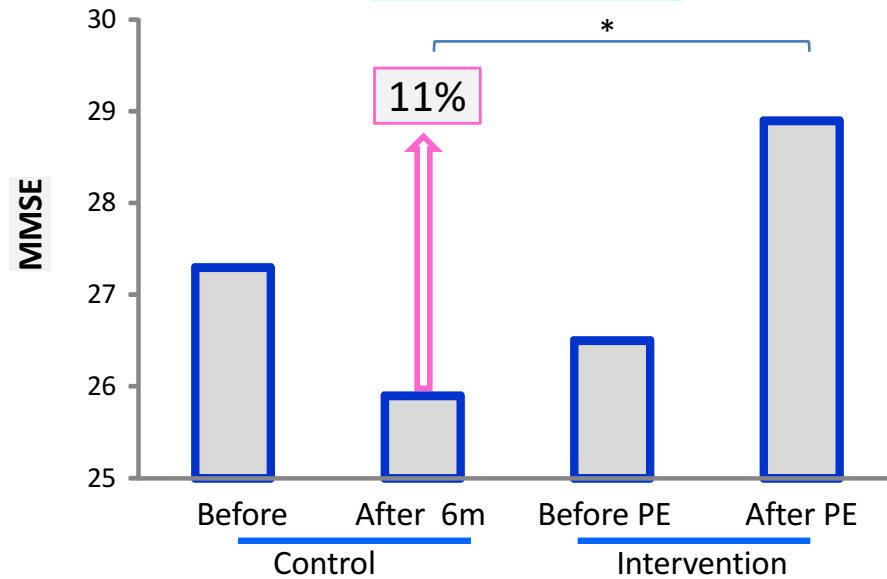
Visits to PCP



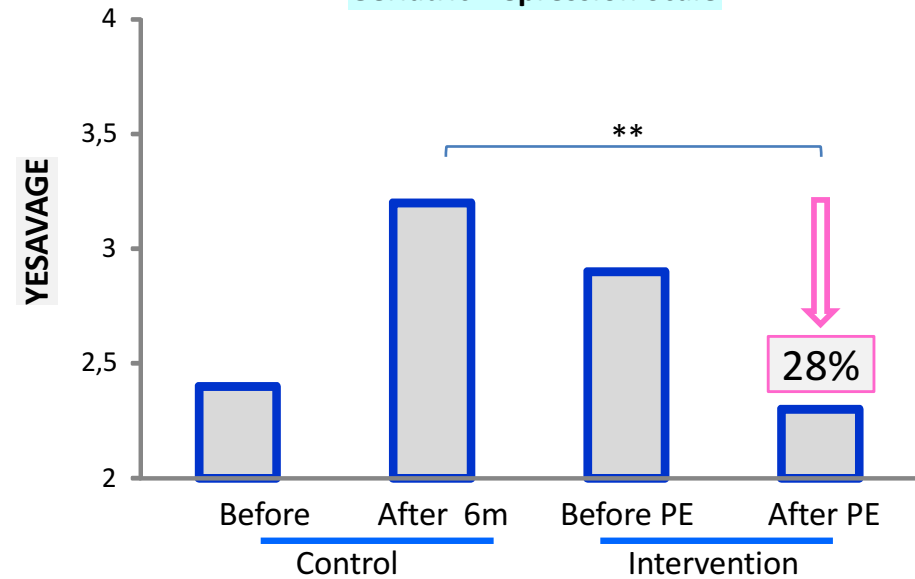
Duke (Social Support)



Cognitive impairment



Geriatric Depression Scale



Outline

 Aging is normal: Reflections of a gerontologist

 Interventions for healthy aging

 Epilogue: successful aging

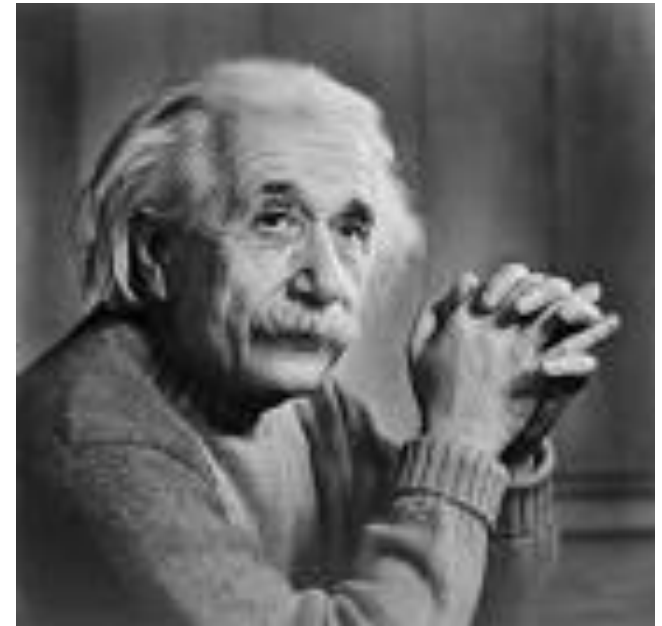
OUR AIM: successful aging



La imagen no existe sin el observador (W Heisenberg)

Successful aging

🌿 People like you and I, though mortal, of course, **do not grow old no matter how long we live.** What I mean is that we never cease to stand like curious children before the great Mystery into which we were born

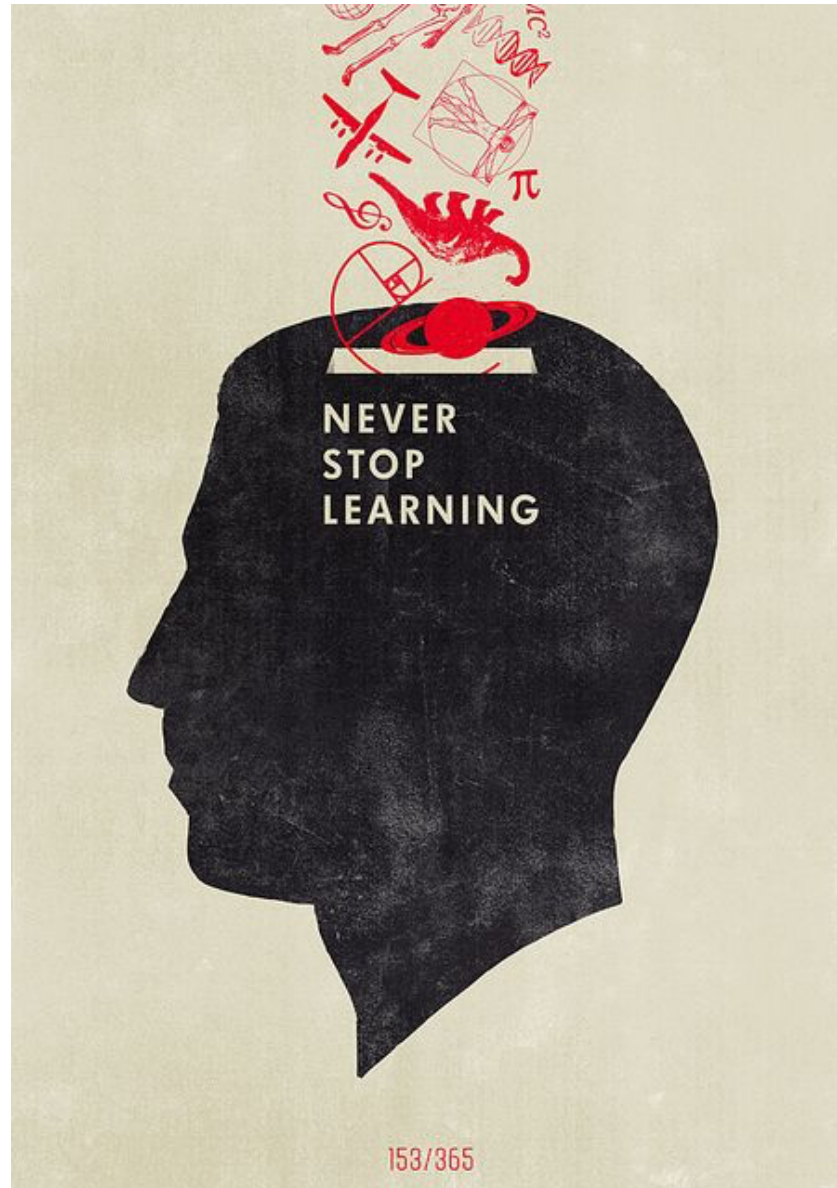


AE. to Otto Juliusberger, close friend and doctor

Successful aging



The secret of successful aging...



VNIVERSITAT
E VALÈNCIA (👤) Facultat de Medicina i Odontologia
VIÑA'S LAB



THANK YOU



Freshage

Age and [Exercise](#) Research Group