Approccio multidisciplinare al pz anziano: gestione delle comorbidità, terapia di supporto e qualità di vita

Il punto di vista del geriatra

G.F Colloca

È strano avere la stessa età degli anziani

LUCIO GARDIN

La scorsa settimana sono andato a Rovereto, la città che mi ha dato i genitali.

Passeggiando per le vie a un certo punto vedo una signora anziana. Di quelle con gli occhietti vispi e il tipico sorriso rassicurante di chi ne ha viste tante nella vita. Mi sorride. Il suo volto mi sembra famigliare. Forse è la mamma di qualche mio compagno delle elementari. Mi avvicino, e per non spaventarla esordisco con un sorriso e scandisco bene le parole perché potrebbe anche essere sorda: «Buo-na-sera signora, mi scu-si, ma noi ci cono-scia-mo?». E lei, con tono leggermente sadico: «Sì deficiente, ero la to compagna de classe alle elementari». Un secondo di silenzio. Forse due. E poi un pensiero mi attraversa la mente: però è strano avere la stessa età degli anziani.

C'è una truffa in corso. È una truffa psicologica, sottile, silenziosa. Non ci sono testimoni, nessun referto, nessuna denuncia. Ma tutti noi, prima o poi, ci caschiamo. La truffa si chiama: «Mi sento ancora un ragazzo». Siamo in molti che stiamo invecchiando (beh, tutti lo fanno), ma dentro ci sentiamo ancora ragazzi. Giovani dentro ma con l'ernia di fuori.

Certe mattine mi guardo allo specchio e mi viene da chiamare mia mamma: «Mamma! C'è un vecchio in bagno che sta usando il mio spazzolino!». E invece sono io. È strano. Se mi guardo allo specchio, il cervello mi mostra un ragazzo pieno di vita. Ma il mio corpo spesso ha una sua autonomia. Si stanca prima di me. Si siede anche quando io vorrei restare in piedi. Alle volte mi dà contro.

Il punto è che siamo cresciuti in un'epoca in cui i sessantenni erano considerati vecchi, ma oggi non è più così. Oggi a sessant'anni, vai in palestra, fai trekking, ti iscrivi a un corso di rafting, assumi un fisioterapista perché ti aiuti a mettere le scarpe. Io ad esempio ho [**§ anni (scusate, la mia tastiera non arriva a certi numeri), eppure, ho ancora la testa di un trentenne.

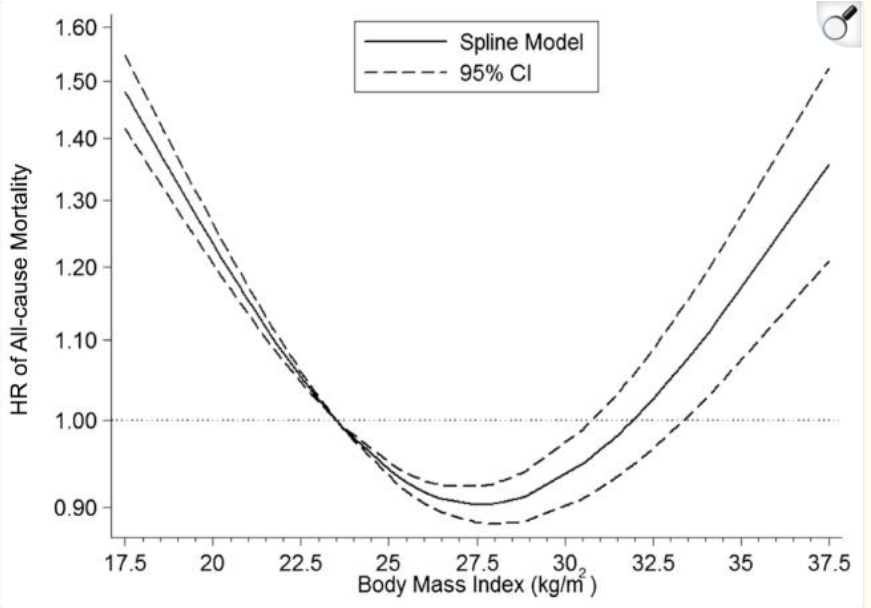
Mi emoziono per una canzone, sogno ancora di fare viaggi improbabili, guardo il mondo con l'entusiasmo di chi ha appena imparato a fare il nodo alla cravatta. E forse il segreto è questo. Il segreto non è non invecchiare (giacché l'alternativa a farlo non è nemmeno da considerare), ma invecchiare senza smettere di stupirsi. Continuare a ridere come ragazzini, anche quando il tuo corpo emette rumori che non ricordavi di avergli autorizzato. E accettare il fatto che si è giovani finché si ha la capacità di sognare e meravigliarsi. Ed è bellissimo. Almeno finché non devi alzarti da un divano basso.

www.luciogardin.it

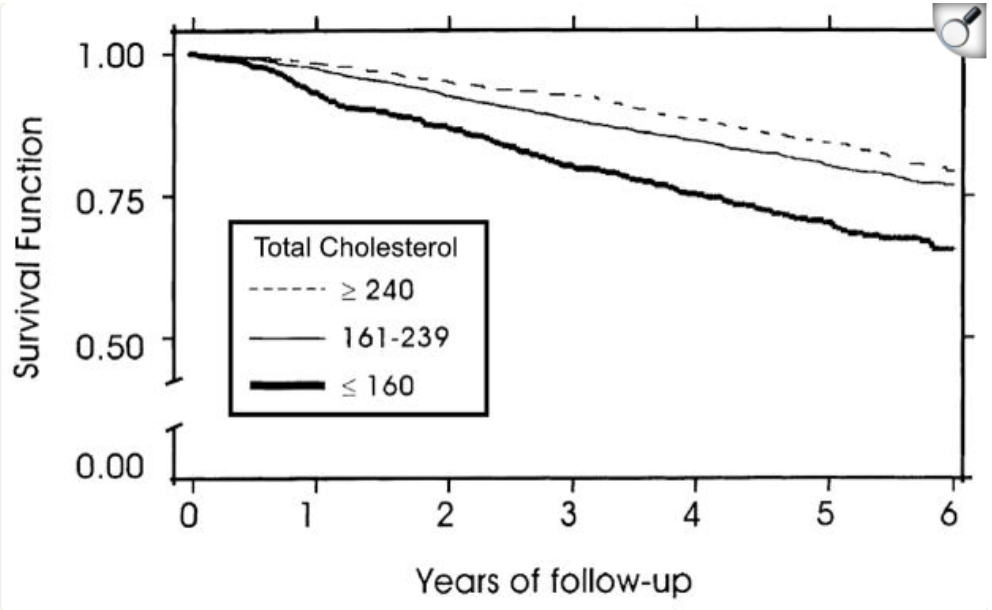
REVERSE EPIDEMIOLOGY

Risk factor paradoxes

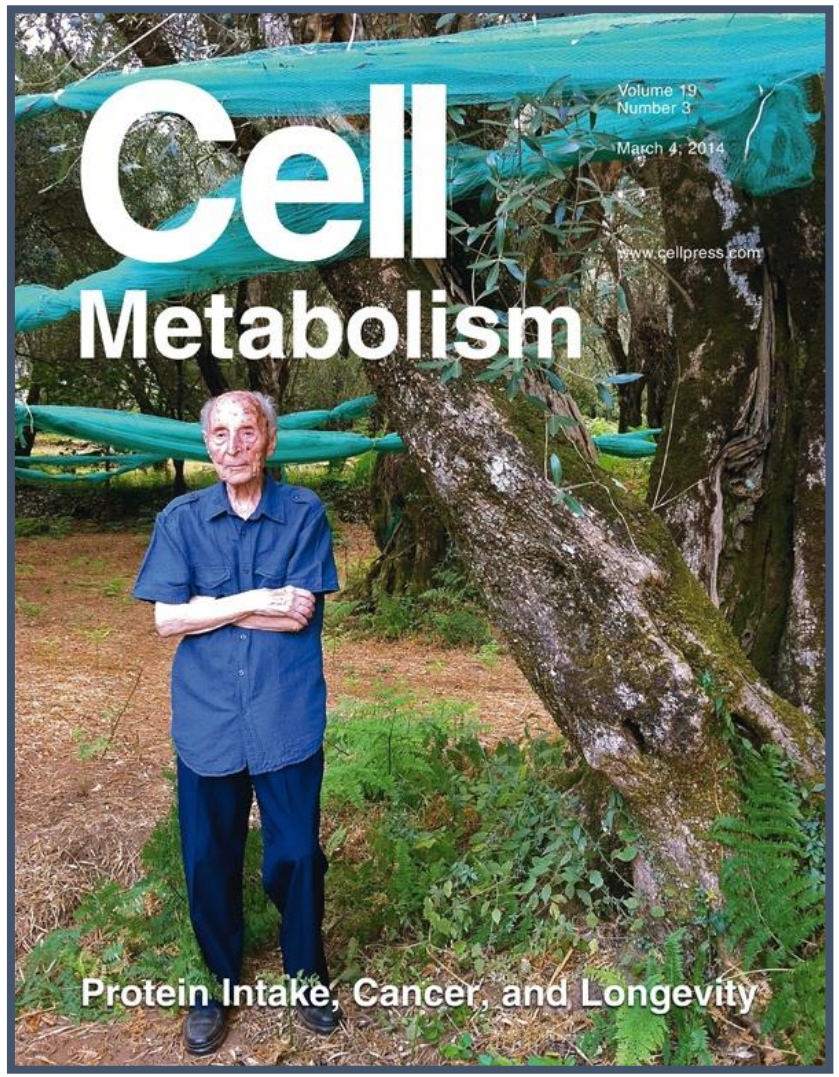
WEIGHT AND BODY COMPOSITION: IS OBESITY FAVORABLE?



SERUM CHOLESTEROLS: IS HYPERCHOLESTEROLEMIA DESIRABLE?



J Am Med Dir Assoc. 2015 Sep 9;16(11):933–939



Low Protein Intake Is Associated with a Major Reduction in IGF-1, Cancer, and Overall Mortality in the 65 and Younger but Not Older Population

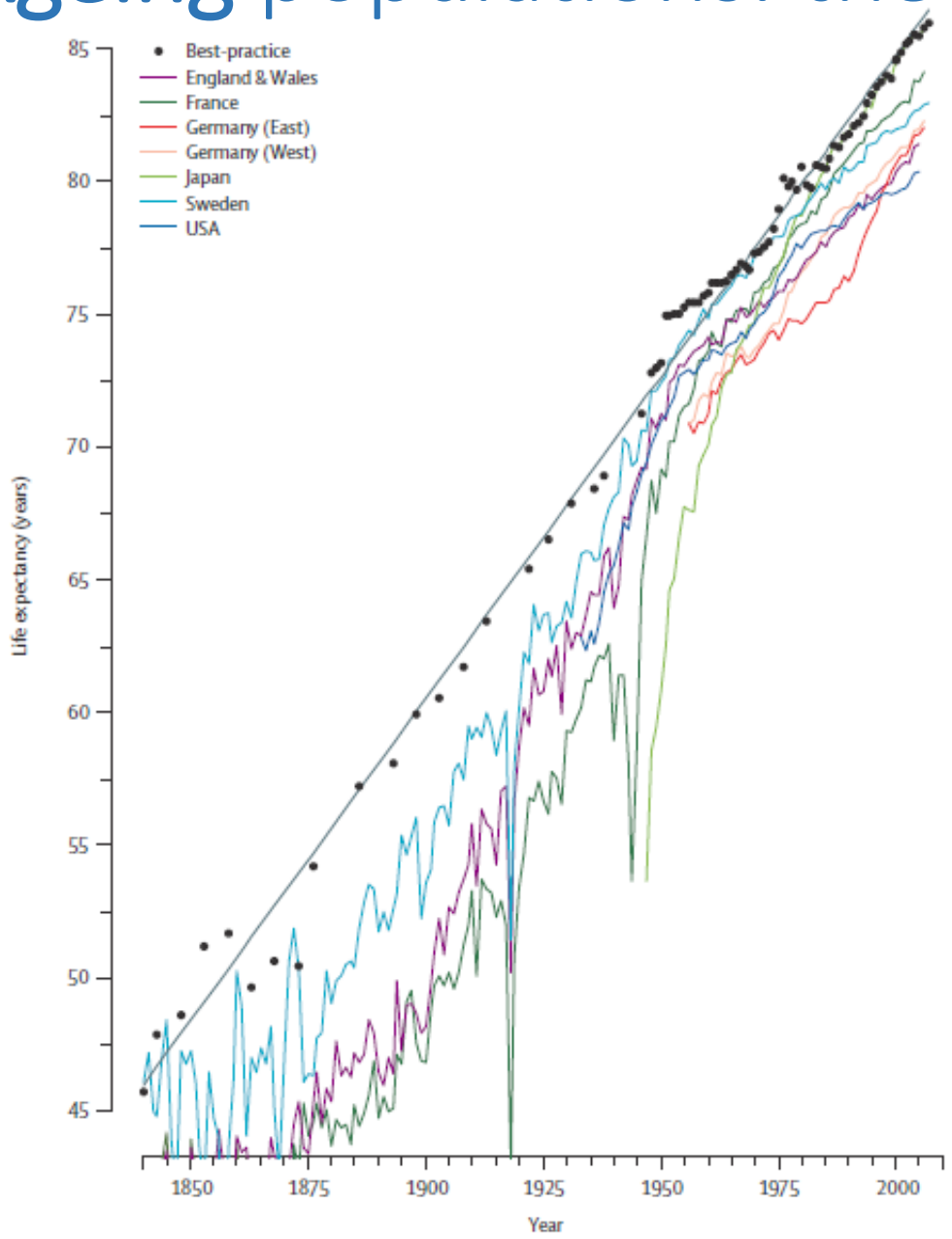
Morgan E. Levine,[1,11] Jorge A. Suarez,[1,2,11] Sebastian Brandhorst,[1,2] Priya Balasubramanian,[1,2] Chia-Wei Cheng,[1,2] Federica Madia,[1,3] Luigi Fontana,[4,5,6] Mario G. Mirisola,[1,2,7] Jaime Guevara-Aguirre,[8] Junxiang Wan,[1,2] Giuseppe Passarino,[9] Brian K. Kennedy,[10] Min Wei,[1,2] Pinchas Cohen,[1,2] Eileen M. Crimmins,[1] and Valter D. Longo[1,2,*]

Mice and humans with growth hormone receptor/IGF-1 deficiencies display major reductions in age-related diseases. Because protein restriction reduces GHR-IGF-1 activity, we examined links between protein intake and mortality. Respondents aged 50–65 reporting high protein intake had a 75% increase in overall mortality and a 4-fold increase in cancer death risk during the following 18 years. These associations were either abolished or attenuated if the proteins were plant derived. Conversely, high protein intake was associated with reduced cancer and overall mortality in respondents over 65, but a 5-fold increase in diabetes mortality across all ages. Mouse studies confirmed the effect of high protein intake and GHR-IGF-1 signaling on the incidence and progression of breast and melanoma tumors, but also the detrimental effects of a low protein diet in the very old. These results suggest that low protein intake during middle age followed by moderate to high protein consumption in old adults may optimize healthspan and longevity.

Cell Metabolism *19*, 407–417, March 4, 2014

Aging is a gradual, continuous process of natural change that begins in early adulthood. During early middle age, many bodily functions begin to gradually decline. People do not become old or elderly at any specific age.

Ageing populations: the challenges ahead



	2000	2001	2002	2003	2004	2005	2006	2007
Canada	102	102	103	103	103	104	104	104
Denmark	99	99	100	100	101	101	101	101
France	102	102	103	103	103	104	104	104
Germany	99	100	100	100	101	101	101	102
Italy	102	102	102	103	103	103	104	104
Japan	104	105	105	105	106	106	106	107
UK	100	101	101	101	102	102	103	103
USA	101	102	102	103	103	103	104	104

Data are ages in years. Baseline data were obtained from the Human Mortality Database and refer to the total population of the respective countries.

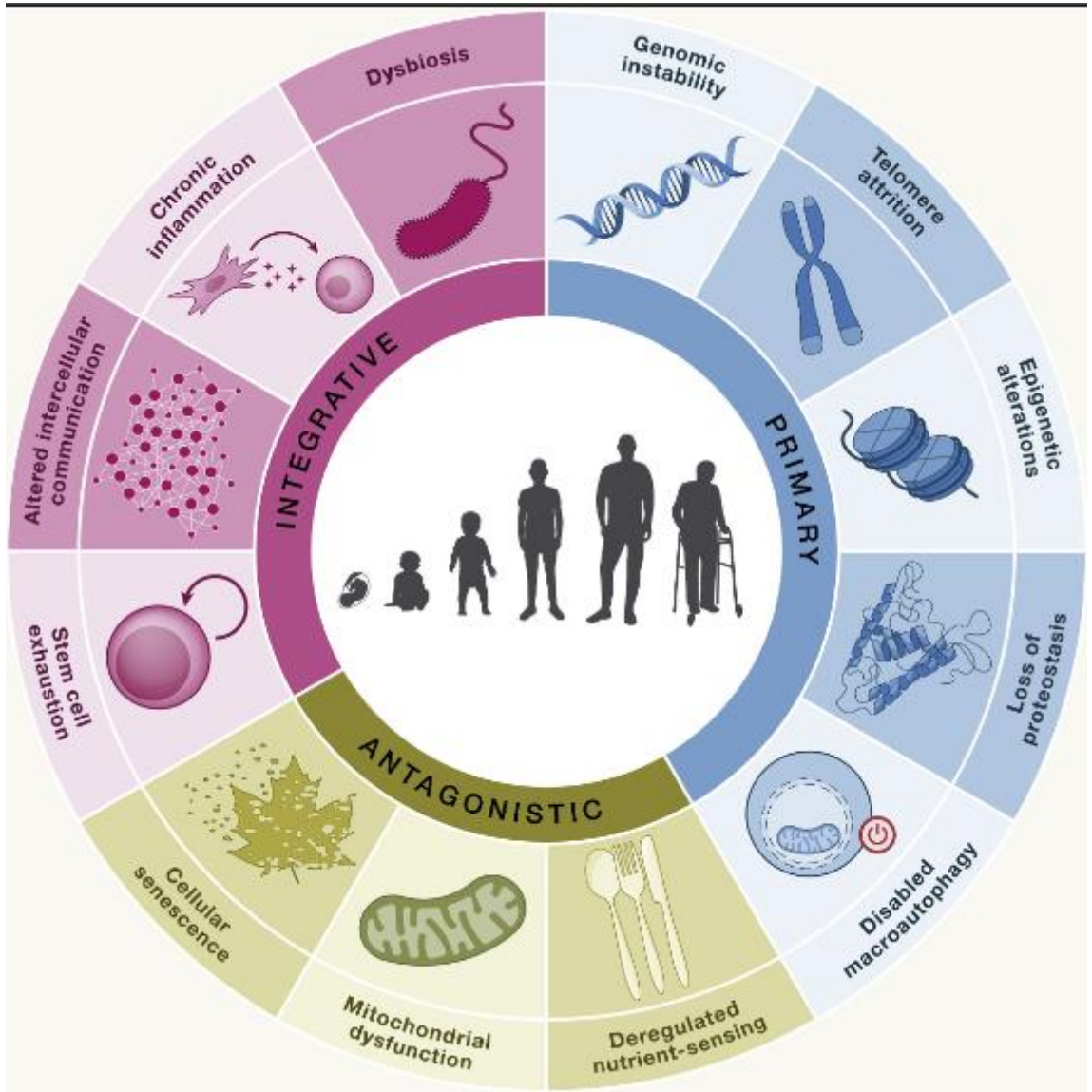
***Table 1*: Oldest age at which at least 50% of a birth cohort is still alive in eight countries**

Lancet 2009; 374: 1196-208

Table 3. **Estimated Life Expectancy, by Comorbidity Groups***

Age, *y*	Life Expectancy in Men, *y*							Life Expectancy in Women, *y*						
	Average U.S. Population†	Comorbidity						Average U.S. Population†	Comorbidity					
		None	Low/ Medium	High	Diabetes‡	COPD§	CHF‖		None	Low/ Medium	High	Diabetes‡	COPD§	CHF‖
All races														
66	15.4	18.5	15.7	9.9	14.7	12.2	7.4	18.4	22.5	18.4	12.0	16.1	15.4	8.0
70	12.8	16.3	13.5	8.9	13.1	11.0	7.0	15.4	19.3	15.7	10.8	14.7	13.3	8.0
75	9.9	12.7	11.0	7.4	10.3	8.9	5.8	12.0	15.3	12.4	8.5	11.4	10.8	7.1
80	7.4	9.8	8.2	5.8	7.4	7.0	4.8	9.0	11.6	9.4	6.6	8.5	8.0	5.8
85	5.5	7.2	5.8	4.2	5.5	5.1	3.7	6.6	8.7	7.0	5.1	6.2	6.2	4.7
90	3.9	5.1	3.9	3.0	3.7	3.7	3.0	4.7	5.7	4.7	3.5	4.4	4.4	3.5
White persons														
66	15.5	18.6	16.1	9.9	14.8	12.2	7.9	18.5	22.6	18.5	12.0	16.2	14.7	8.5
70	12.9	16.3	13.9	8.9	13.2	11.0	7.0	15.5	19.4	15.8	10.8	14.0	12.7	8.0
75	9.9	12.8	10.7	7.4	10.3	8.9	5.8	12.0	15.3	12.4	8.5	11.4	10.2	7.0
80	7.4	9.9	8.2	5.4	7.4	6.6	4.8	9.0	11.7	9.0	6.6	8.5	8.0	5.8
85	5.4	7.2	5.8	4.2	5.4	4.8	3.6	6.6	8.2	6.6	5.0	6.2	6.2	4.7
90	3.9	5.0	3.9	3.0	3.6	3.6	3.0	4.7	5.7	4.7	3.8	4.3	4.3	3.5
Black persons														
66	13.5	16.3	14.2	9.1	13.5	11.9	7.1	17.0	21.3	17.8	10.9	17.0	17.0	8.1
70	11.4	14.7	12.4	7.9	11.4	9.5	6.4	14.4	18.7	15.3	9.9	14.7	13.8	8.1
75	9.1	11.9	10.0	6.4	9.4	7.9	5.2	11.5	15.3	12.5	8.5	11.5	11.8	7.2
80	7.1	9.8	8.0	5.2	7.7	6.8	4.5	9.0	12.1	10.0	6.9	9.3	9.0	6.1
85	5.5	7.3	6.3	4.5	5.5	5.2	3.8	6.9	9.0	7.5	5.5	6.5	6.9	5.2
90	4.2	5.7	4.7	3.6	4.5	3.1	3.4	5.2	6.7	5.7	4.1	5.2	5.2	4.1

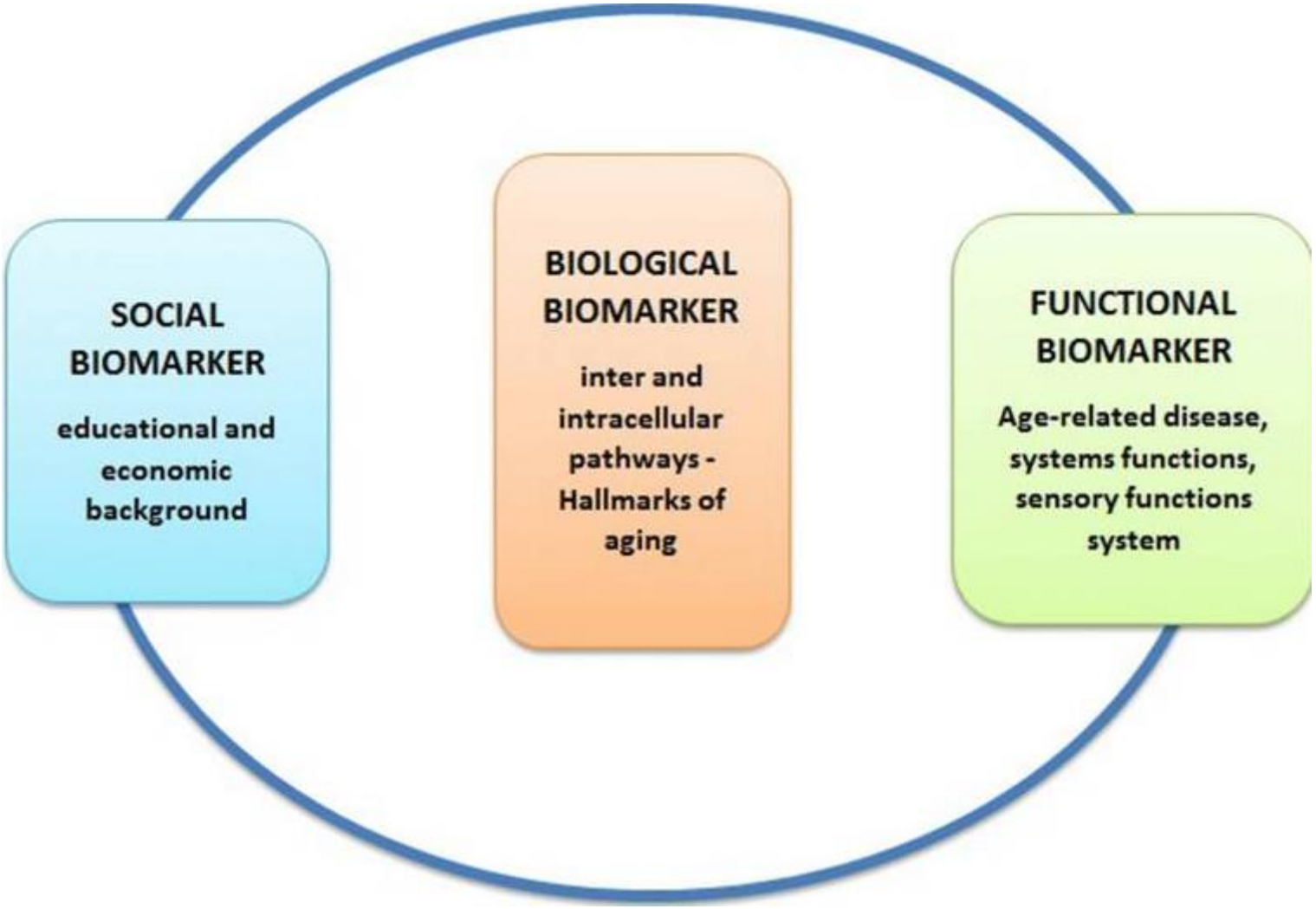
CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease.
* Rounded to the nearest tenth.
† From the 2000 U.S. decennial life table at the chronological age.
‡ Includes diabetes only or diabetes with other conditions except COPD and CHF.
§ Includes COPD only or COPD with other conditions except CHF.
‖ Includes CHF only or CHF with other conditions.



Genomic instability
Telomere attrition
epigenetic alterations
loss of proteostasis
Disabled macroautophagy
deregulated nutrient-sensing
mitochondrial dysfunction
cellular senescence
stem cell exhaustion
altered intercellular communication
chronic inflammation
dysbiosis.

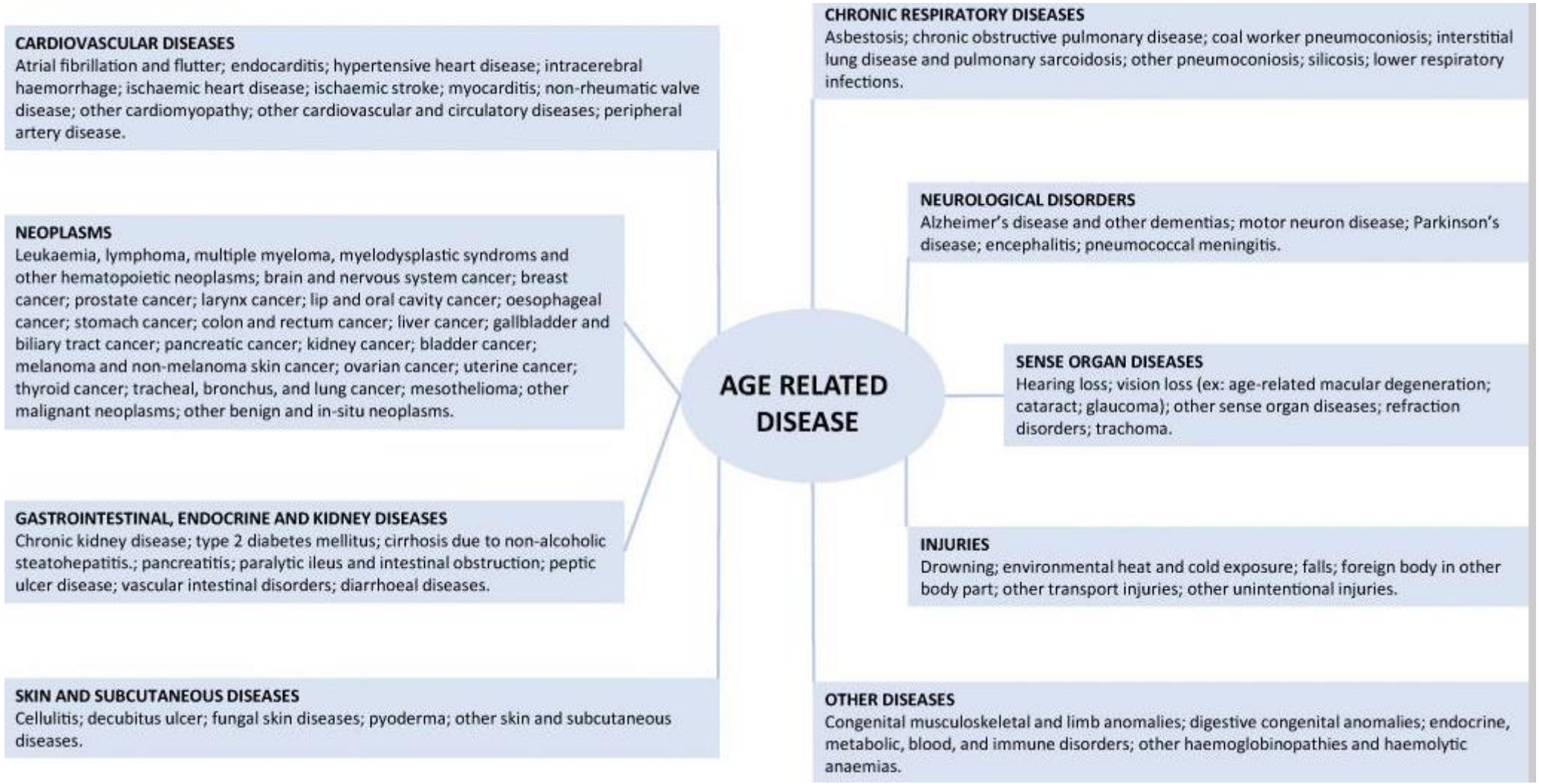
These hallmarks are interconnected among each other

Mechanisms connecting different clusters of biomarkers



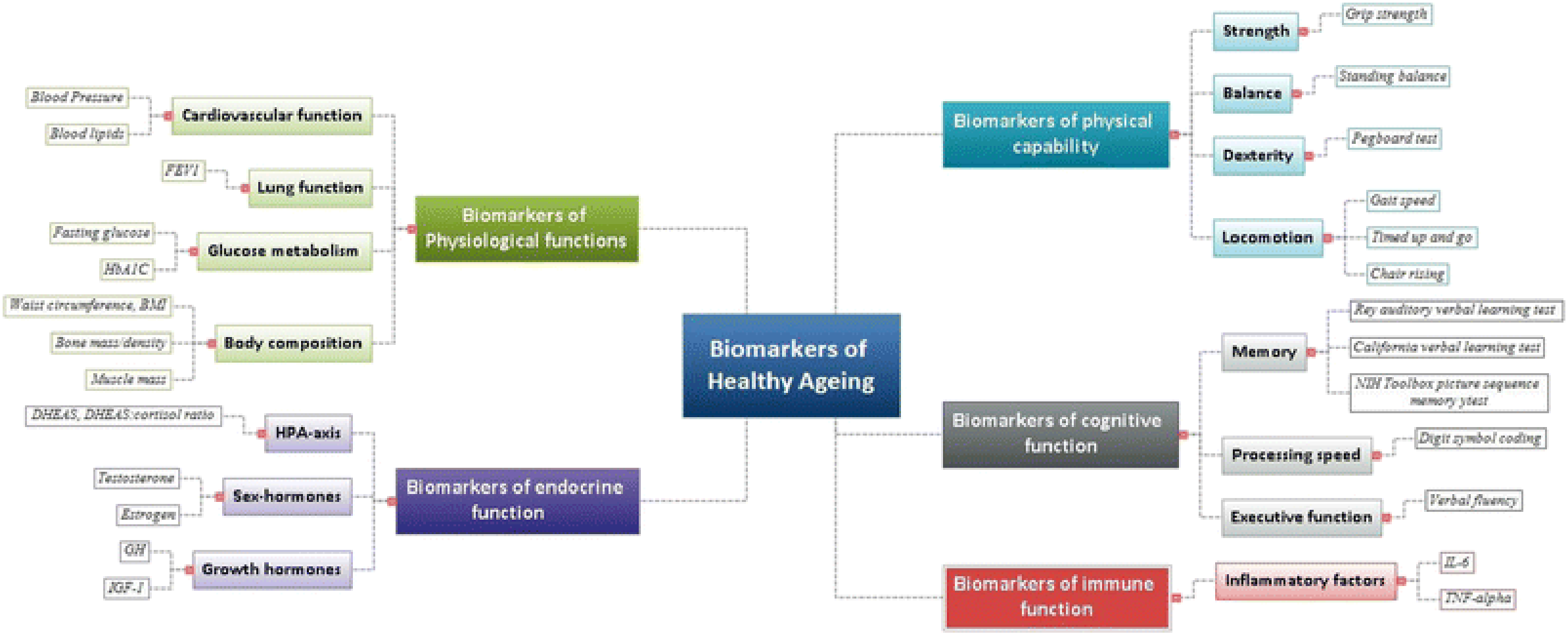
Colloca G. Curr Oncol Rep. 2020; 22(11): 115.

Age-related diseases



Colloca G. Curr Oncol Rep. 2020; 22(11): 115.

Panel of biomarkers of Healthy Ageing



Lara et al. BMC Medicine (2015) 13:222

Biomarkers of ageing

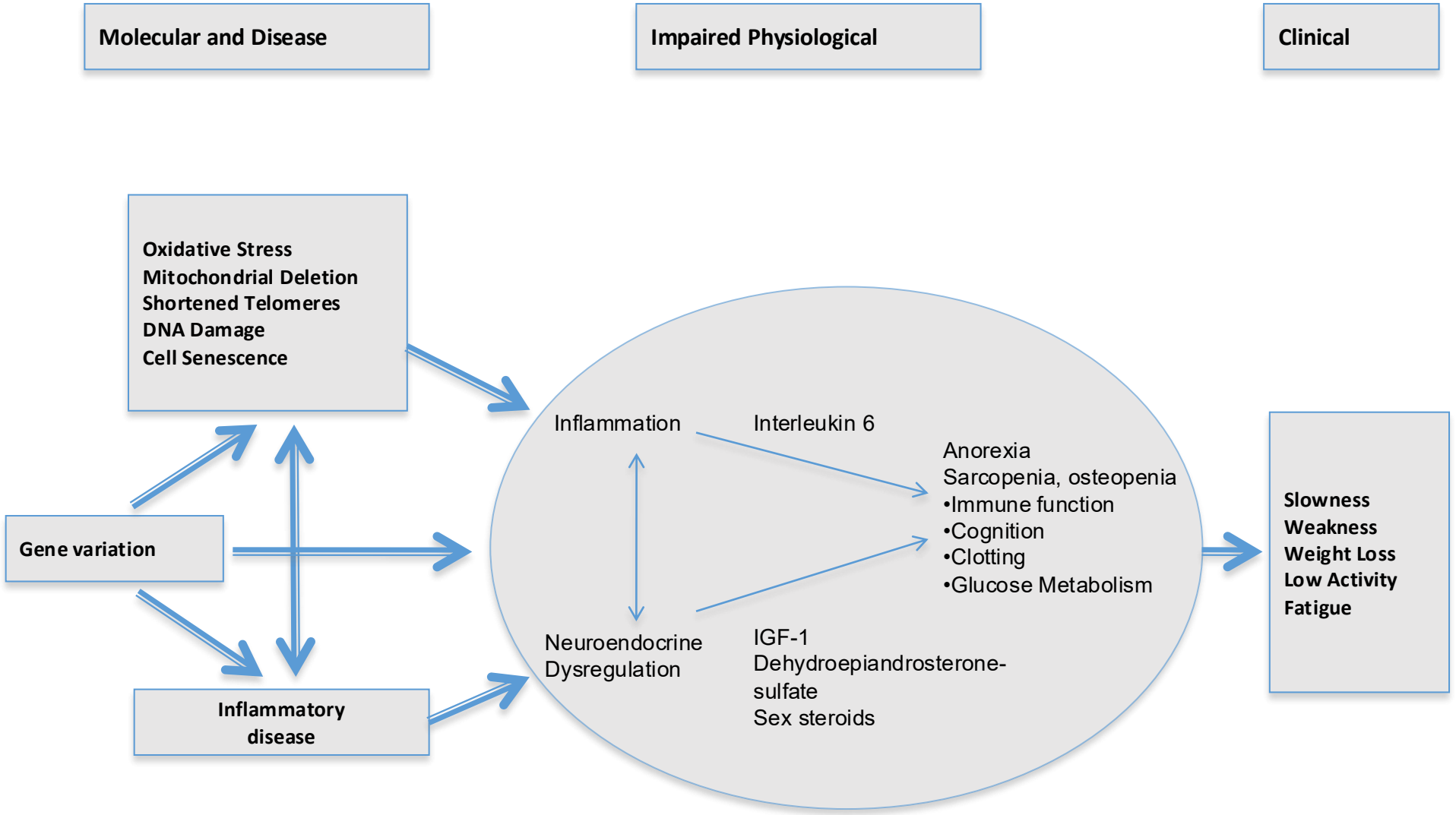
vs

Biomarkers of Healthy Ageing

Understanding the Dynamics of the Aging Process

changes in:
dynamic biological,
physiological,
environmental,
psychological,
behavioral,
and social processes

The National Institute on Aging: Strategic Directions for Research, 2020-2025



Walston J, Ferrucci L,Fried L, J Am Geriatr Soc. 2006 Jun;54(6):991-1001

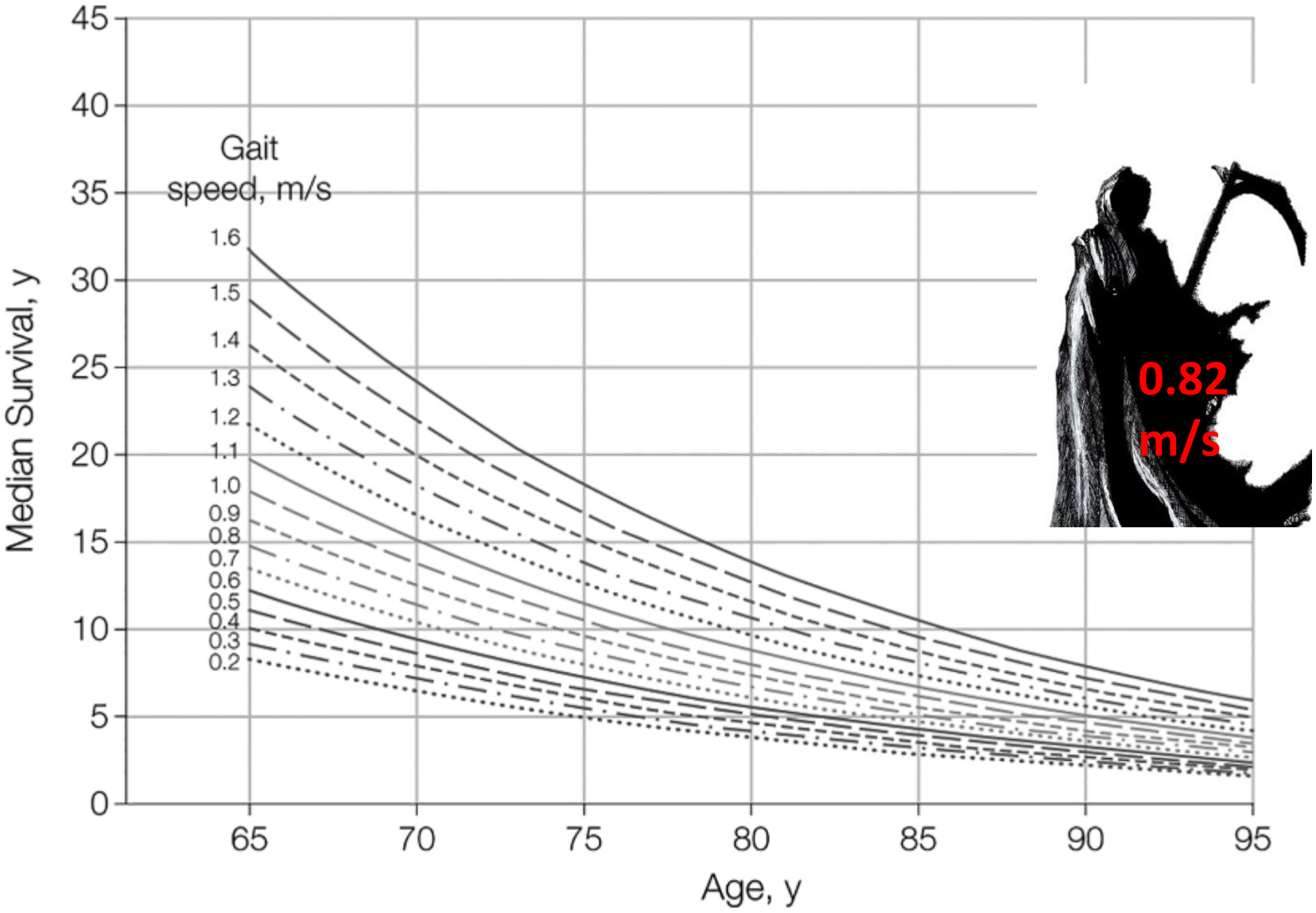
“Frailty Phenotype”

- Weight loss
- Slow walking speed
- Low levels of physical activity
- Subjective exhaustion
- Weakness (Low grip strength)

- 3-5 is “frail”
- 1-2 is “intermediate”
- 0 is “not frail”

Fried LP, Tangen, Walston et al. J Ger Med Sci 2001

Predicted Median Life Expectancy by Age and Gait Speed



Studenski S, et al. JAMA 2011 305(1)50

A global clinical measure of fitness and frailty in older people

Box 1: The CSHA Clinical Frailty Scale

1 *Very fit* — robust, active, energetic, well motivated and fit; these people commonly exercise regularly and are in the most fit group for their age

2 *Well* — without active disease, but less fit than people in category 1

3 *Well, with treated comorbid disease* — disease symptoms are well controlled compared with those in category 4

4 *Apparently vulnerable* — although not frankly dependent, these people commonly complain of being "slowed up" or have disease symptoms

5 *Mildly frail* — with limited dependence on others for instrumental activities of daily living

6 *Moderately frail* — help is needed with both instrumental and non-instrumental activities of daily living

7 *Severely frail* — completely dependent on others for the activities of daily living, or terminally ill

Note: CSHA = Canadian Study of Health and Aging.

Box 2: Tools for measuring degree of frailty that were compared with the CSHA Clinical Frailty Scale*

- Modified Mini-Mental State Examination[22] (3MS), in which a score† of 77 or less indicates cognitive impairment
- Cumulative Illness Rating Scale,[23] a comorbidity measure that has been validated with autopsies
- A history† of falls, delirium, cognitive impairment or dementia (as per DSM-III-R criteria for the diagnosis of dementia)[24]
- CSHA rules-based definition of frailty,[12] which categorizes subjects as 0 (having no cognitive or functional impairment), 1 (isolated urinary incontinence), 2 (dependent in 1 ADL or having a diagnosis of CIND) or 3 (dependent in at least 2 ADLs, having mobility impairment or having a diagnosis of dementia)
- CSHA Frailty Index, a count of 70 deficits (listed in Appendix 1), including the presence and severity of current diseases, ability in ADLs and physical signs from clinical and neurologic exams. (A person with 7 deficits, for example, would have an index score of 7/70 = 0.10. The relative frailty or fitness of a patient can be calculated as a percentage difference from the average score for people of that age.) To indicate severity, each deficit not restricted by its nature to two values (i.e., 0 or 1 for absence or presence, respectively) was assigned three (0, 0.5 or 1) or four values (0, 0.33, 0.67 or 1.0), as appropriate
- CSHA Function Scale (based on the extensively validated Older American Resources Survey), which scores the patient on each of 12 ADLs (some instrumental) as 0 (the patient is independent in carrying out this ADL), 1 (needs assistance) or 2 (is incapable)

Note: CSHA = Canadian Study of Health and Aging, 3MS = Modified Mini-Mental State Examination, ADL = activity of daily living, CIND = cognitive impairment, no dementia.
*Except for the 3MS, a higher score on these tests represents greater morbidity.
†The clinicians assessing study participants on the CHSA Clinical Frailty Scale were aware of these factors in the medical history but blinded to scores from all the other indexes listed, except for results from the 3MS (as indicated).

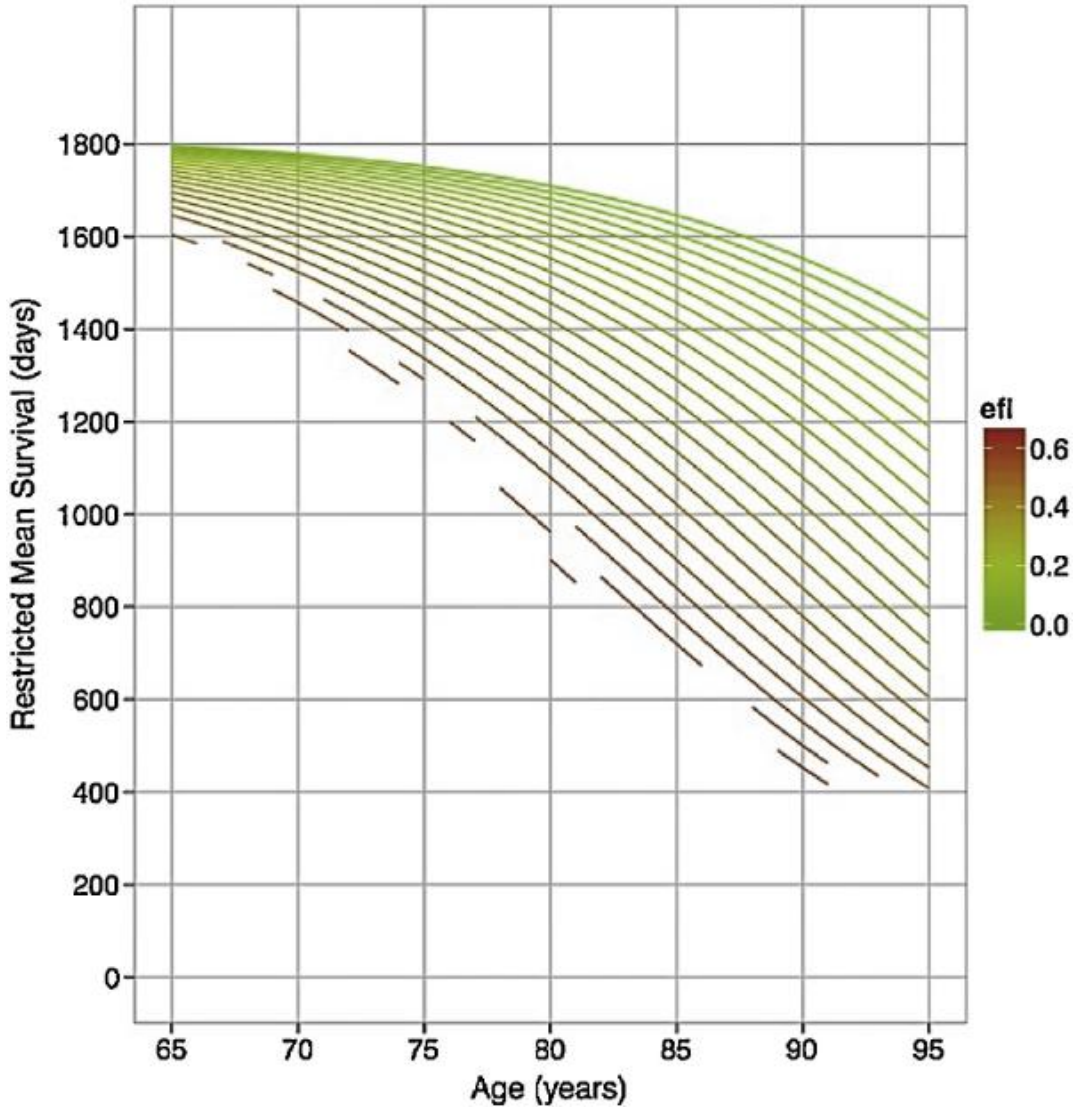
Rockwood K, Song X, Mitnitski A. *CMAJ. 2005 Aug 30;173(5):489-95*

A global clinical measure of fitness and frailty in older people

Appendix 1: List of variables used by the Canadian Study of Health and Aging to construct the 70-item CSHA Frailty Index

- Changes in everyday activities
- Head and neck problems
- Poor muscle tone in neck
- Bradykinesia, facial
- Problems getting dressed
- Problems with bathing
- Problems carrying out personal grooming
- Urinary incontinence
- Toileting problems
- Bulk difficulties
- Rectal problems
- Gastrointestinal problems
- Problems cooking
- Sucking problems
- Problems going out alone
- Impaired mobility
- Musculoskeletal problems
- Bradykinesia of the limbs
- Poor muscle tone in limbs
- Poor limb coordination
- Poor coordination, trunk
- Poor standing posture
- Irregular gait pattern
- Falls
- Mood problems
- Feeling sad, blue, depressed
- History of depressed mood
- Tiredness all the time
- Depression (clinical impression)
- Sleep changes
- Restlessness
- Memory changes
- Short-term memory impairment
- Long-term memory impairment
- Changes in general mental functioning
- Onset of cognitive symptoms
- Clouding or delirium
- Paranoid features
- History relevant to cognitive impairment or loss
- Family history relevant to cognitive impairment or loss
- Impaired vibration
- Tremor at rest
- Postural tremor
- Intention tremor
- History of Parkinson's disease
- Family history of degenerative disease
- Seizures, partial complex
- Seizures, generalized
- Syncope or blackouts
- Headache
- Cerebrovascular problems
- History of stroke
- History of diabetes mellitus
- Arterial hypertension
- Peripheral pulses
- Cardiac problems
- Myocardial infarction
- Arrhythmia
- Congestive heart failure
- Lung problems
- Respiratory problems
- History of thyroid disease
- Thyroid problems
- Skin problems
- Malignant disease
- Breast problems
- Abdominal problems
- Presence of snout reflex
- Presence of the palmomental reflex
- Other medical history

Age-related deficit accumulation and the diseases of ageing



$$FrailtyIndexscore = \frac{Numberofdeficitsinanindividual}{Totalnumberofdeficitsmeasured}$$

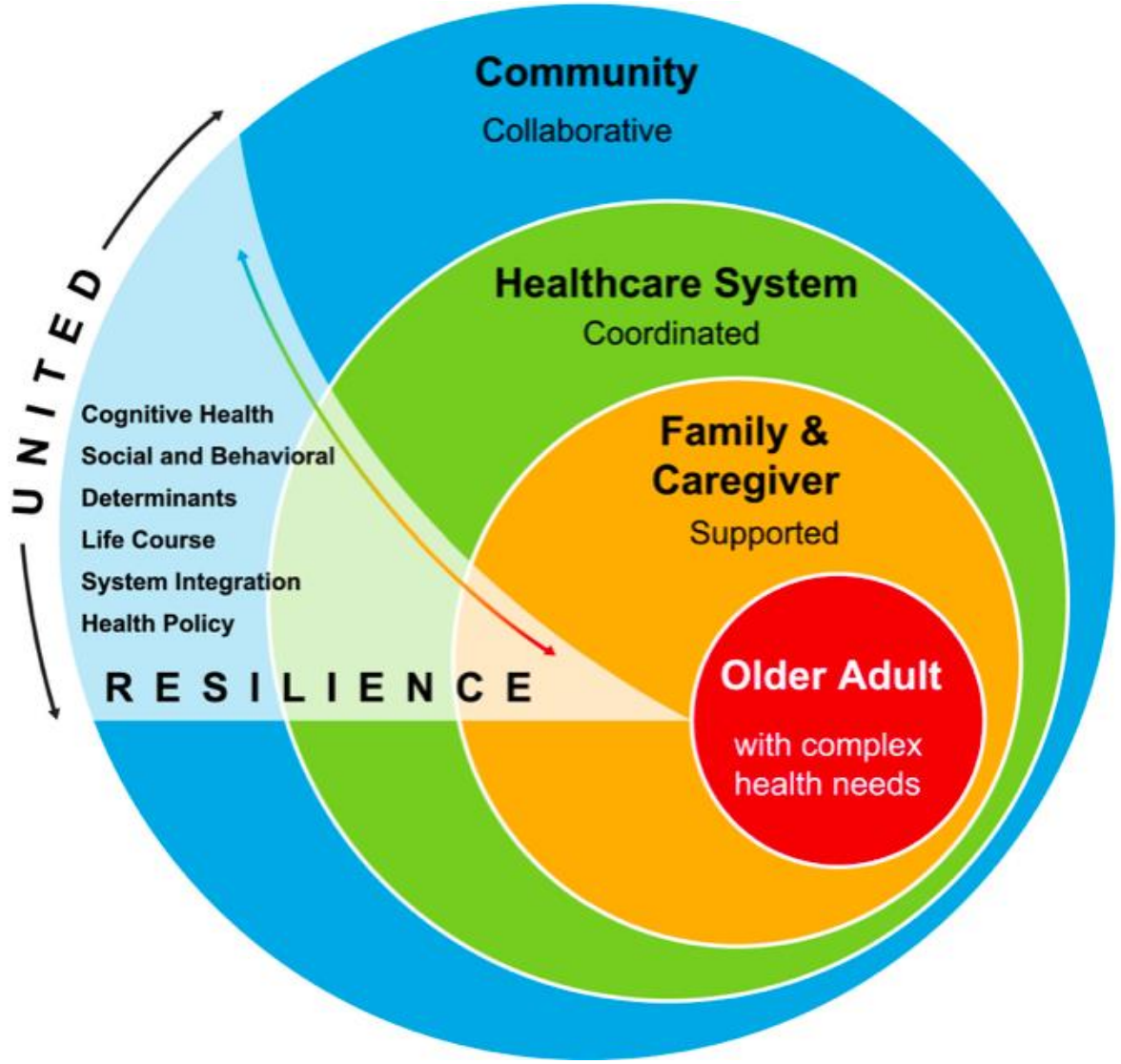
K. Rockwood and S.E. Howlett Mechanisms of Ageing and Development 180 (2019) 107–116108

Frail/complex patient

- Multimorbidity
- Multiple drugs
- Function deficits
  - Cognitive deficit
  - Physical deficit
- Financial toxicity
- Affective problems
- Social problems
- Incontinence
- Malnutrition
- Anemia
- Falls
- Sarcopenia
- Osteoporosis

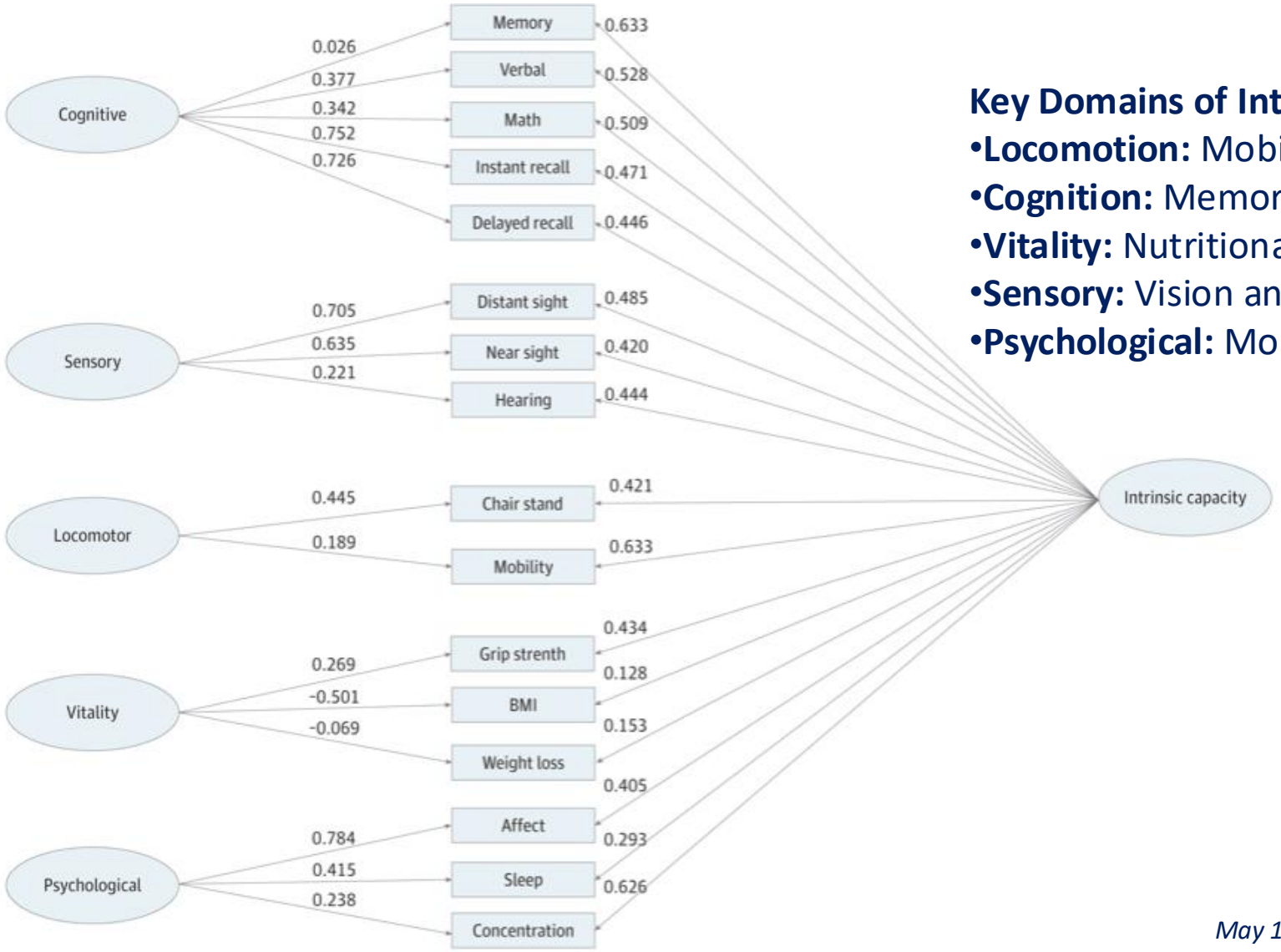
Geriatric Syndromes

Reimagining Resilience in Aging



The American Journal of Geriatric Psychiatry, Volume 33, Issue 9, 1005 - 1017

Intrinsic Capacity Across 15 Countries in the Survey of Health, Aging, and Retirement in Europe



Key Domains of Intrinsic Capacity (WHO Framework)

- **Locomotion:** Mobility, gait speed, and balance.
- **Cognition:** Memory, attention, and executive function.
- **Vitality:** Nutritional status, metabolic health.
- **Sensory:** Vision and hearing capabilities.
- **Psychological:** Mood, mental health, and resilience.

May 12, 2025. doi:10.1001/jamanetworkopen

Defining Intrinsic Capacity: The WHO-ICOPE Model

"The composite of all the physical and mental capacities that an individual can draw upon at any point in time."

— WHO World Report on Ageing and Health, 2015; Cesari et al., J Gerontol A, 2018

COGNITION

Memory, executive function, attention

LOCOMOTION

Gait speed, grip strength, SPPB

VITALITY

Nutrition, energy metabolism, muscle mass

PSYCHOLOGICAL

Mood, depression screening (PHQ-9)

SENSORY

Vision & hearing – functional independence

WHO ICOPE Handbook 2019 • Cesari M et al. J Gerontol A 2018;73:1653–1660 • PMC8947834

KEY CONCEPTUAL DISTINCTION

Intrinsic Capacity vs. Frailty: Two Distinct but Related Constructs

Belloni G & Cesari M, Front Med 2019;6:133 (PMID 31275941)

Intrinsic Capacity	Frailty
Positive, function-centred	Deficit-centred, risk-focused
Community-wide, population level	Clinical, individual risk
Longitudinal trajectories	Cross-sectional state
Potential & reserves	Vulnerability & stressors
5 modifiable domains	Phenotype or deficit accumulation
Entry point for prehabilitation	Entry point for care planning

Advanced frailty may represent a condition of profound IC reduction — the two are complementary along a continuum of ageing.

The ICOPE Screening Tool: Implementation & Validation

ICOPE Step 1 — Screening (community / primary care)

COGNITION	3-word recall + clock drawing	**PSYCHOLOGY**	PHQ-2 → PHQ-9
MOBILITY	SPPB / Gait speed (<0.8 m/s)	**VISION**	Self-reported visual impairment
VITALITY	MNA-SF / unintentional weight loss	**HEARING**	Whisper test / audiometry referral

ICOPE Step 2 — In-depth CGA (geriatric specialist)

- Sensitivity (INSPIRE-T cohort, n=603): 42–97% per domain
- High specificity (>70%) for most domains
- Vision: very high sensitivity (97.2%) but low specificity (2.7%) → reflex referral recommended

Virecoulon Giudici K et al. J Gerontol A 2024;79(7):glae112 (PMID 38676323) • WHO ICOPE Handbook 2019

Intrinsic Capacity in the Cancer Patient: Conceptual Interaction

IC ↔ Frailty relationship
Frailty is considered a cross-sectional snapshot of IC. The two are distinct but complementary — both needed for complete geriatric assessment. Advanced frailty may represent profound IC reduction (Belloni & Cesari, 2019).

Cancer as an IC accelerant
Cancer and antineoplastic treatments directly impair IC domains via inflammation, sarcopenia, neuropathy, and chemobrain — creating a vicious cycle (Hamaker et al., JGO 2023).

Belloni G, Cesari M. Front Med 2019;6:133 • Hamaker M et al. J Geriatr Oncol 2023;14(2):101421 (PMID 36657249)

IC Assessment to Guide Treatment Decision-Making

How IC informs oncological decisions

🟢 Fit (high IC): standard-dose chemotherapy / aggressive treatment intent

🟡 Vulnerable (intermediate IC): dose reduction, prehabilitation, close monitoring

🔴 Frail (low IC): goals-of-care discussion, best supportive care, palliative intent

Guidelines & Evidence Base

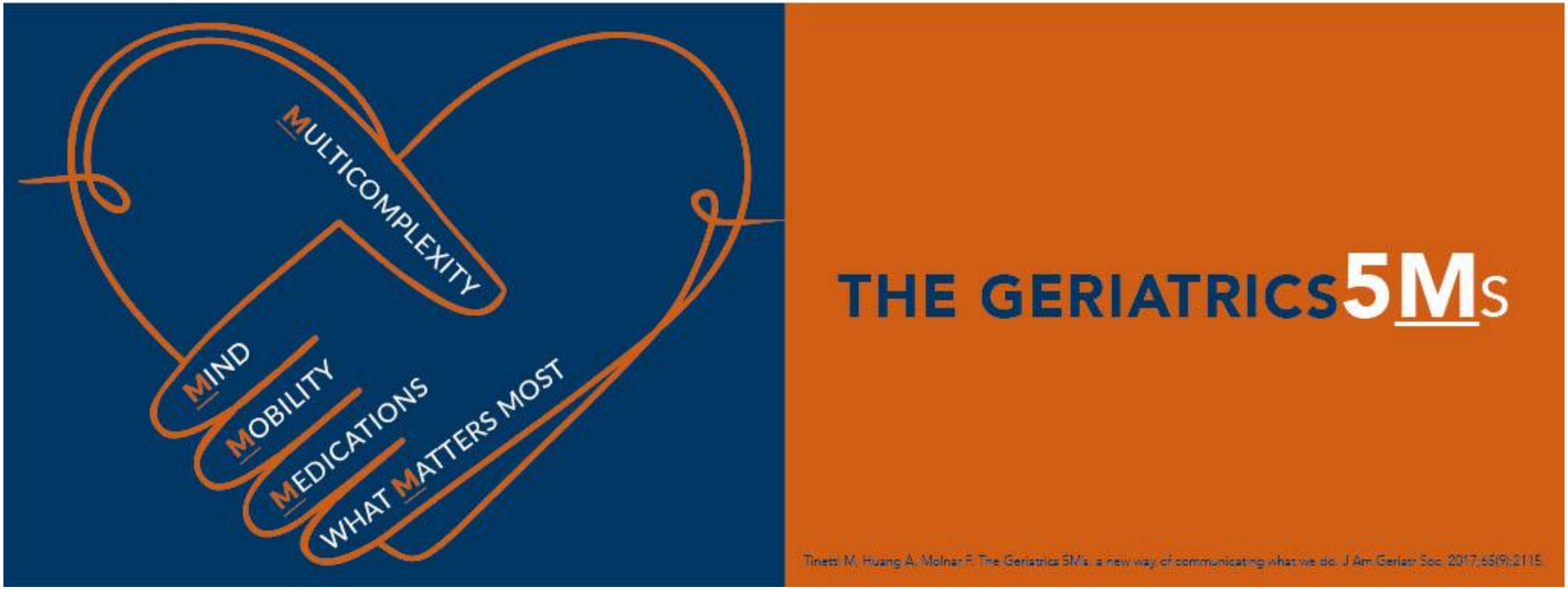
ASCO 2023 GA Guideline
GA recommended for all patients ≥65 receiving systemic therapy. Intervention reduces chemotherapy toxicity, improves QoL.

SIOG Recommendations
G8 as first-line screen → GA for abnormal scores → IC-informed treatment plan.

JNCI Meta-analysis 2025 (n=58 studies)
Frailty/IC assessments predict: survival, toxicity, treatment tolerance, functional decline, and hospitalisation in systemic cancer therapy.

Pearce J et al. JNCI 2025;117(7):1316 • ASCO GA Guideline JCO 2018/2023 • Williams GR et al. JCO Oncol Pract 2023;19(9):718

Key point


MULTICOMPLEXITY
MIND
MOBILITY
MEDICATIONS
WHAT MATTERS MOST
THE GERIATRICS 5Ms
Tinetti M, Huang A, Molnar F. The Geriatrics 5Ms: a new way of communicating what we do. J Am Geriatr Soc. 2017;65(9):2115