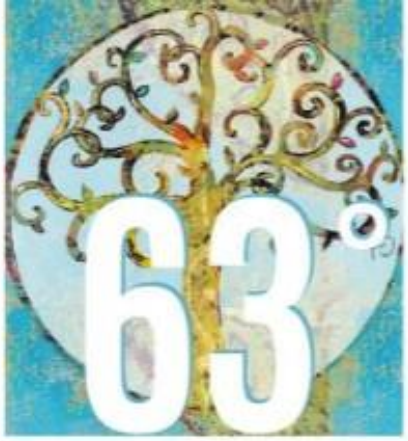


63° CONGRESSO NAZIONALE SIGG

GLI ANZIANI: LE RADICI DA PRESERVARE

ROMA 28 novembre 01 dicembre 2018 Auditorium della Tecnica, Roma

Fragilità, età biologica e resilienza: è solo una questione di terminologia o sono problemi clinici differenti?

Matteo Cesari

UNIVERSITÀ DEGLI STUDI DI MILANO

FONDAZIONE IRCCS CA' GRANDA
OSPEDALE MAGGIORE POLICLINICO
Sistema Sanitario Regione Lombardia

INTERNATIONAL

105-Year-Old Cyclist Rides 14 Miles In An Hour En Route To A World Record

January 4, 2017 · 2:44 PM ET

Robert Marchand (age 105yo)

26.925 kilometers in an hour

-50.6% compared to respective worldrecord

Age and Ageing 2016; **45:** 729–733
doi: 10.1093/ageing/afw111
Published electronically 4 July 2016

Centenarian athletes: Examples of ultimate human performance?

ROMUALD LEPERS[1], PAUL J. STAPLEY[2], THOMAS CATTAGNI[3]

JAMDA 14 (2013) 392–397

JAMDA

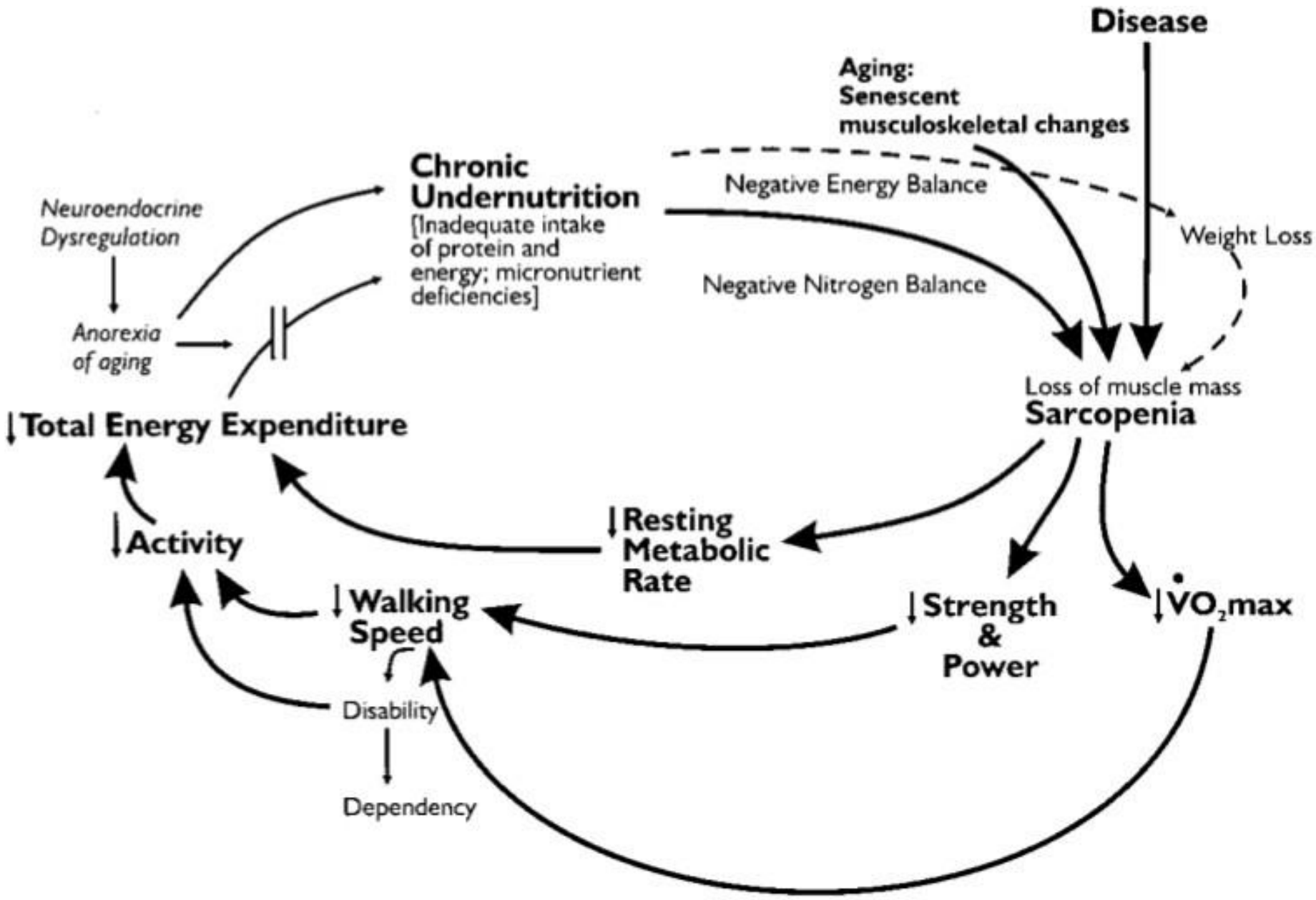
journal homepage: www.jamda.com

Special Article

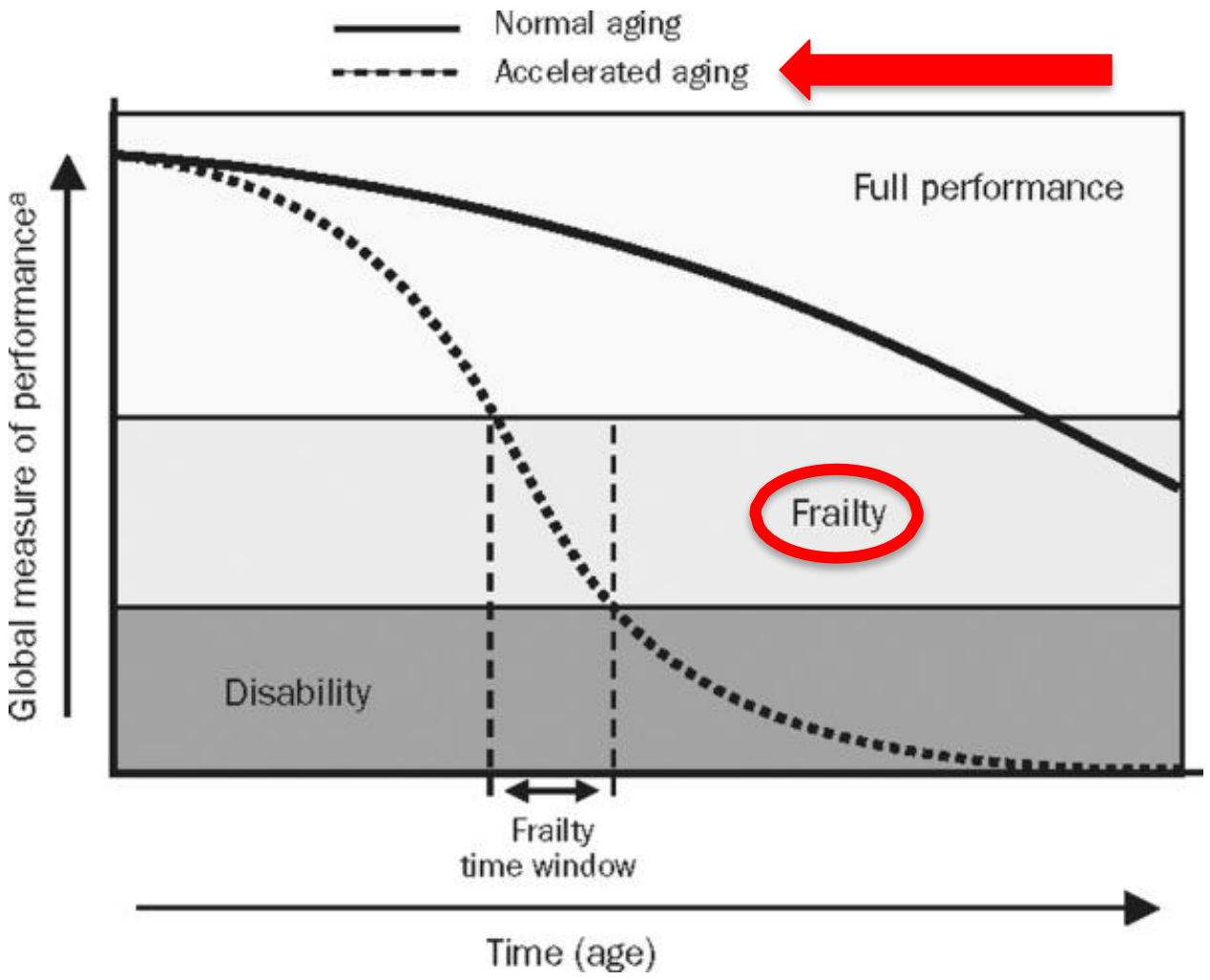
Frailty Consensus: A Call to Action

John E. Morley MB, BCh [a,*], Bruno Vellas MD [b,c], G. Abellan van Kan MD [b,c], Stefan D. Anker MD, PhD [d,e], Juergen M. Bauer MD, PhD [f], Roberto Bernabei MD [g], Matteo Cesari MD, PhD [b,c], W.C. Chumlea PhD [h], Wolfram Doehner MD, PhD [d,i], Jonathan Evans MD [j], Linda P. Fried MD, MPH [k], Jack M. Guralnik MD, PhD [l], Paul R. Katz MD, CMD [m], Theodore K. Malmstrom PhD [a,n], Roger J. McCarter PhD [o], Luis M. Gutierrez Robledo MD, PhD [p], Ken Rockwood MD [q], Stephan von Haehling MD, PhD [r], Maurits F. Vandewoude MD, PhD [s], Jeremy Walston MD [t]

"..A medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death..."

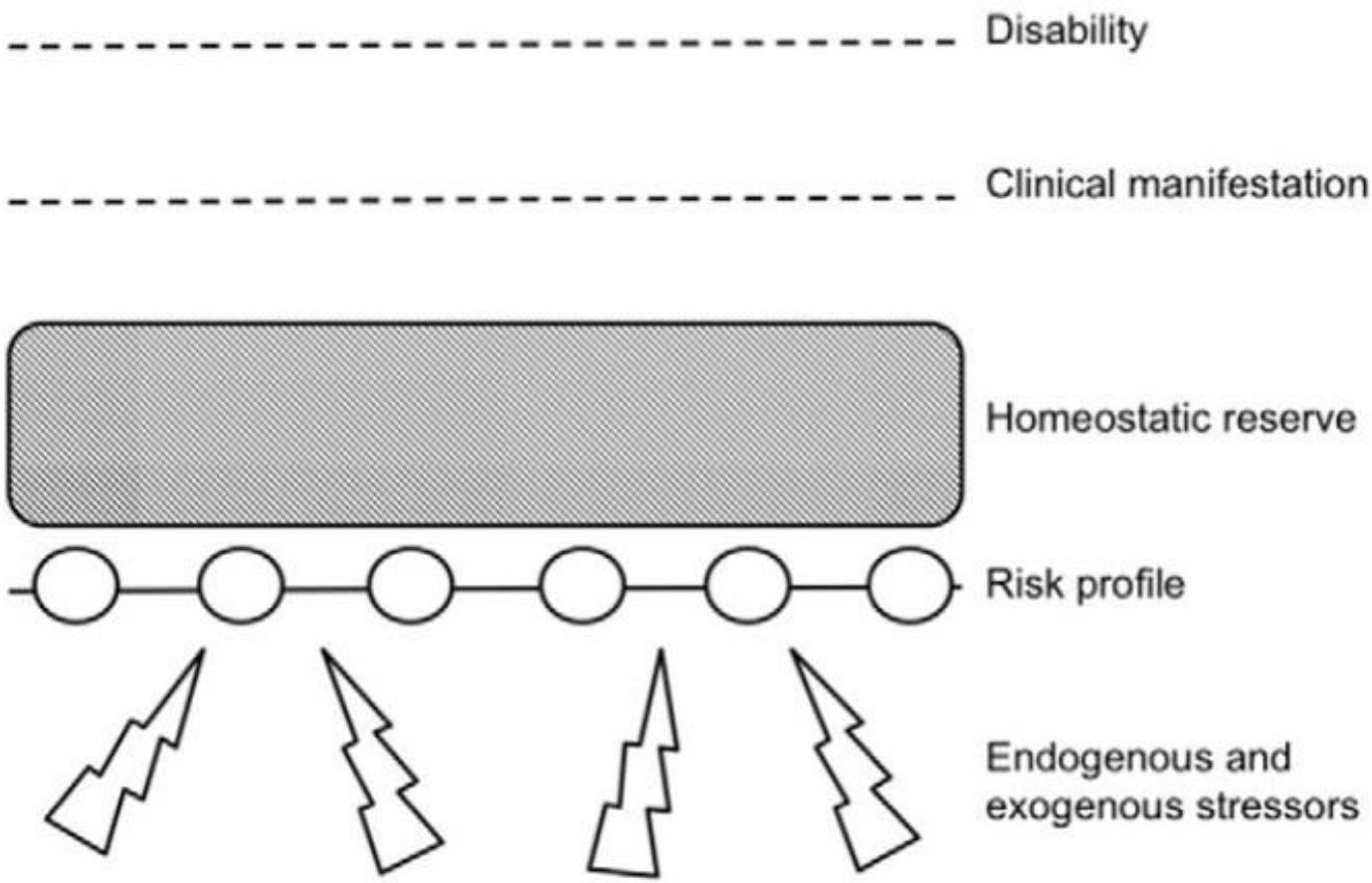


Fried LP, Walston J. Failure to thrieve. In: Hazzard WR et al, eds. *Principles of Geriatric Medicine and Gerontology*. McGraw-Hill, 1998



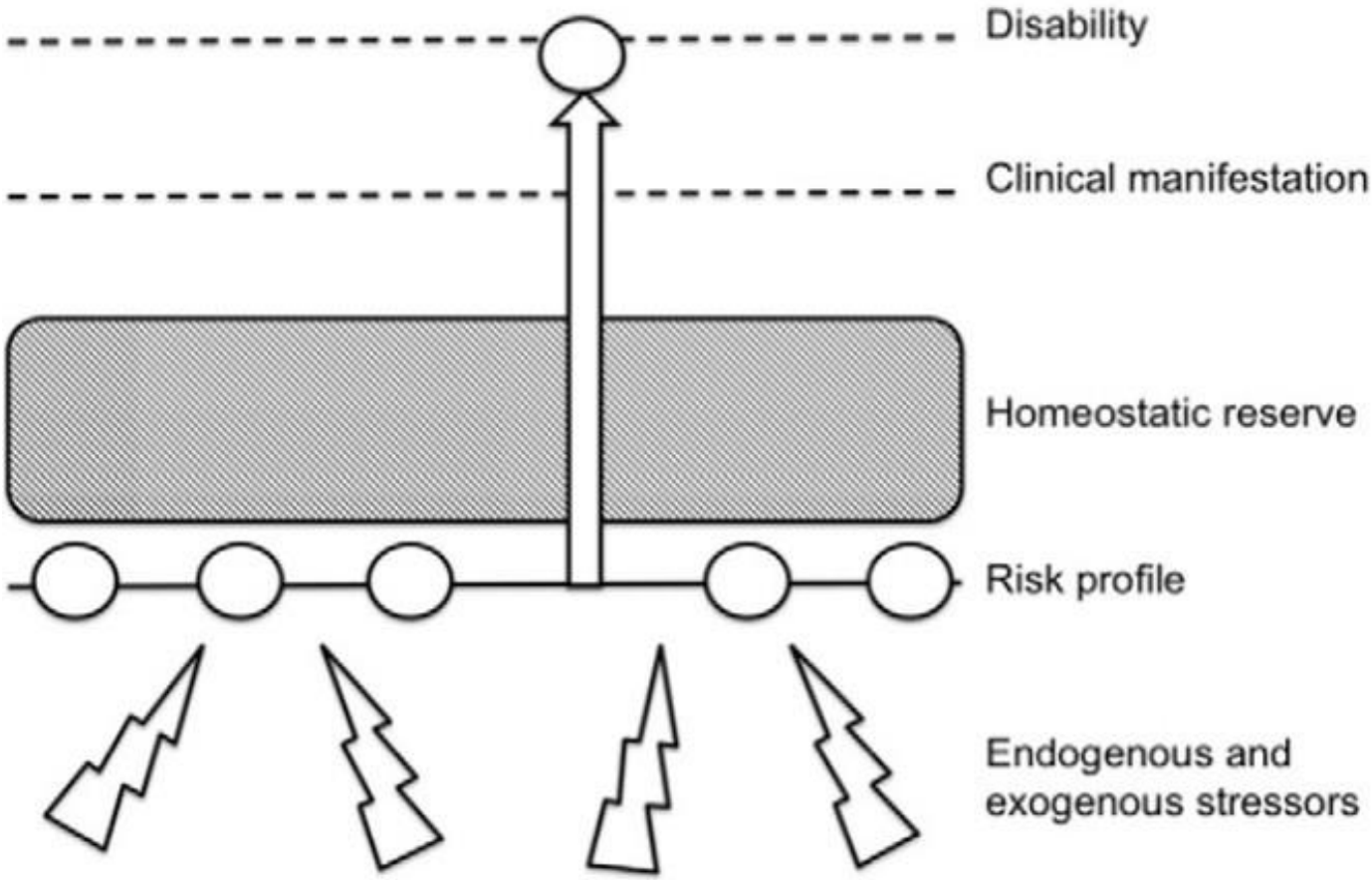
Ferrucci L et al. *JEndocrinol Invest* 2002;25:10-5
Singh M et al. *Mayo Clin Proc* 2008;83:1146-53

A. Optimal homeostatic balance



Cesari et al. *Eur J Intern Med* 2016;35:1-9
Studenski S. *J Nutr Health Aging* 2009;13:729-32
Ferrucci L et al. *Genus* 2005;LXI:39-53

B. Model of disease in young/adult individuals

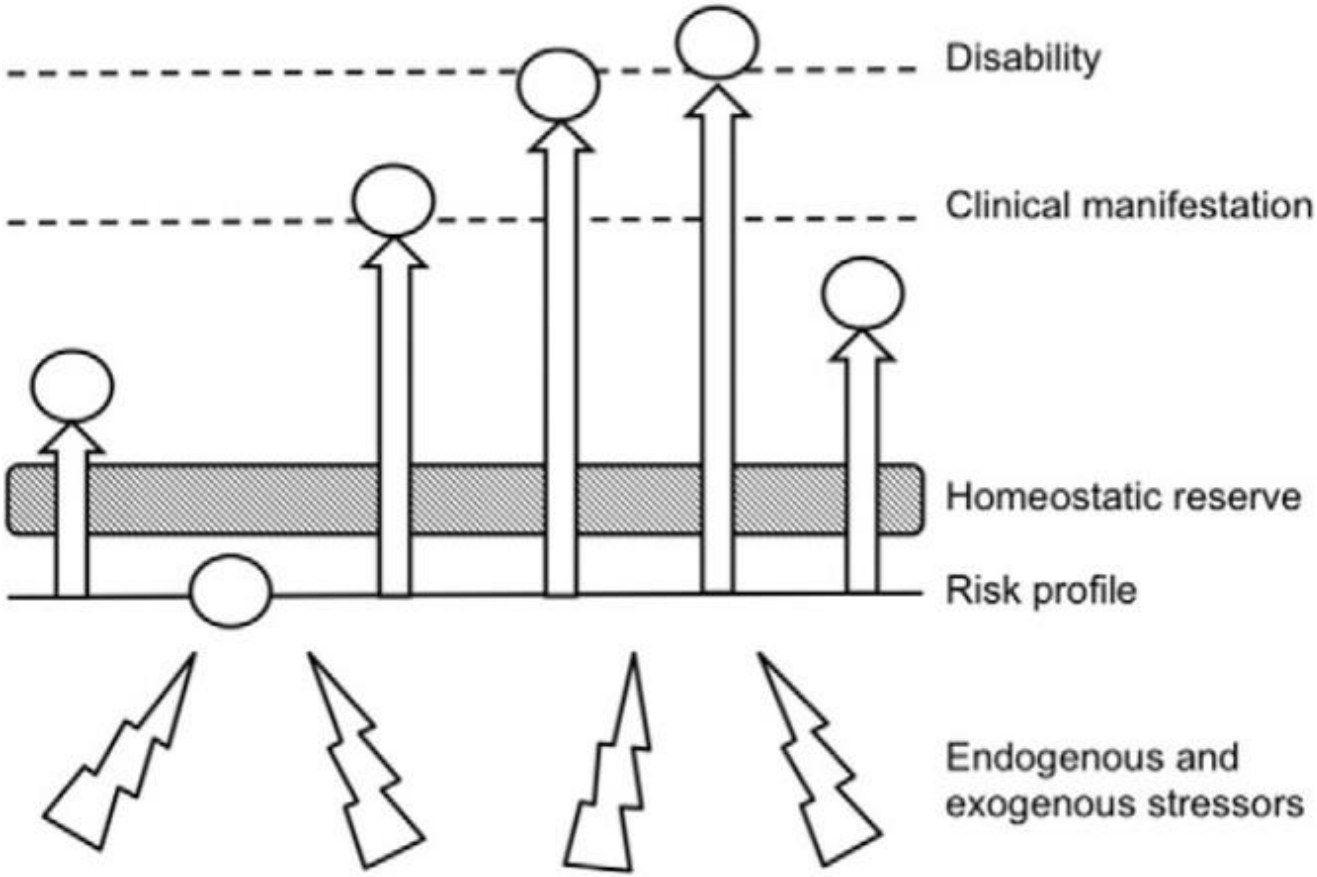


Cesari et al. *Eur J Intern Med* 2016;35:1-9

Studenski S. *J Nutr Health Aging* 2009;13:729-32

Ferrucci L et al. *Genus* 2005;LXI:39-53

C. Frailty



Cesari et al. *Eur J Intern Med* 2016;35:1-9
Studenski S. *J Nutr Health Aging* 2009;13:729-32
Ferrucci L et al. *Genus* 2005;LXI:39-53

The Frailty Phenotype

Table 1. Operationalizing a Phenotype of Frailty

A. *Characteristics of Frailty*	B. *Cardiovascular Health Study Measure**
Shrinking: Weight loss (unintentional) Sarcopenia (loss of muscle mass)	Baseline: >10 lbs lost unintentionally in prior year
Weakness	Grip strength: lowest 20% (by gender, body mass index)
Poor endurance; Exhaustion	"Exhaustion" (self-report)
Slowness	Walking time/15 feet: slowest 20% (by gender, height)
Low activity	Kcals/week: lowest 20% males: <383 Kcals/week females: <270 Kcals/week
	C. *Presence of Frailty*
	Positive for frailty phenotype: ≥3 criteria present
	Intermediate or prefrail: 1 or 2 criteria present

*See Appendix.

Fried LP et al. *JGerontol A Biol Sci Med Sci* 2001;56:M146-56

Research Article
TheScientificWorld (2001) 1, 323–336
ISSN 1532-2246; DOI 10.1100/tsw.2001.58

TheScientificWorld
www.thescientificworld.com

Accumulation of Deficits as a Proxy Measure of Aging

Arnold B. Mitnitski[1,2], Alexander J. Mogilner, and Kenneth Rockwood[2,*]

[1]Department of Mechanical Engineering, Ecole Polytechnique, Montreal P.O. Box 6079, Station Centre-ville Montreal, Quebec H3C 3A7; [2]Queen Elizabeth II, Health Sciences Centre, Geriatric Medicine Research Unit, Room 1421,5955 Veterans' Memorial Lane, Halifax, Nova Scotia B3H 2E1

"… a method for appraising health status in elderly people. A **Frailty Index** was defined as the proportion of accumulated deficits (symptoms, signs, functional impairments, and laboratory abnormalities). It serves as an individual state variable, reflecting severity of illness and proximity to death…"

Biogerontology (2013) 14:709–717
DOI 10.1007/s10522-013-9446-3

RESEARCH ARTICLE

Assessing biological aging: the origin of deficit accumulation

Arnold Mitnitski · Xiaowei Song · Kenneth Rockwood

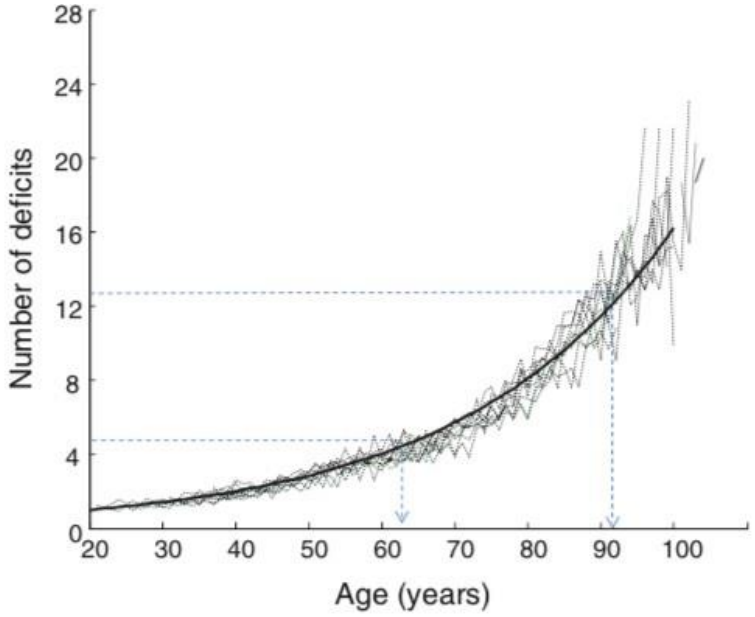


Fig. 1 Age trajectories of the mean number of deficits. *Thin lines* are the cross-sectional data for the nine consecutive two-years cycles plotted against age. The *solid line* is the best exponential fit with the exponent of 0.035 (±0.02)

Chronological Age vs Biological Age

Chronological age: the number of years a person has been alive

Biological age *(or physiological age):* the description of an individual's development based on biomarkers (i.e., molecular or cellular events). It measures the declining integrity of multiple organs

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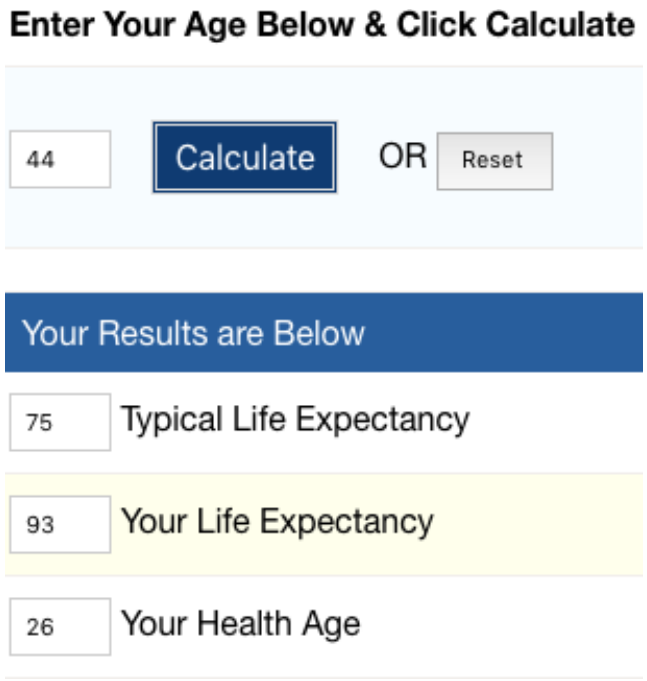
Biological age *(or physiological age):* the description of an individual's development based on biomarkers (i.e., molecular or cellular events). It measures the declining integrity of multiple organs



To a broader extent, biological age captures how old a person seems

It takes into consideration the clinical aspect of the individual as well as lifestyle factors (e.g., diet, exercise, sleeping habits, happiness)

Proc Natl Acad Sci U S A 2015;112:E4104-10

Quantification of biological aging in young adults

Daniel W. Belsky[a,b,1], Avshalom Caspi[c,d,e,f], Renate Houts[c], Harvey J. Cohen[a], David L. Corcoran[e], Andrea Danese[f,g], HonaLee Harrington[c], Salomon Israel[h], Morgan E. Levine[i], Jonathan D. Schaefer[c], Karen Sugden[c], Ben Williams[c], Anatoli I. Yashin[b], Richie Poulton[j], and Terrie E. Moffitt[c,d,e,f]

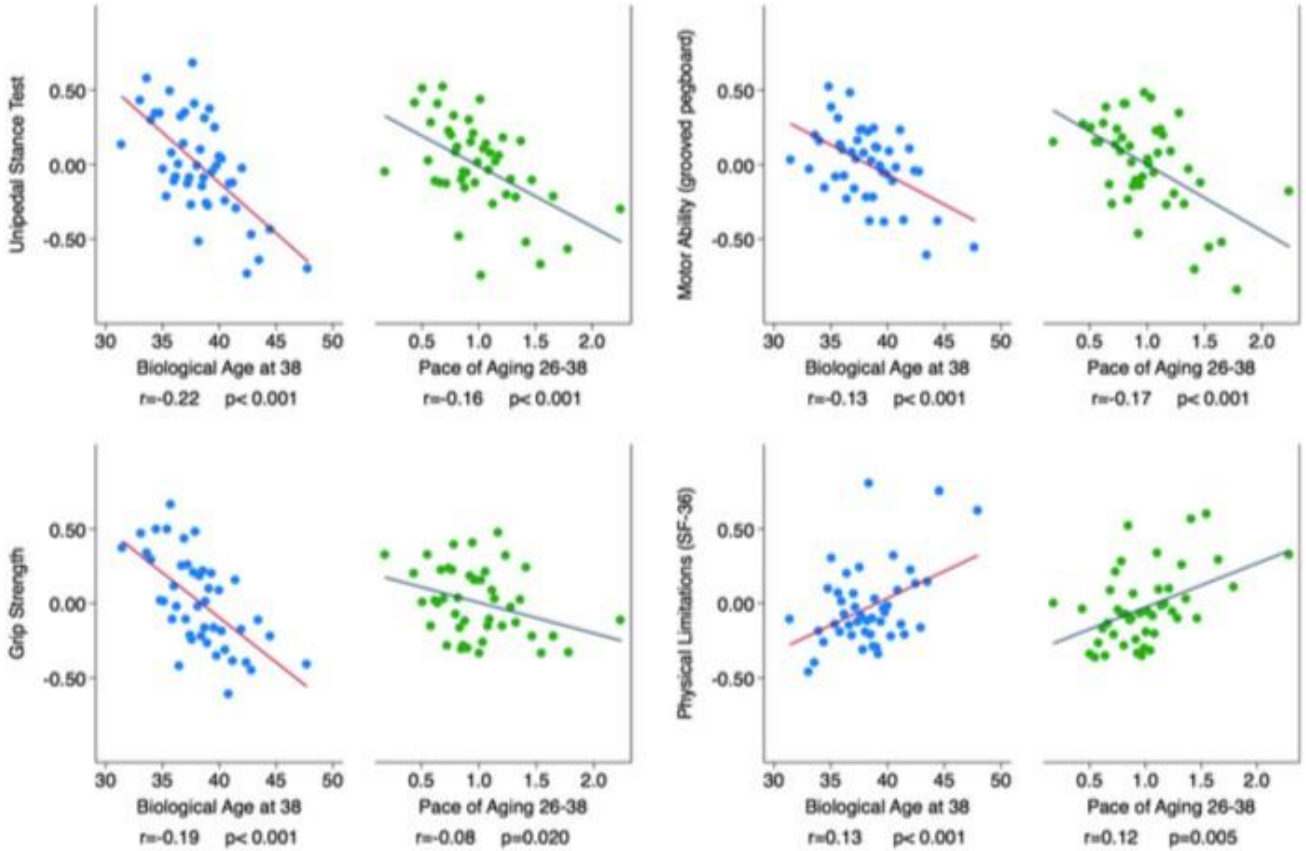


Fig. 5. Healthy adults who were aging faster exhibited deficits in physical functioning relative to slower-aging peers. The figure shows binned scatter plots of the associations of Biological Age and Pace of Aging with tests of physical functioning (unipedal stance test, grooved pegboard test, grip strength) and study members' reports of their physical limitations. In each graph, Biological Age associations are plotted on the left in blue (red regression line) and Pace of Aging associations are plotted on the right in green (navy regression line). Plotted points show means for bins of data from 20 Dunedin Study members. Effect size and regression line were calculated from the raw data.

Mitnitski et al. BMC Medicine
DOI 10.1186/s12916-015-0400-x

BMC Medicine

RESEARCH ARTICLE Open Access

Age-related frailty and its association with biological markers of ageing

Arnold Mitnitski[1], Joanna Collerton[2], Carmen Martin-Ruiz[3], Carol Jagger[2], Thomas von Zglinicki[4], Kenneth Rockwood[5] and Thomas B. L. Kirkwood[4*]

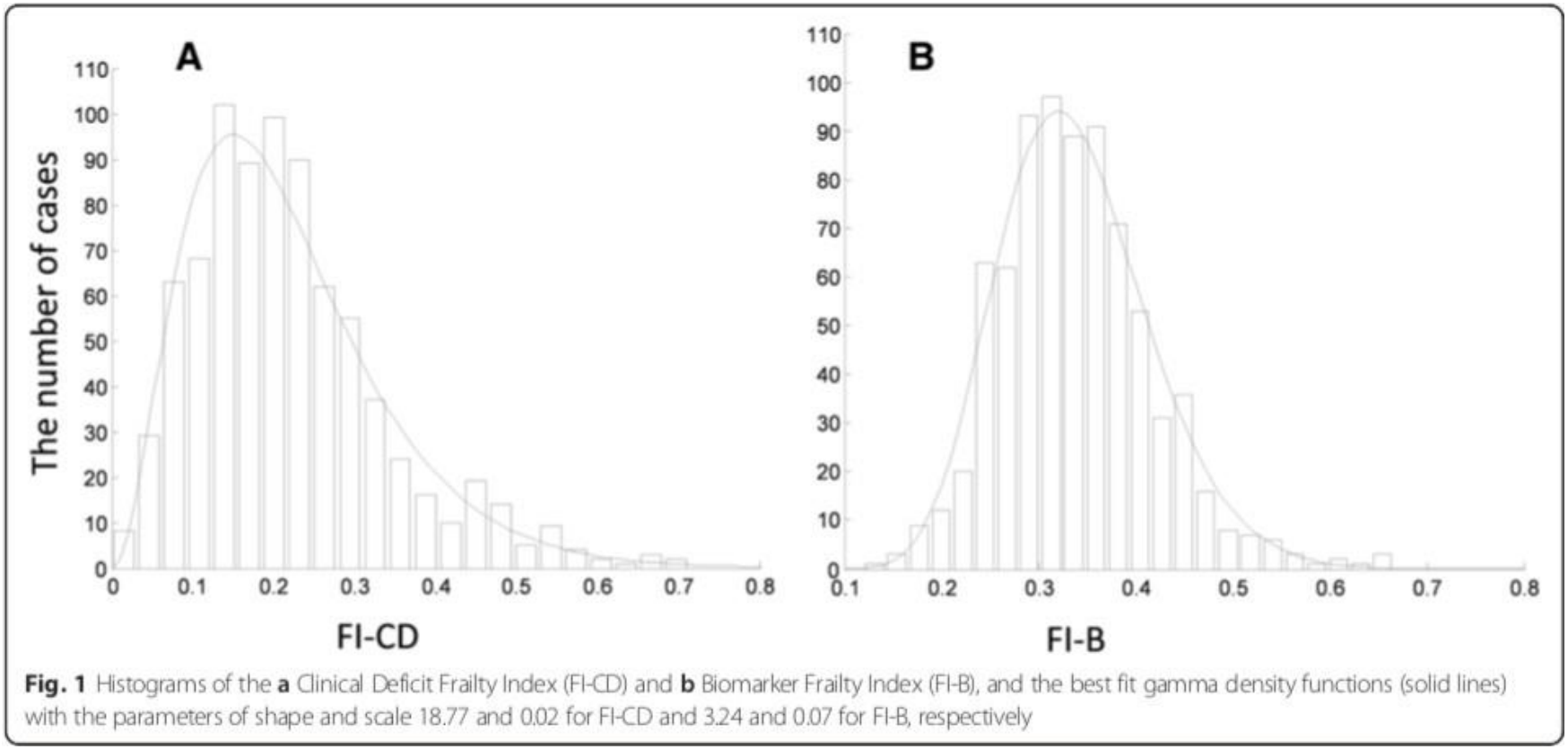


Fig. 1 Histograms of the **a** Clinical Deficit Frailty Index (FI-CD) and **b** Biomarker Frailty Index (FI-B), and the best fit gamma density functions (solid lines) with the parameters of shape and scale 18.77 and 0.02 for FI-CD and 3.24 and 0.07 for FI-B, respectively

OPEN

Molecular Psychiatry (2018) 23, 1385–1392

www.nature.com/mp

ORIGINAL ARTICLE

Brain age predicts mortality

JH Cole[1], SJ Ritchie[2,3], ME Bastin[2,4], MC Valdés Hernández[2,4], S Muñoz Maniega[2,4], N Royle[2,4], J Corley[2,3], A Pattie[2,3], SE Harris[2,5], Q Zhang[6], NR Wray[6,7], P Redmond[3], RE Marioni[2,5,7], JM Starr[2], SR Cox[2,3], JM Wardlaw[2,4], DJ Sharp[1] and IJ Deary[2,3]

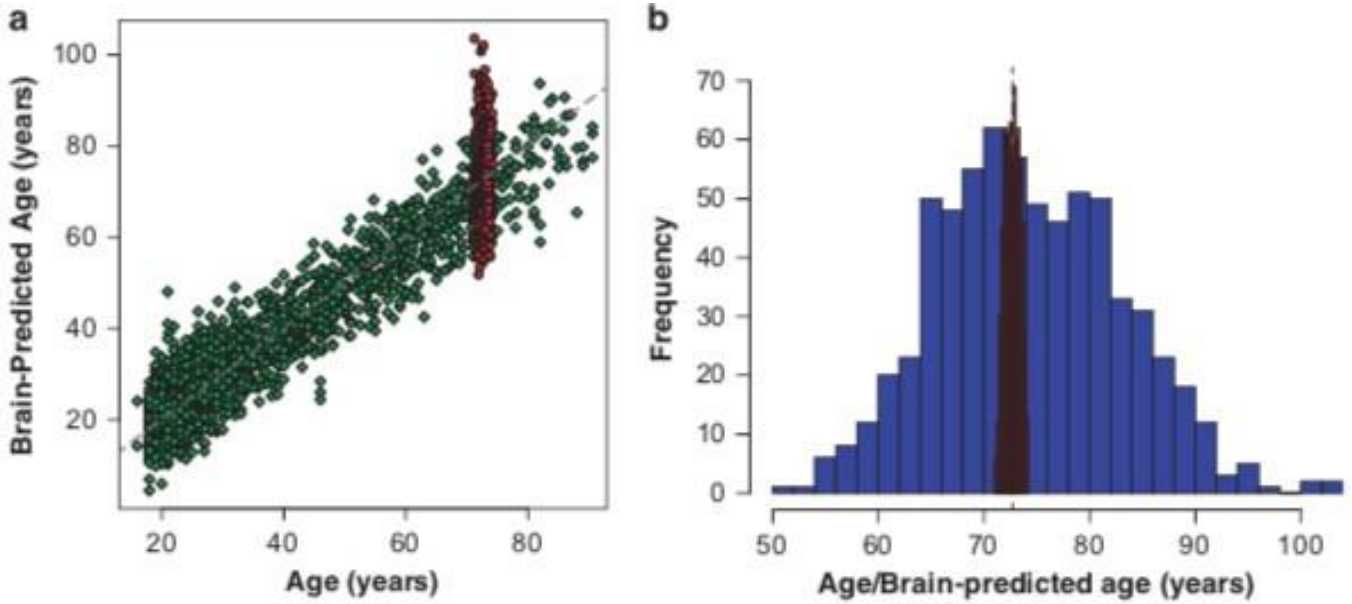


Figure 2. Brain-predicted age using structural neuroimaging in LBC1936. (**a**) Scatterplot showing the relationship between chronological age and brain-predicted age in the independent healthy cohort used as the training data (green diamonds) and the LBC1936 participants used as the test set (red circles). (**b**) Histogram showing the distributions of brain-predicted age (in blue) compared to the distribution in chronological age (in red). The substantially wider variability in brain-predicted age is evident. LBC1936, Lothian Birth Cohort 1936.

Resilience

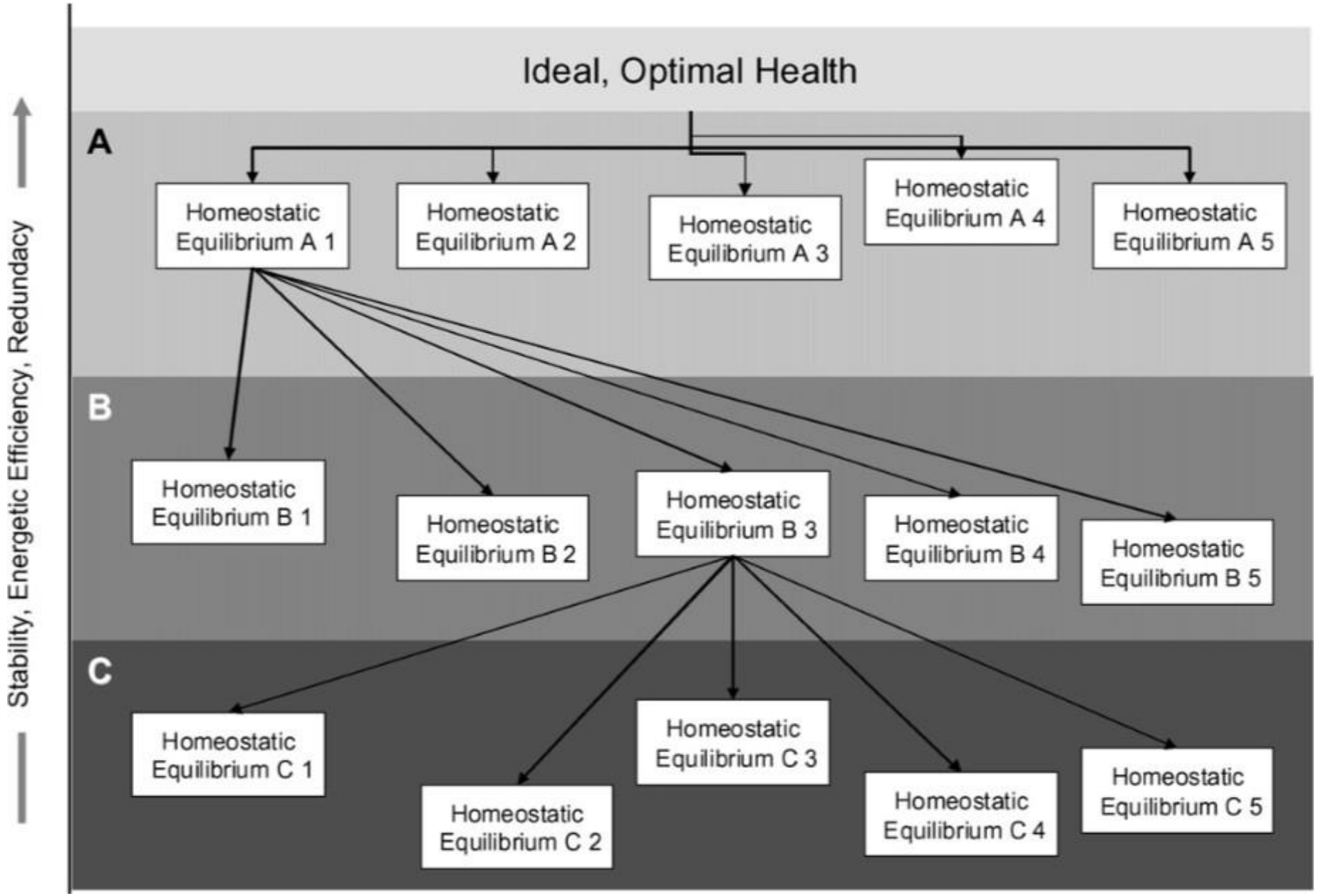
The **capacity** of metals **to resist** deformation presaged interest in individual differences in the resiliency of people under **stress**.

The human **ability to adapt** in the face of tragedy, trauma, adversity, hardship, and ongoing significant life **stressors**

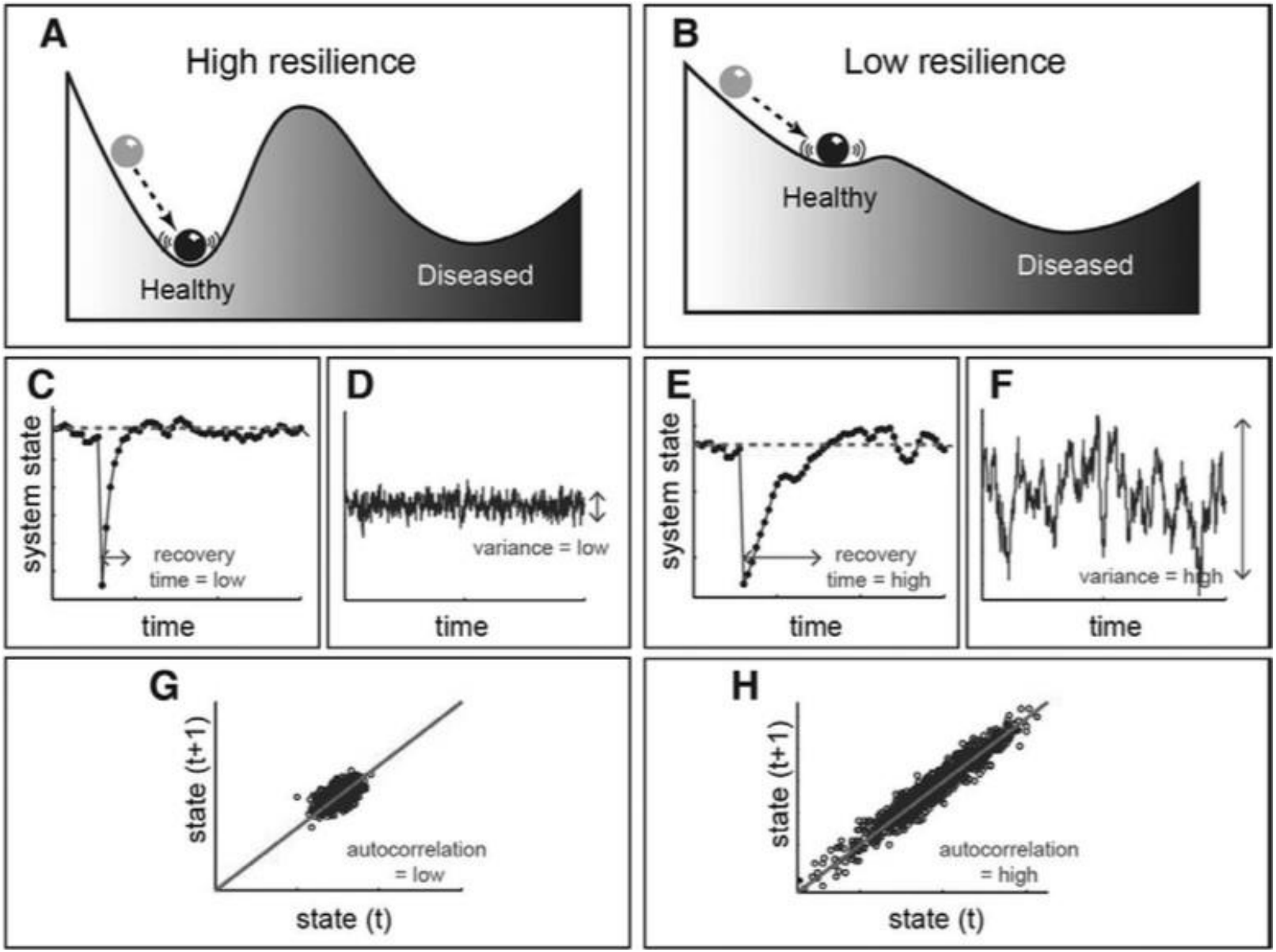
(Psychological) resilience refers to **effective coping and adaptation** although faced with loss, hardship, or **adversity**

(Physical) resilience is a characteristic at the whole person level which determines an individual's **ability to resist** functional decline or recover physical health following a **stressor**

Lazarus RS. *Ann Rev Psychol* 1993;44:1-21
Conti AA, Conti A. *Med Hypotheses*. 2010;74:1090
Tugade MM, Fredrickson BL. *J Pers Soc Psychol* 2004;86:320-333
Whitson HE et al. *J Gerontol A Biol Sci Med Sci*. 2016;71:489–495



Ferrucci L, et al. *Mech Ageing Dev* 2008;129:677-679

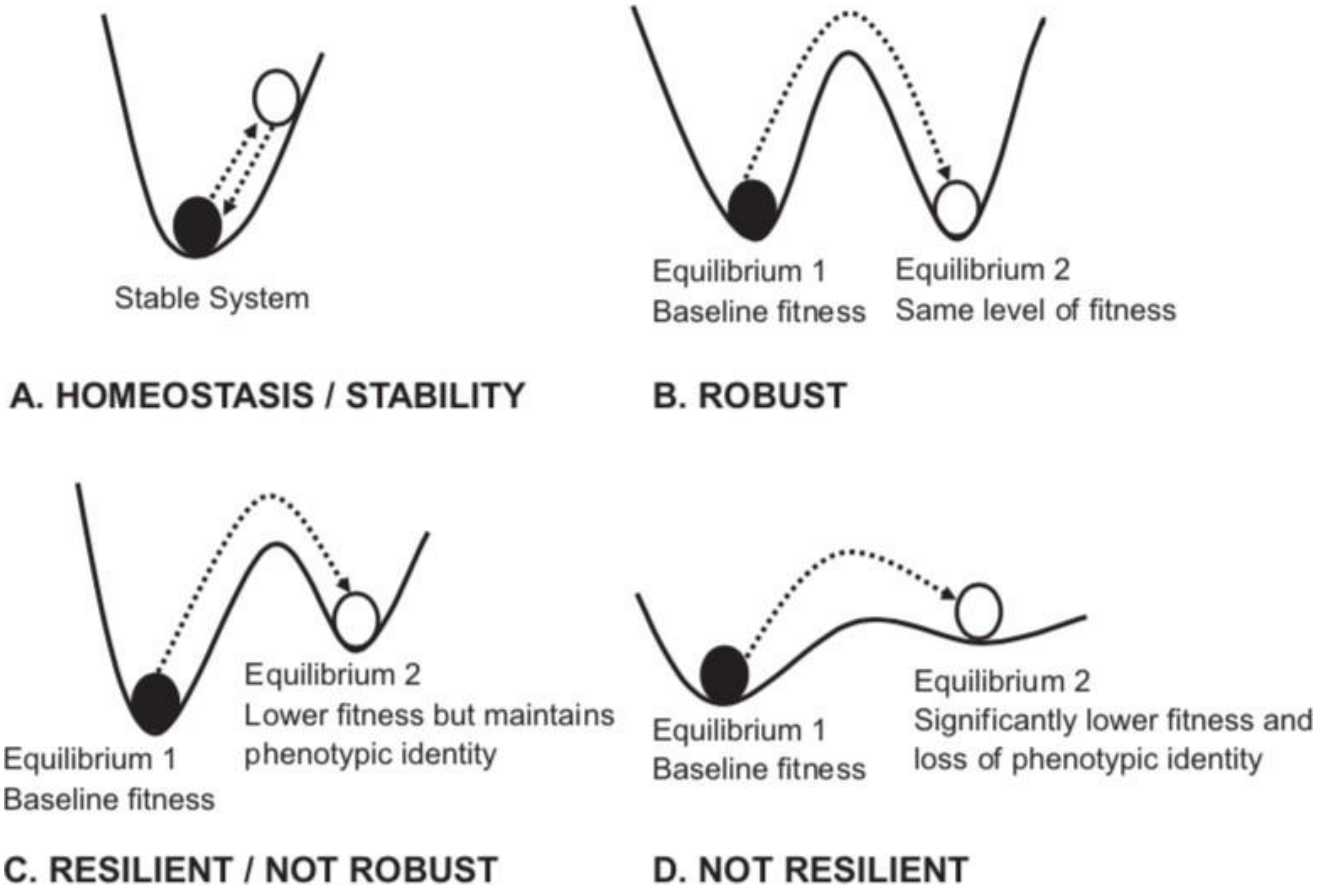


Olde Rikkert MG et al. *Crit Care Med* 2016;44:601-606

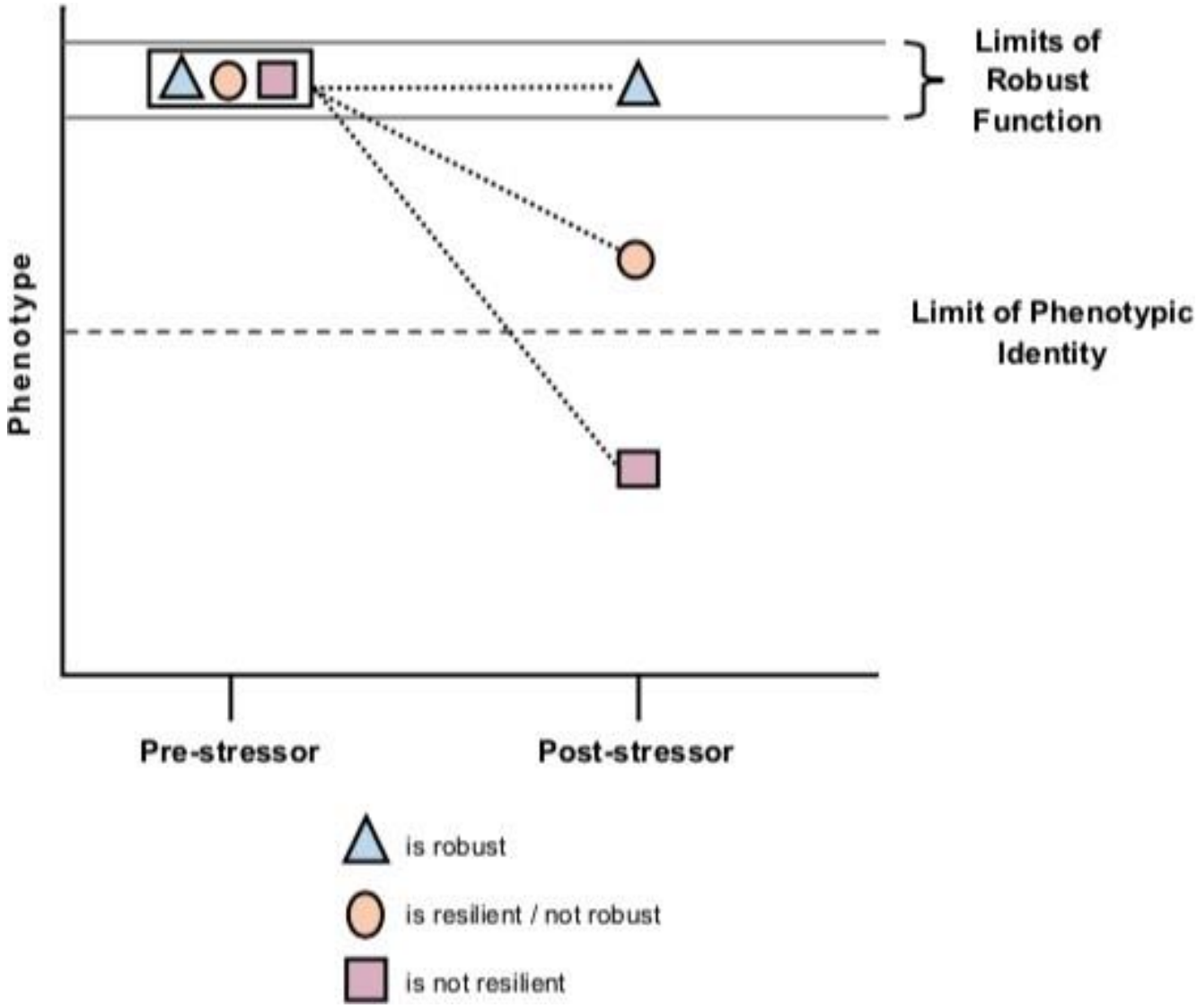
Robustness: ability to resist deviation from original state

versus

Resilience: ability to recover afer deviation



Varadhan R et al. *J Am Geriatr Soc* 2018;66:1455-1458



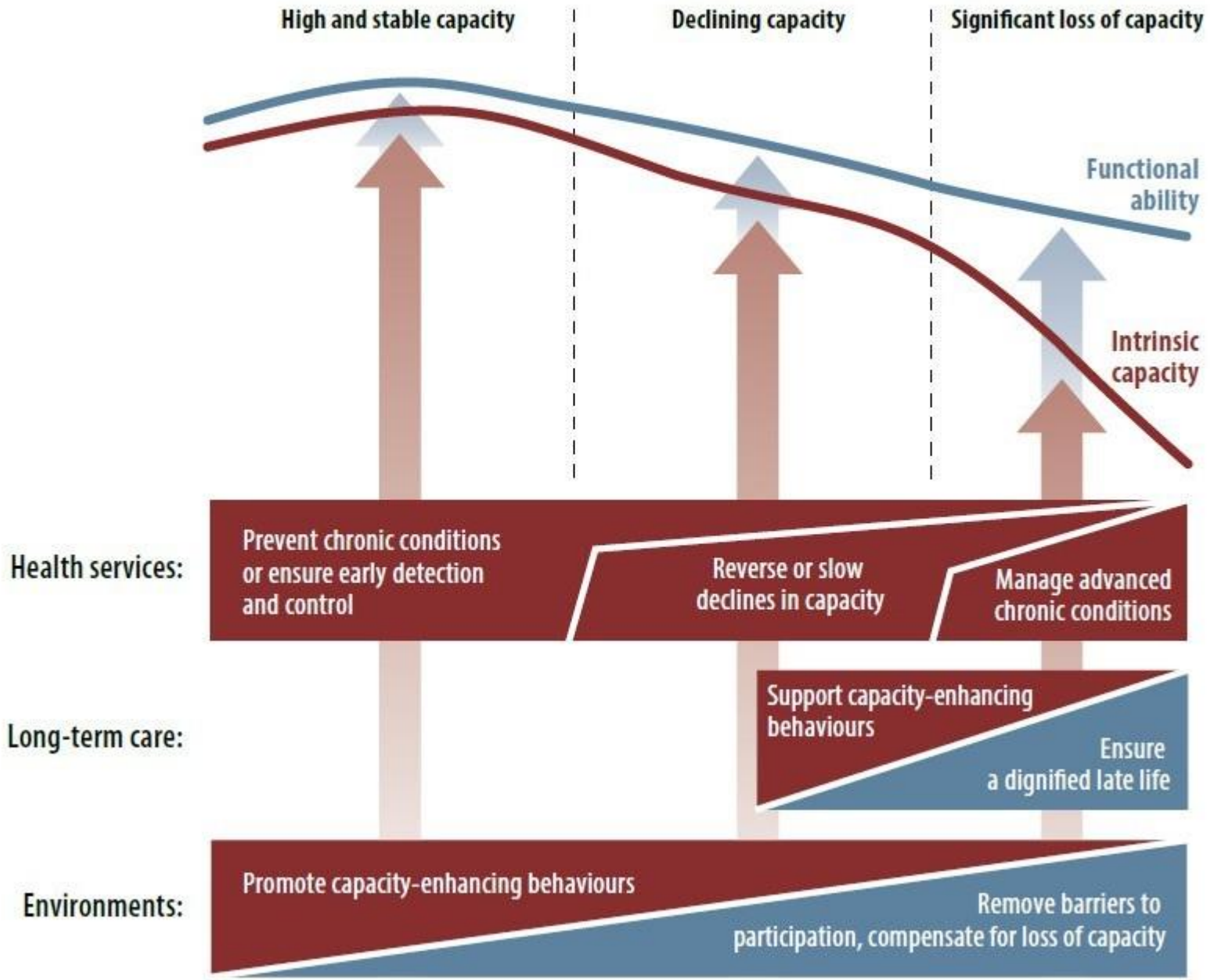
Varadhan R et al. *J Am Geriatr Soc* 2018;66:1455-1458

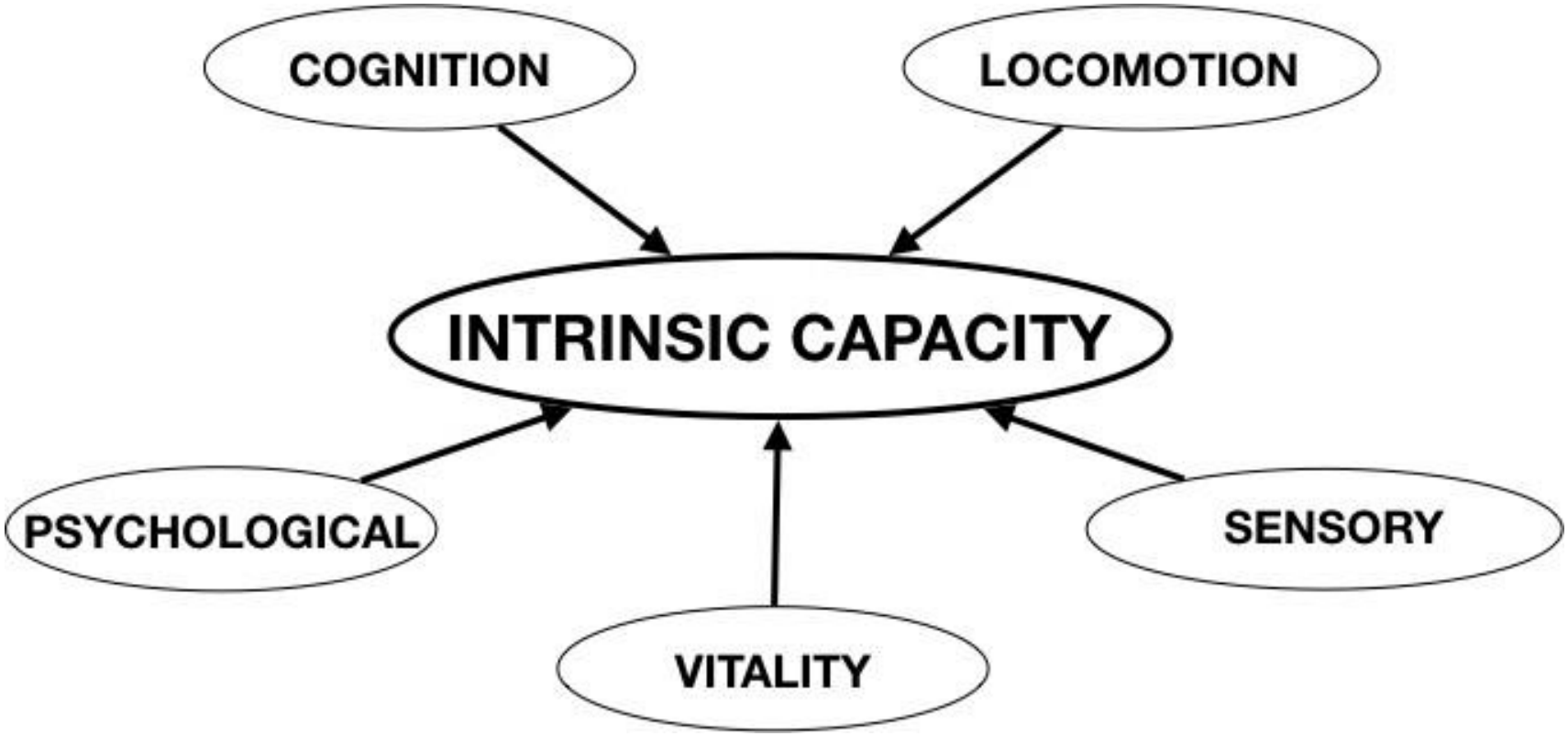
World Health Organization

World Health Organization

WORLD REPORT ON **AGEING AND HEALTH**

Fig. 2.4. **A public-health framework for *Healthy Ageing:* opportunities for public-health action across the life course**





Cesari M et al. *J Gerontol A Biol Sci Med Sci* 2018 ahead of print

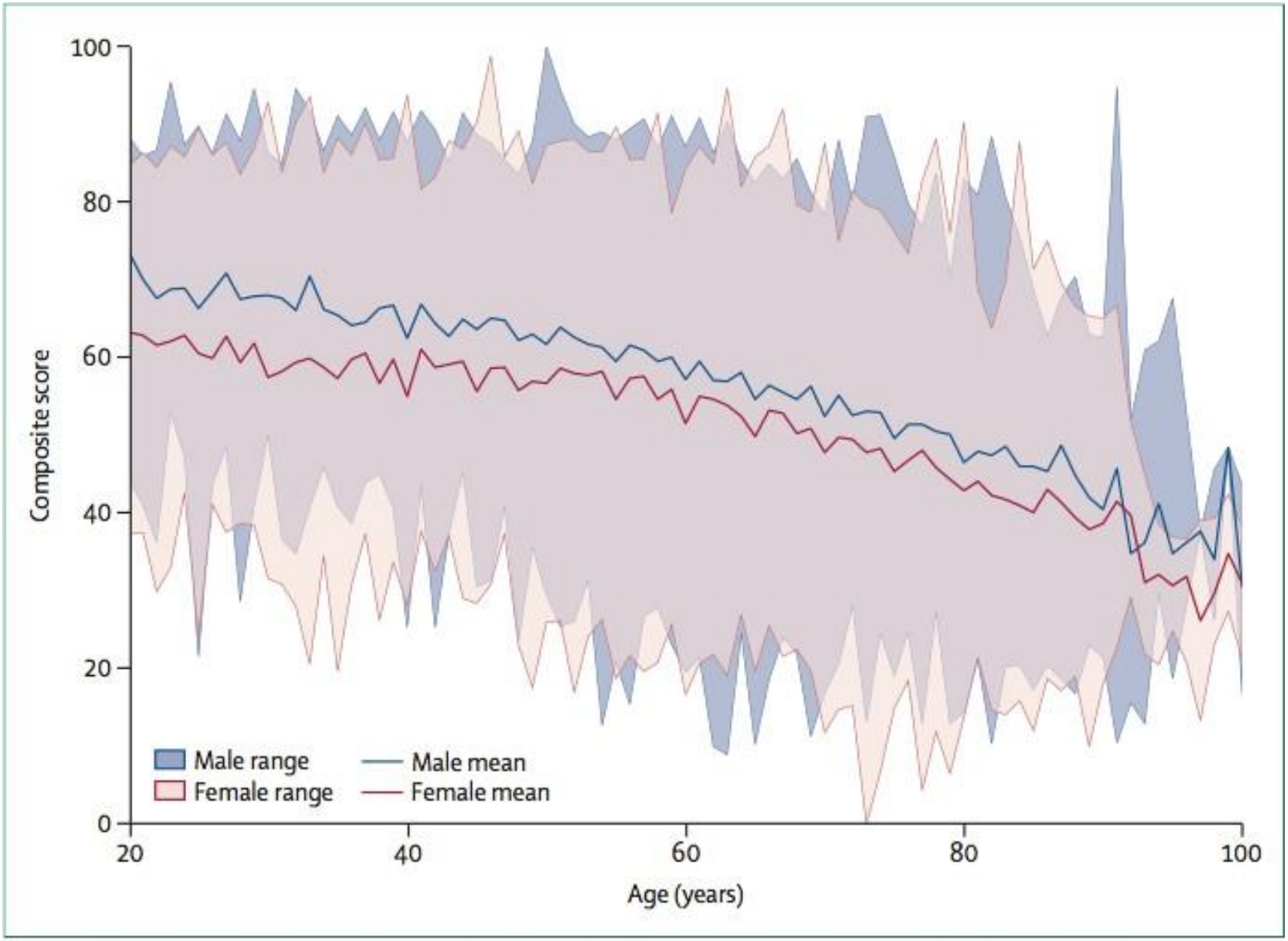


***Figure 3*: Range and mean intrinsic capacity of men and women in countries in the Study on global AGEing and adult health 2007–2010 (wave 1)[42]**

Beard JR, et al. *Lancet* 2015;387:2145-2154

Main differences between the frailty, resilience and intrinsic capacity constructs

Frailty (FI)	Resilience	Intrinsic capacity
Driven by deficits	Driven by adaptability	Driven by reserves
Negative value	Positive value	Positive value
Towards treatment	Towards prevention	Towards prevention
Clinical setting	Research	Community
Cross-sectional design	Dynamic design	Longitudinal design
Sometimes the defining criteria are not predefined	Criteria to be defined	Criteria predefined on the basis of a biological construct
Potentially including the environment	Including the environment	Excluding the environment
No normative data	No normative data	Possible nomograms

Conclusions

Frailty, biological age, and resilience are all associated with negative health outcomes

Frailty is mainly designed for clinical use with the aim of serving as target for adapted geriatric interventions (versus traditional care)

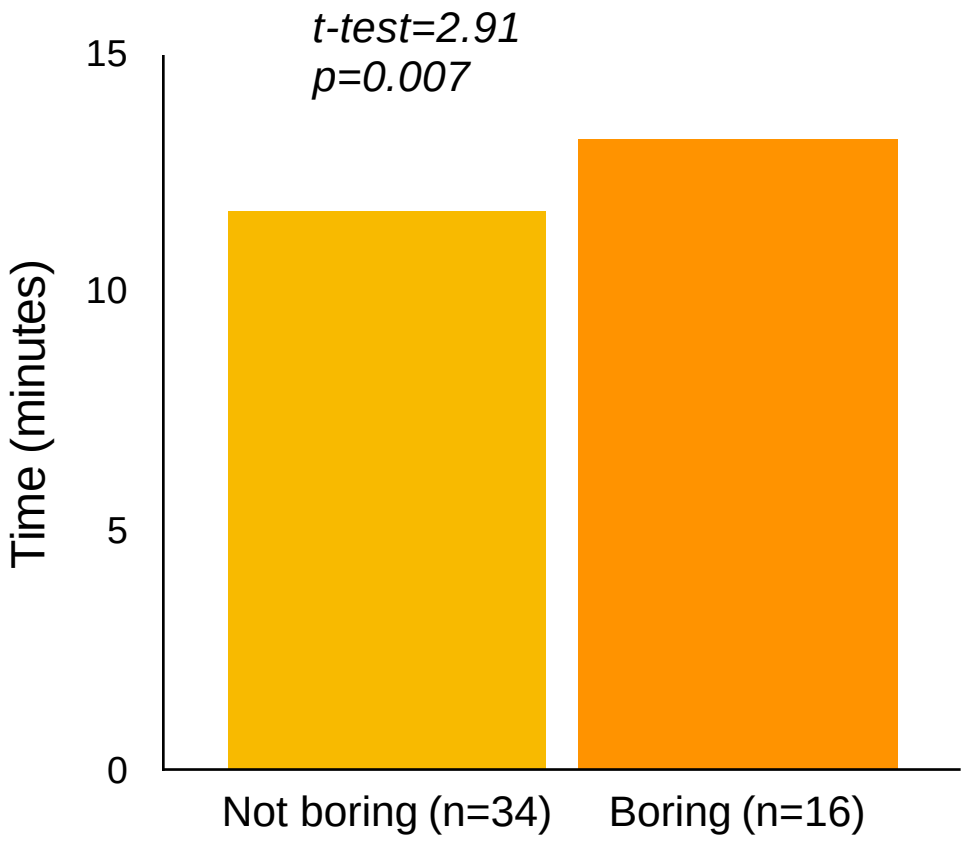
Frailty is sometimes translated with “biological age” for overcoming the obsolete paradigm of chronological age

To date, resilience is largely confined to the research level. Its purpose is to provide a dynamic measure of the individual’s capacity of adapting to stressors

Intrinsic capacity is a promising construct for promoting healthy aging through the valorization of the person’s functions and reserves

All the these construct have been developed to overcome the barriers and limitations burdening the traditional medical approach

nature
International weekly journal of science



Ewers RM. *Nature* 2018;561:464

Thank you!

Matteo Cesari
macesari@gmail.com
@macesari

Boring speakers talk for longer