Multimorbilità e Fragilità nell'Anziano

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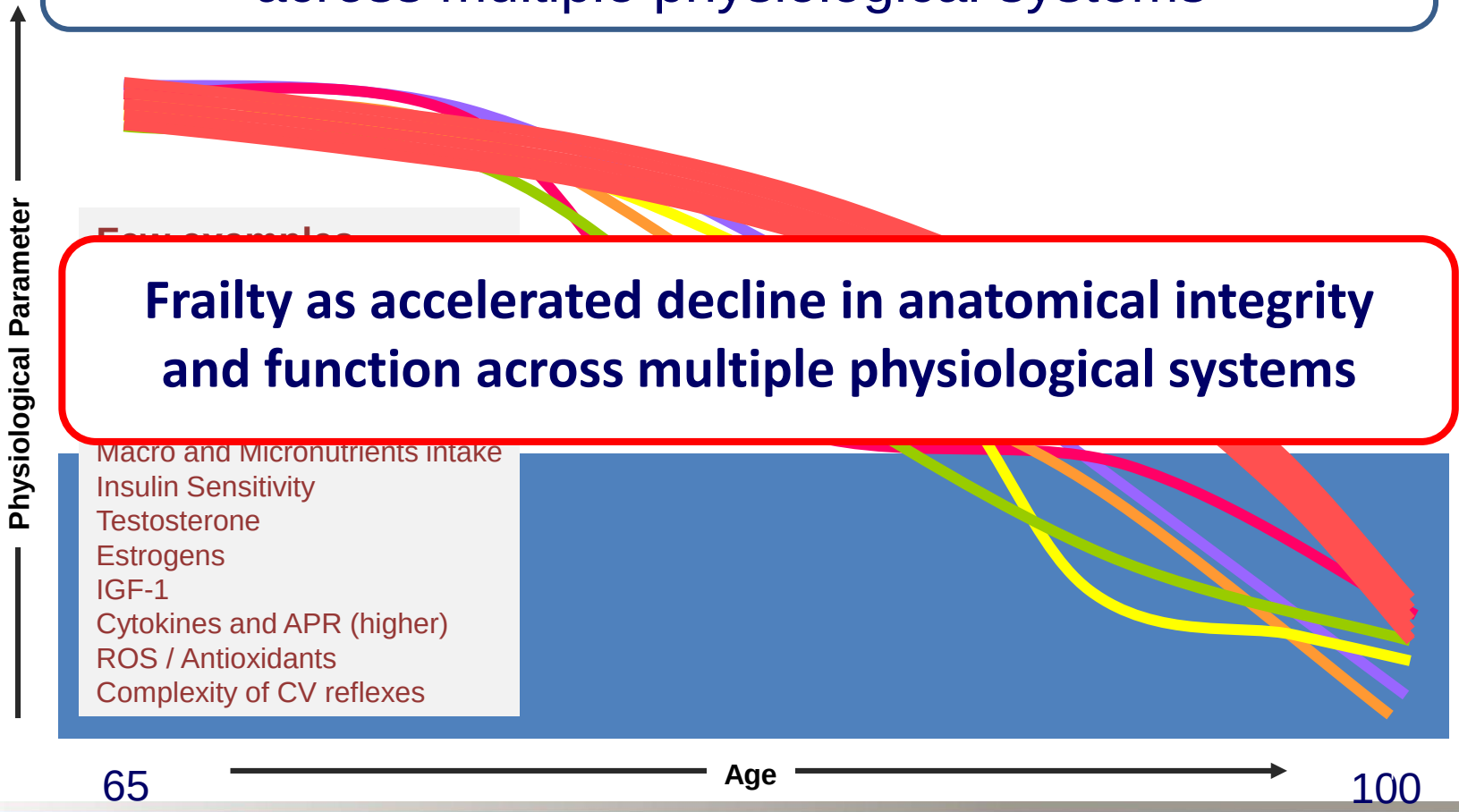
Università di Ferrara
- ex labore fructus -

Aging, homeostatic mechanisms, and function

Progressive decline in anatomical integrity and function across multiple physiological systems



Frailty as accelerated decline in anatomical integrity and function across multiple physiological systems

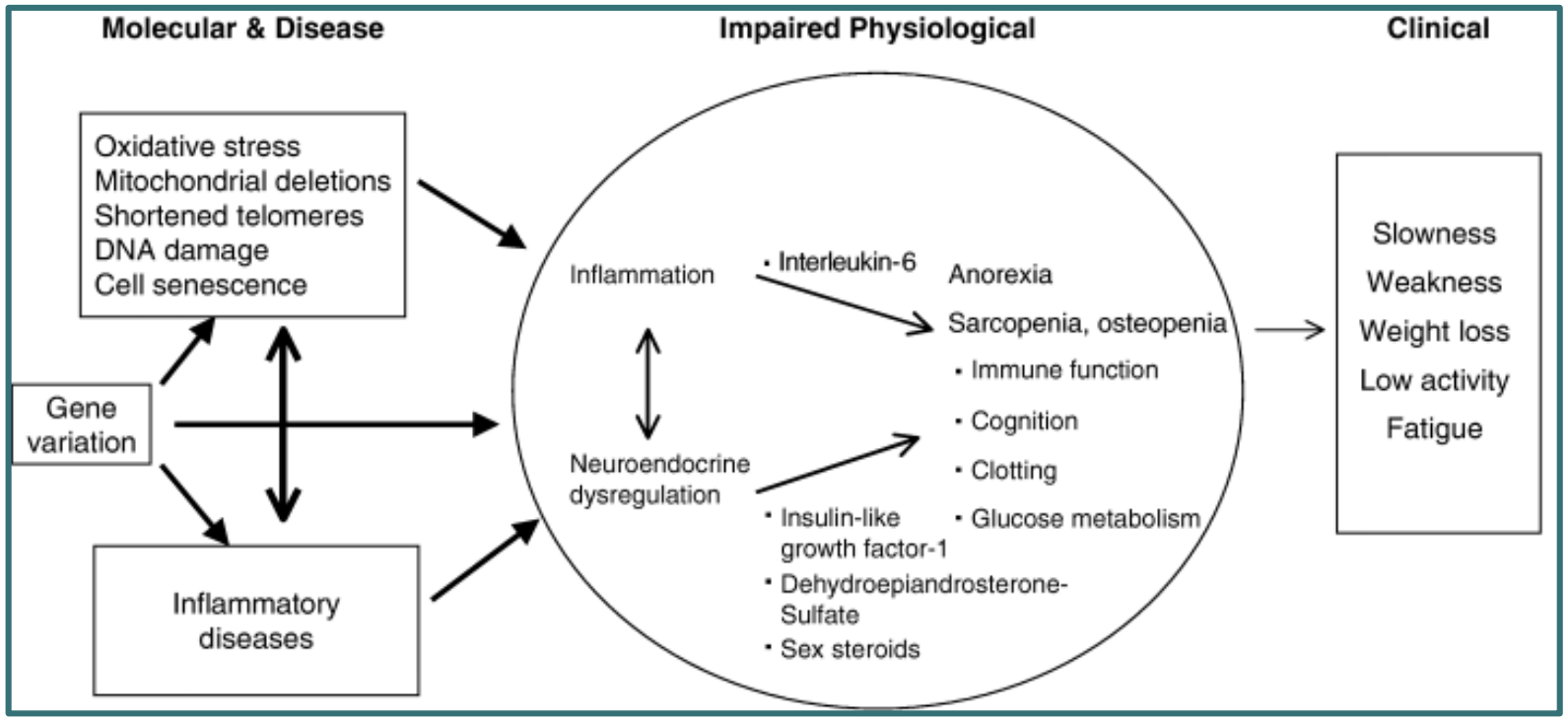
What is Frailty?
Frailty Consensus: A Call to Action

- 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

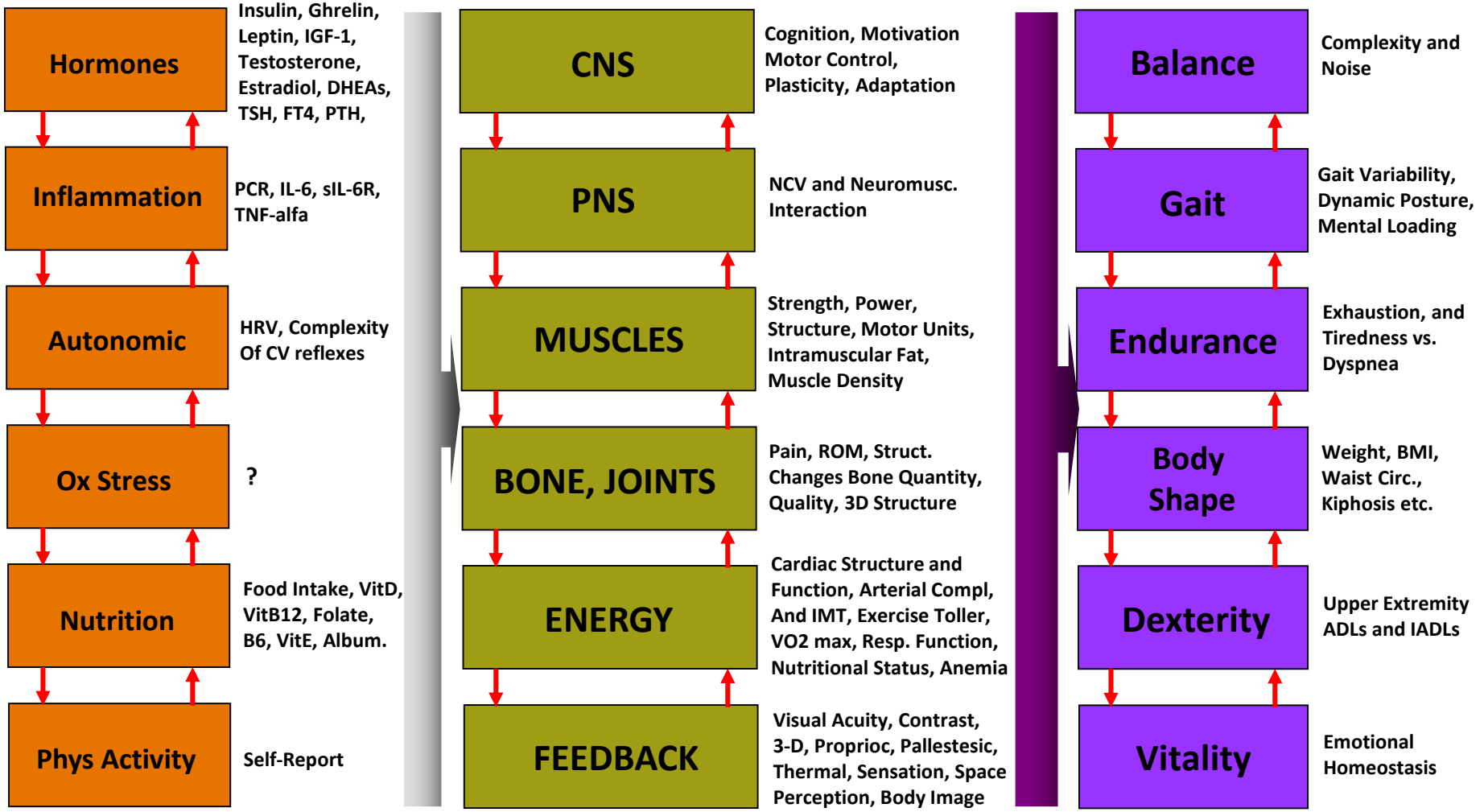
- Frailty can occur as the result of a range of diseases and medical conditions

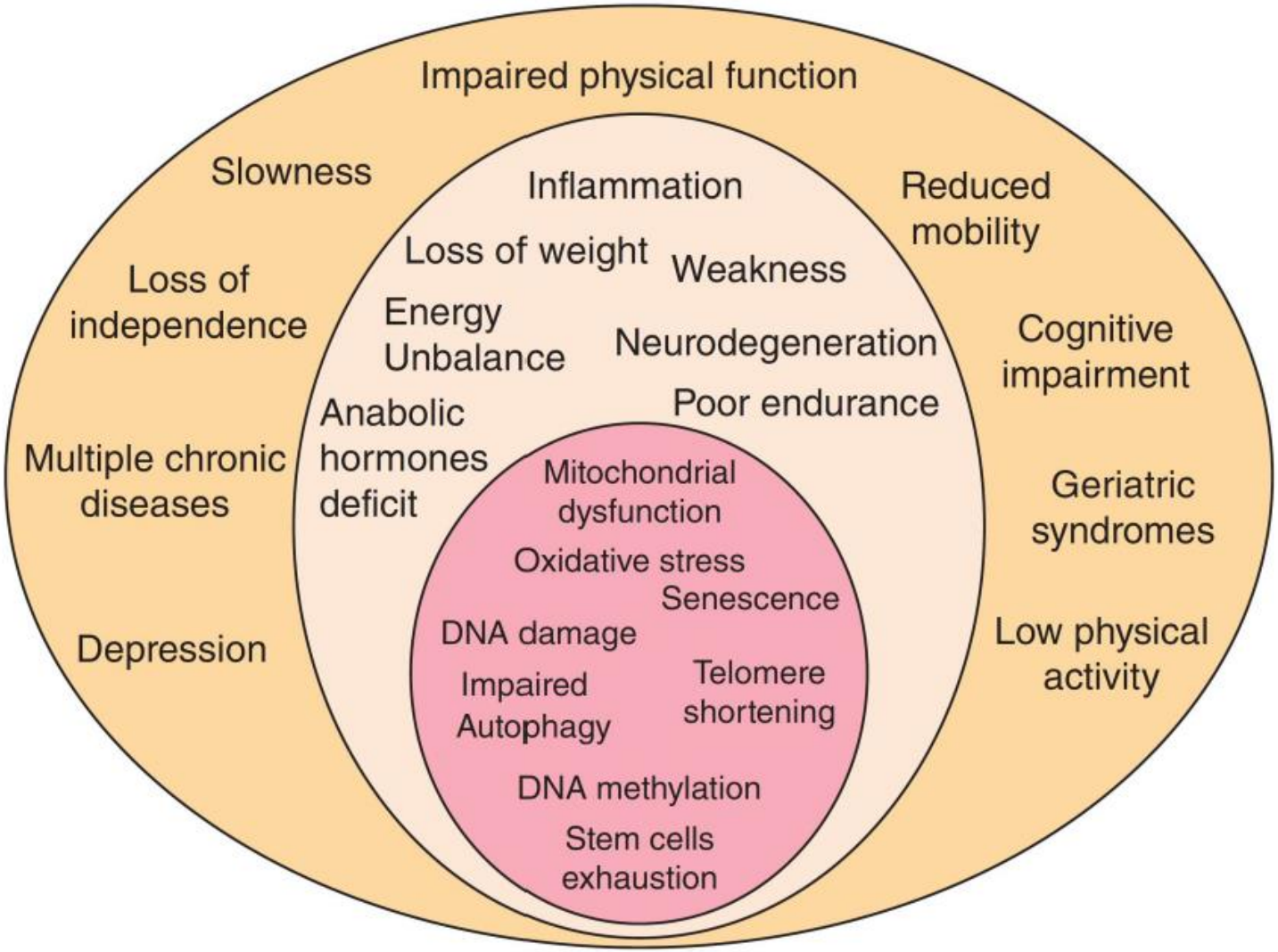
- It is different from disability

Toward a Better Understanding of Physiology and Etiology: Summary from the AGS/NIA Research Conference on Frailty

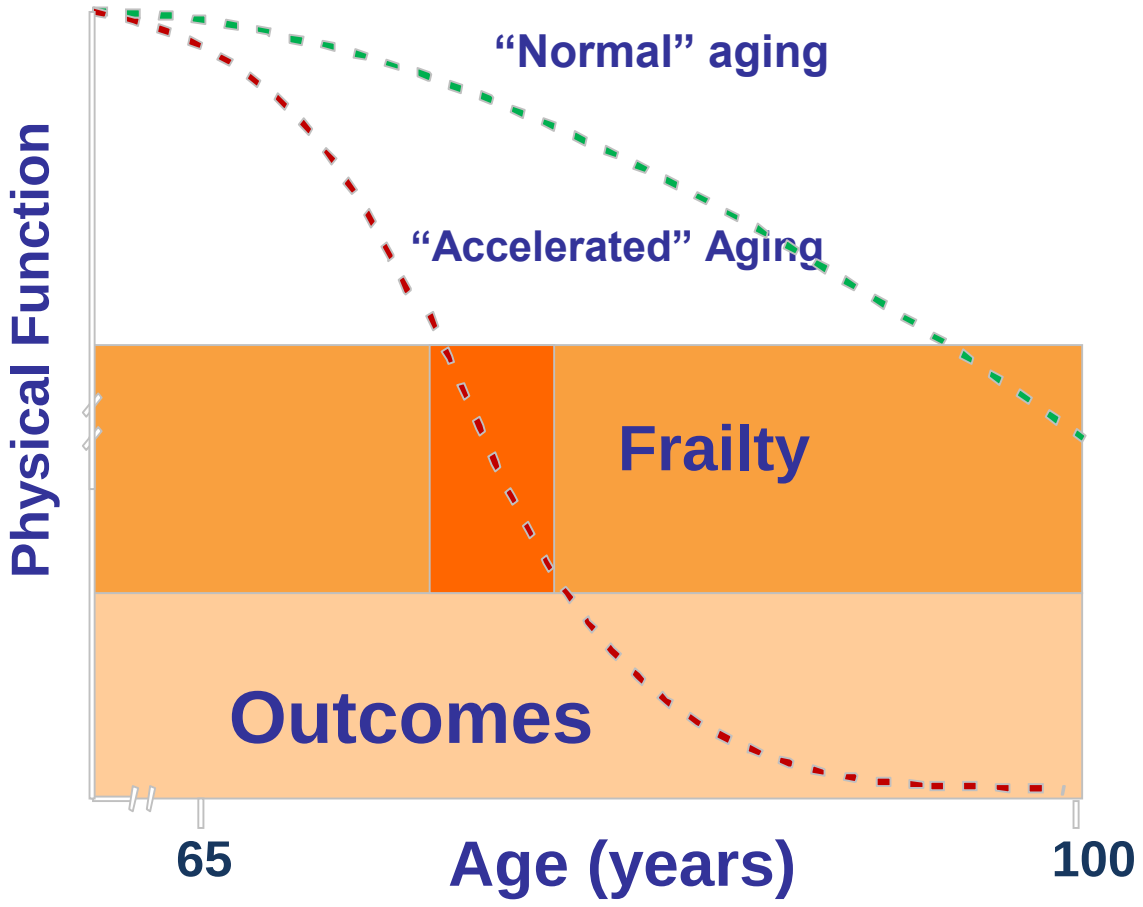


FACING THE COMPLEXITY OF FRAILTY
Multiple Levels of Measure and Interaction



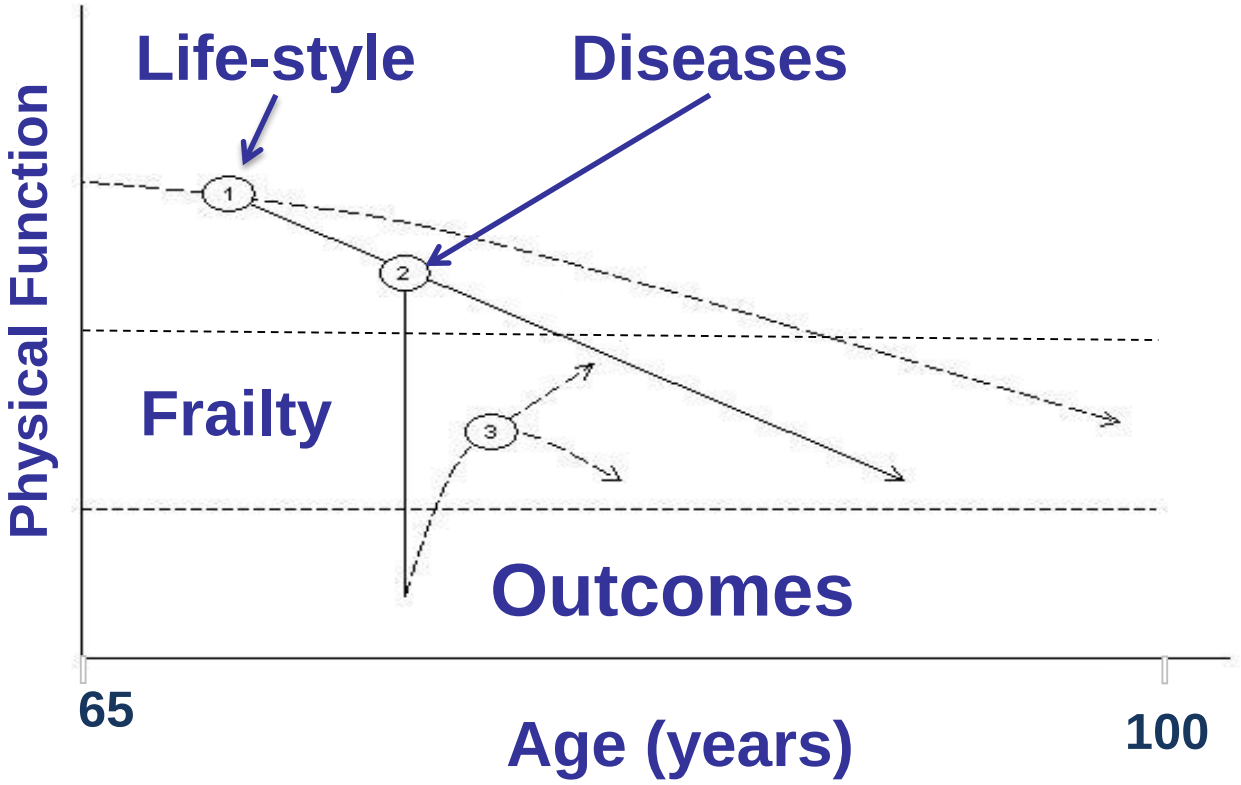

Impaired physical function
Slowness
Loss of independence
Multiple chronic diseases
Depression
Reduced mobility
Cognitive impairment
Geriatric syndromes
Low physical activity
Inflammation
Loss of weight
Weakness
Energy Unbalance
Neurodegeneration
Poor endurance
Anabolic hormones deficit
Mitochondrial dysfunction
Oxidative stress
Senescence
DNA damage
Impaired Autophagy
Telomere shortening
DNA methylation
Stem cells exhaustion

Aging and Functional decline

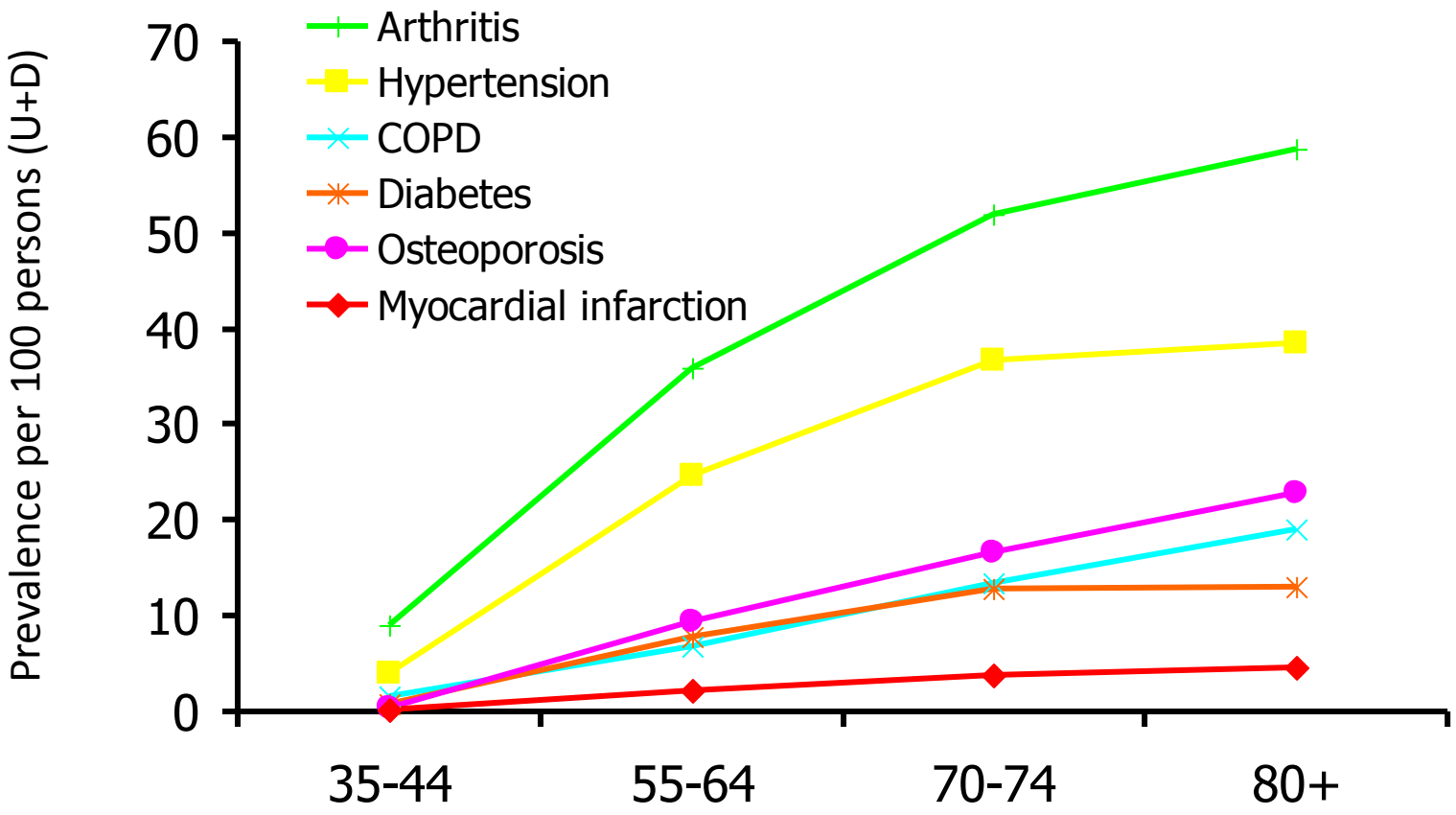


Ferrucci et al. J Endocrinol Invest 2002, modified

Aging and Functional decline

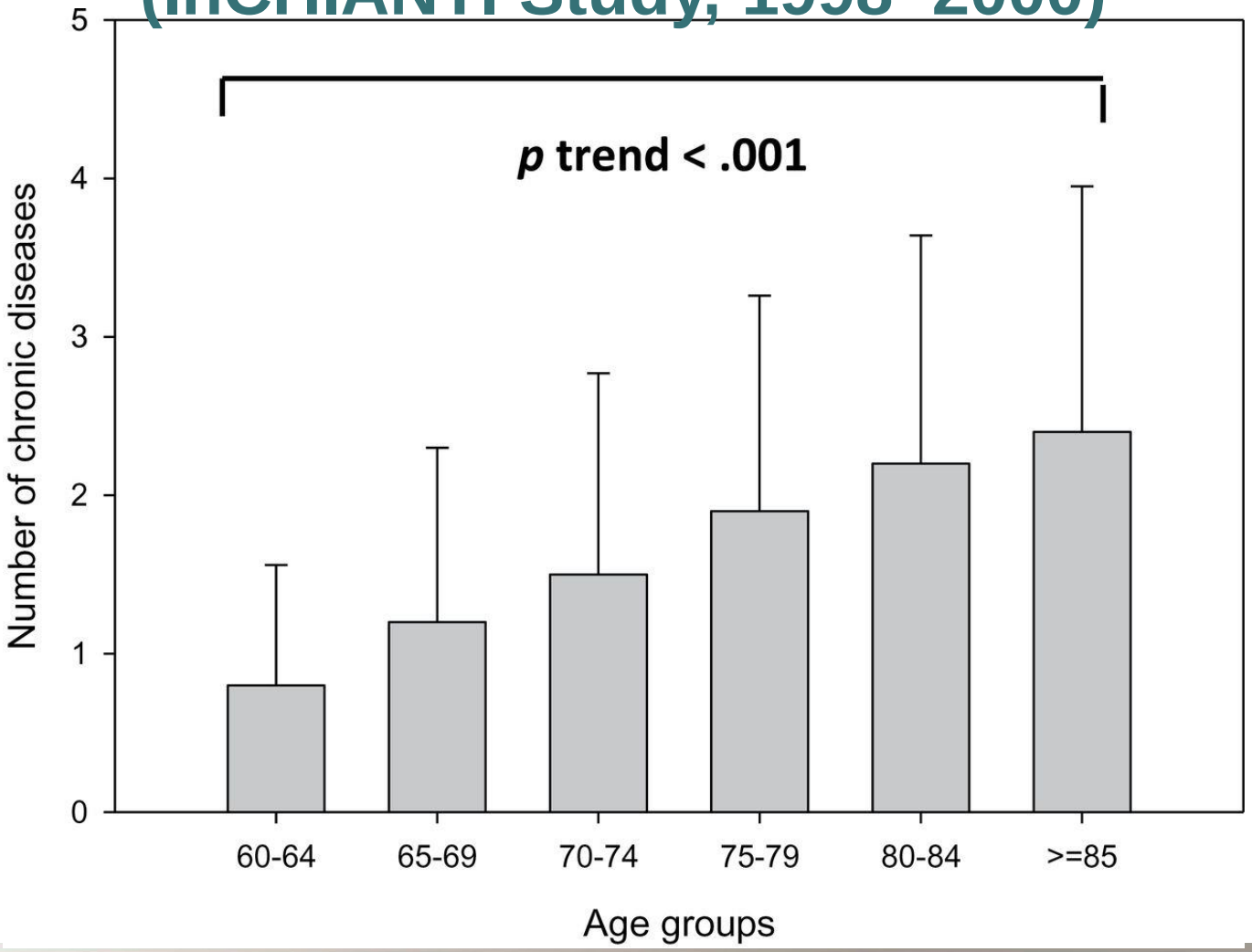


Prevalence of Major Chronic Diseases According to Age, Italy



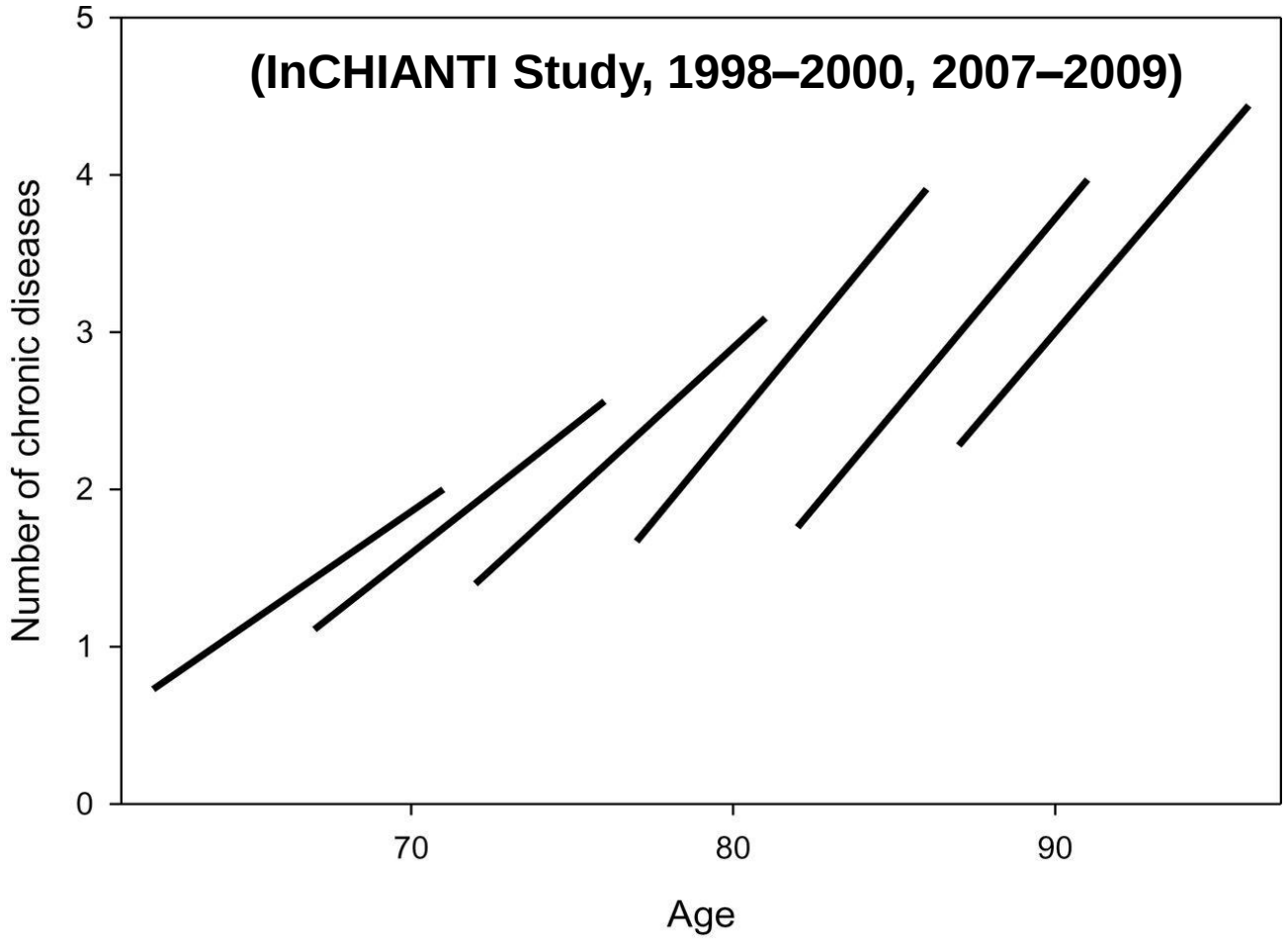
Source: ISTAT data

Number of chronic diseases according to age (InCHIANTI Study, 1998–2000)

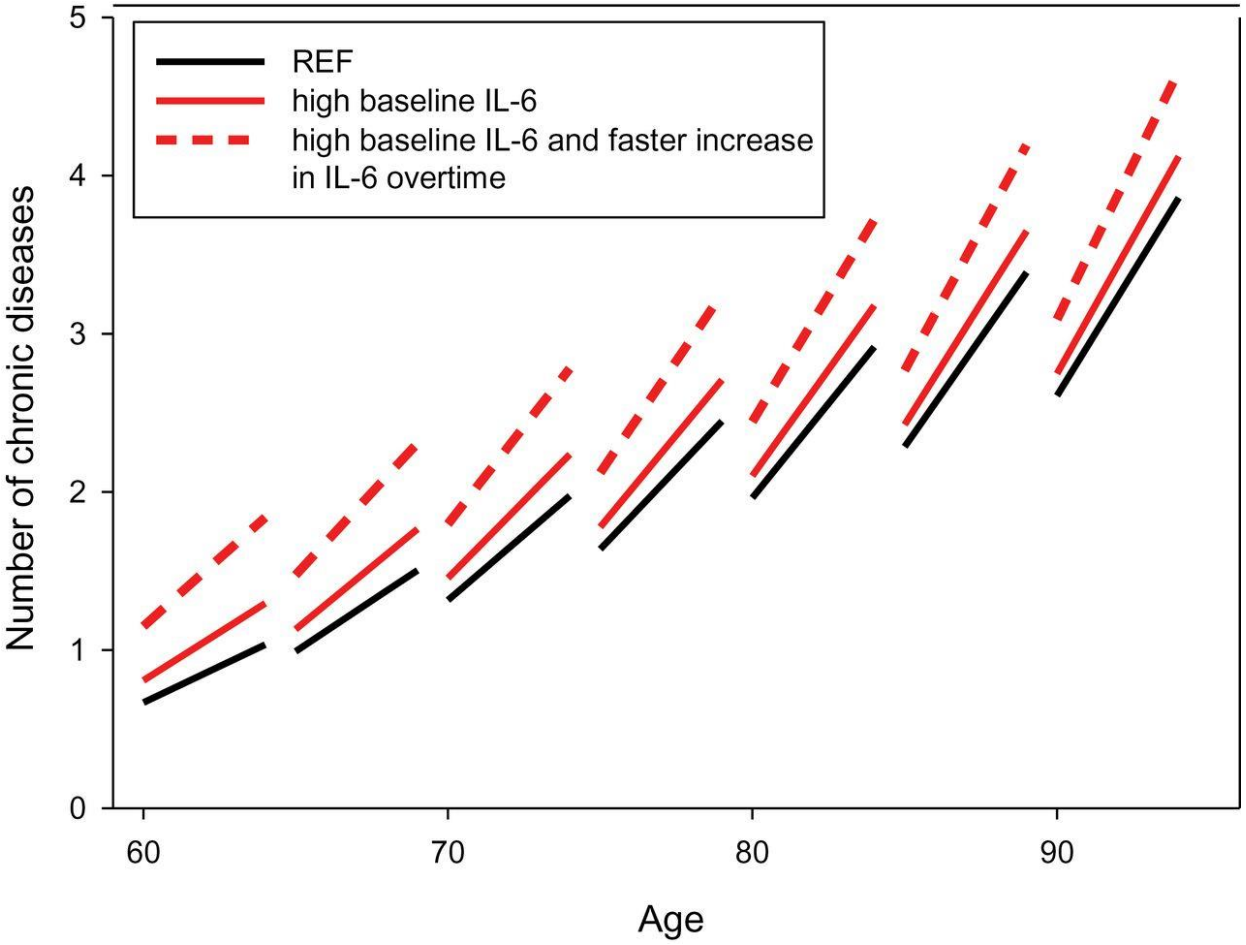


Fabbri E. et al. J Gerontol A Biol Sci Med Sci 2015;70:63-70

Number of Chronic Diseases at Baseline and at 9-year follow-up and average trajectories of multimorbidity

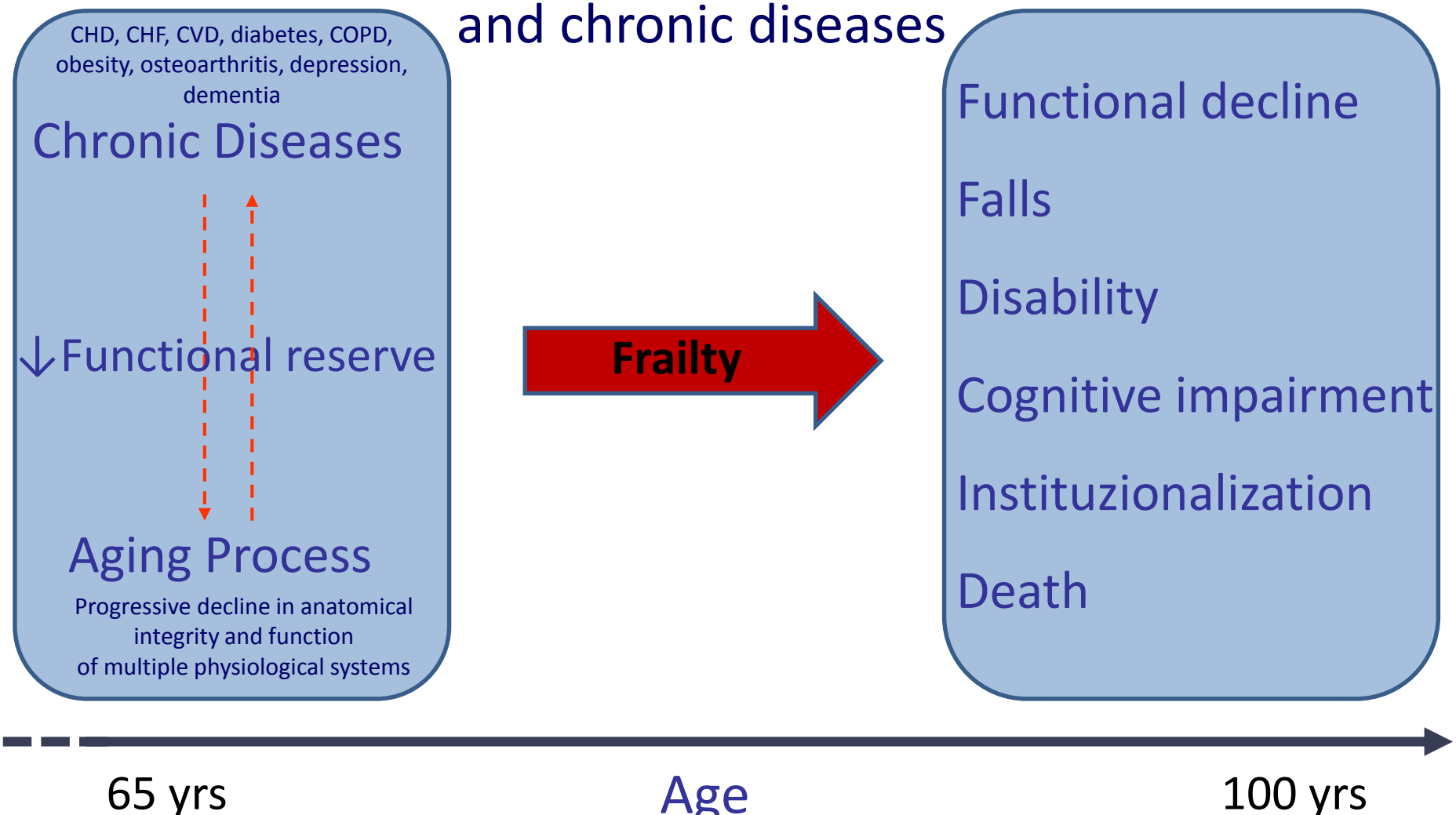


Trajectories of longitudinal increase in number of chronic diseases according to baseline values and rate of increase in IL-6 levels

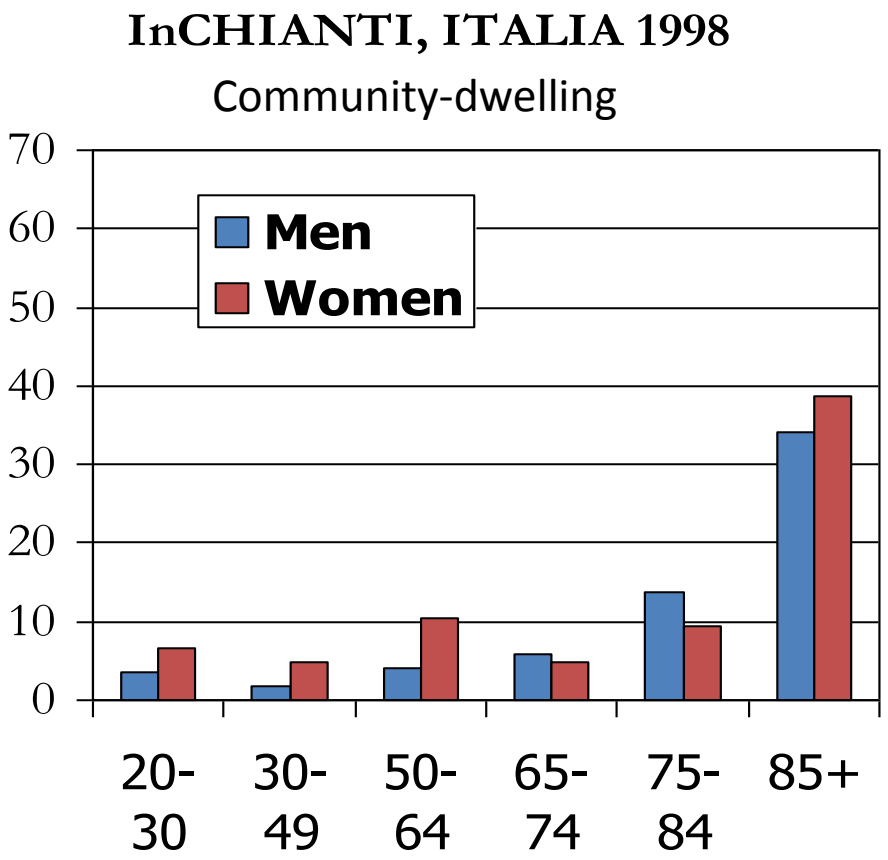


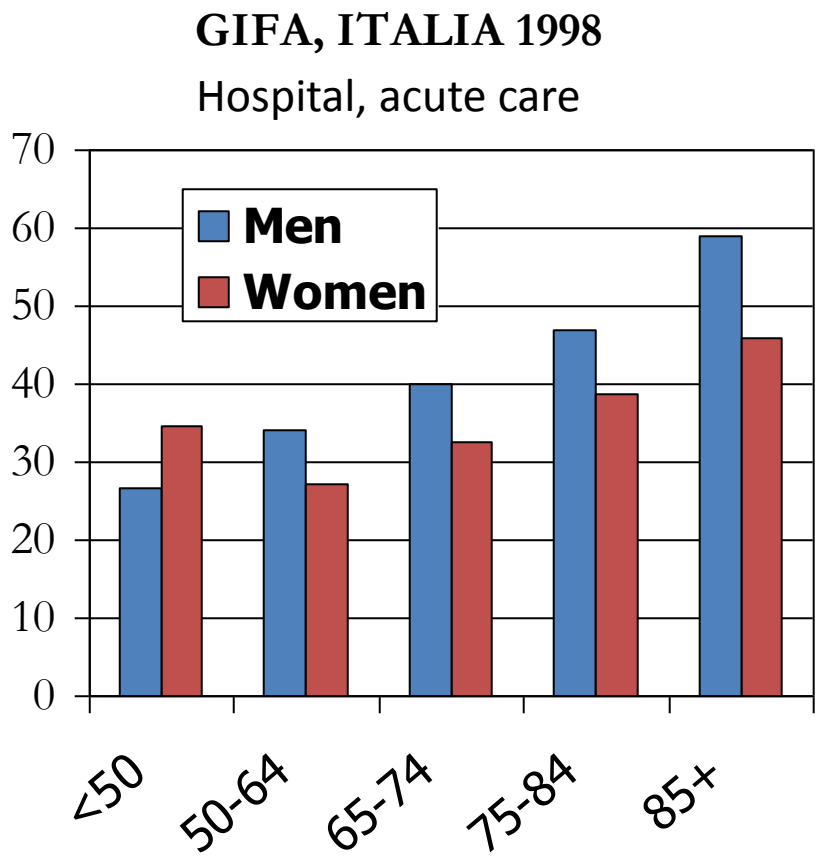
Fabbri E. et al. J Gerontol A Biol Sci Med Sci 2015;70:63-70

Interactions between age-related changes and chronic diseases



Prevalence of anemia according to gender, age, and clinical setting



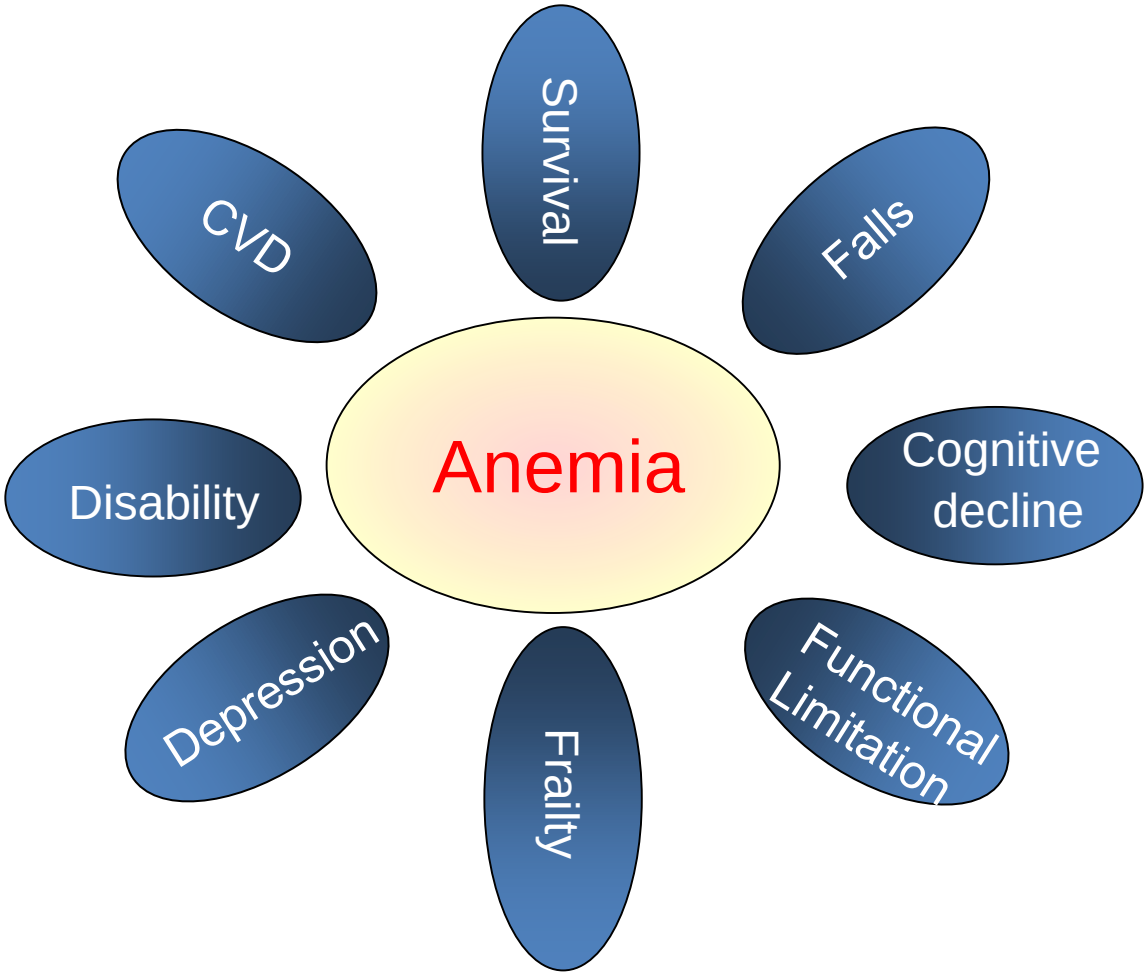


Prognostic value of anemia in terms of disability and mortality in hospitalized geriatric patients: the CRIME study

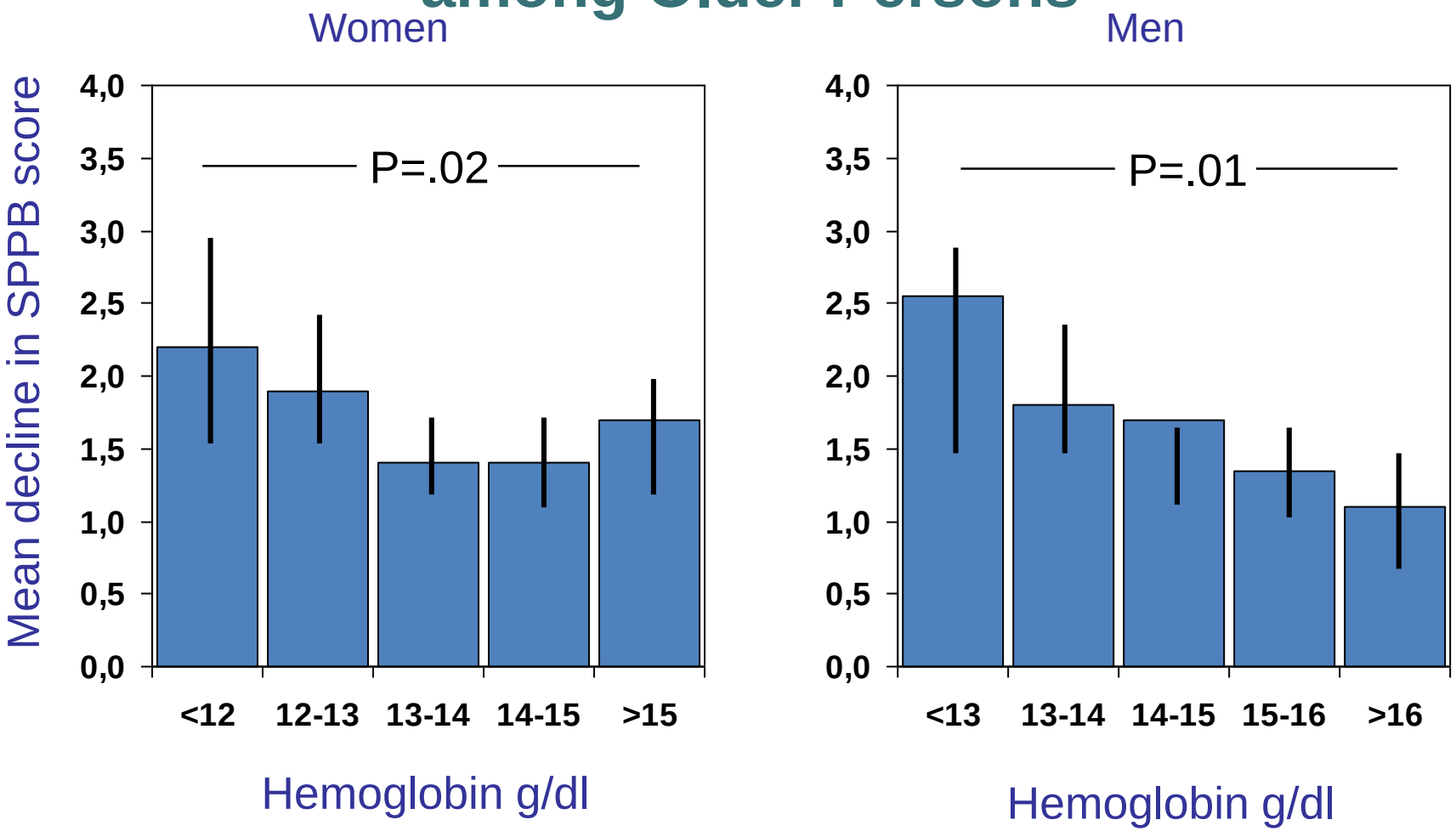
Characteristics	No anemia (n=378)	Mild/moderate anemia (n=343)	Severe anemia (n=175)	P
Female, N (%)	200 (52.9)	199 (58.0)	93 (53.1)	0.338
Age, mean±SD	78.8±7.4	83.1±7.0	82.7±6.7	<0.001
Smoking, N (%)				
Former	133 (35.2)	112 (32.7)	56 (32.0)	
Never-smoker	205 (54.2)	210 (61.2)	107 (61.1)	0.128
BMI (kg/m²), mean±SD	28.0±5.3	25.8±5.0	25.6±4.7	<0.001
Hospitalizations in the last year, N (%)				
One	78 (20.6)	77 (22.4)	43 (24.6)	
More than one	62 (16.4)	90 (26.2)	53 (30.3)	<0.001
Medical conditions, N (%)				
Hypertension	303 (80.2)	240 (70.0)	127 (72.6)	0.005
Coronary heart disease	102 (27.0)	116 (33.8)	56 (32.0)	0.125
Heart failure	74 (19.6)	116 (33.8)	65 (37.1)	<0.001
Diabetes mellitus	99 (26.2)	100 (29.2)	61 (34.9)	0.113
Non-Alzheimer's dementia	38 (10.0)	53 (15.4)	34 (19.4)	0.007
Alzheimer's dementia	17 (4.5)	24 (7.0)	6 (3.4)	0.157
Gastritis	34 (9.0)	48 (14.0)	27 (15.4)	0.041
Peptic ulcer	12 (3.2)	8 (2.3)	16 (9.1)	0.001
Renal failure	63 (16.7)	99 (28.9)	64 (36.6)	<0.001
Cancer	31 (8.2)	48 (14.0)	43 (24.6)	<0.001
Multidimensional assessment				
MMSE, median (IQR)	24 (19, 28)	22 (16, 27)	22 (14, 27)	<0.001
GDS, median (IQR)	3 (2, 6)	4 (2, 7)	4 (3, 7)	0.008
Disability in ADL, N (%)	113 (29.9)	176 (51.3)	108 (61.7)	<0.001
Biochemical parameters (at discharge)				
Albumin (g/dL), mean±SD	3.8±0.5	3.5±0.6	3.4±0.7	<0.001
Creatinine (mg/dL), median (IQR)	1.0 (0.8, 1.2)	1.1 (0.8, 1.4)	1.1 (0.9, 1.5)	<0.001
C-reactive protein (mg/L), median (IQR)	3.7 (1.1, 10.3)	6.3 (2.3, 17.9)	6.0 (1.5, 23.9)	0.035

Brombo G., Volpato S, et al. Geriatric Care 2016;2: 5803

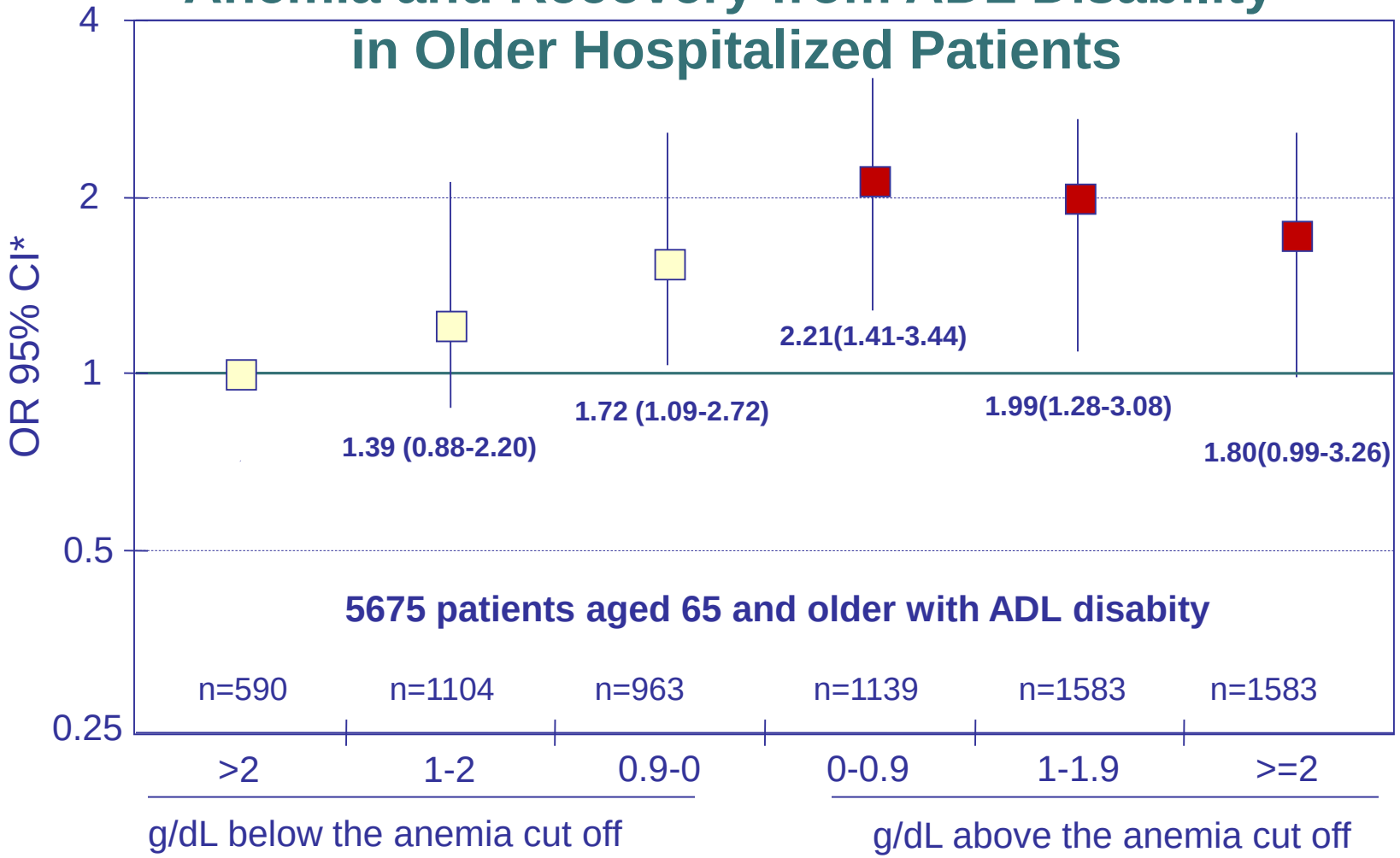
Anemia and Geriatrics Syndromes



Anemia and Decline in Physical Performance among Older Persons



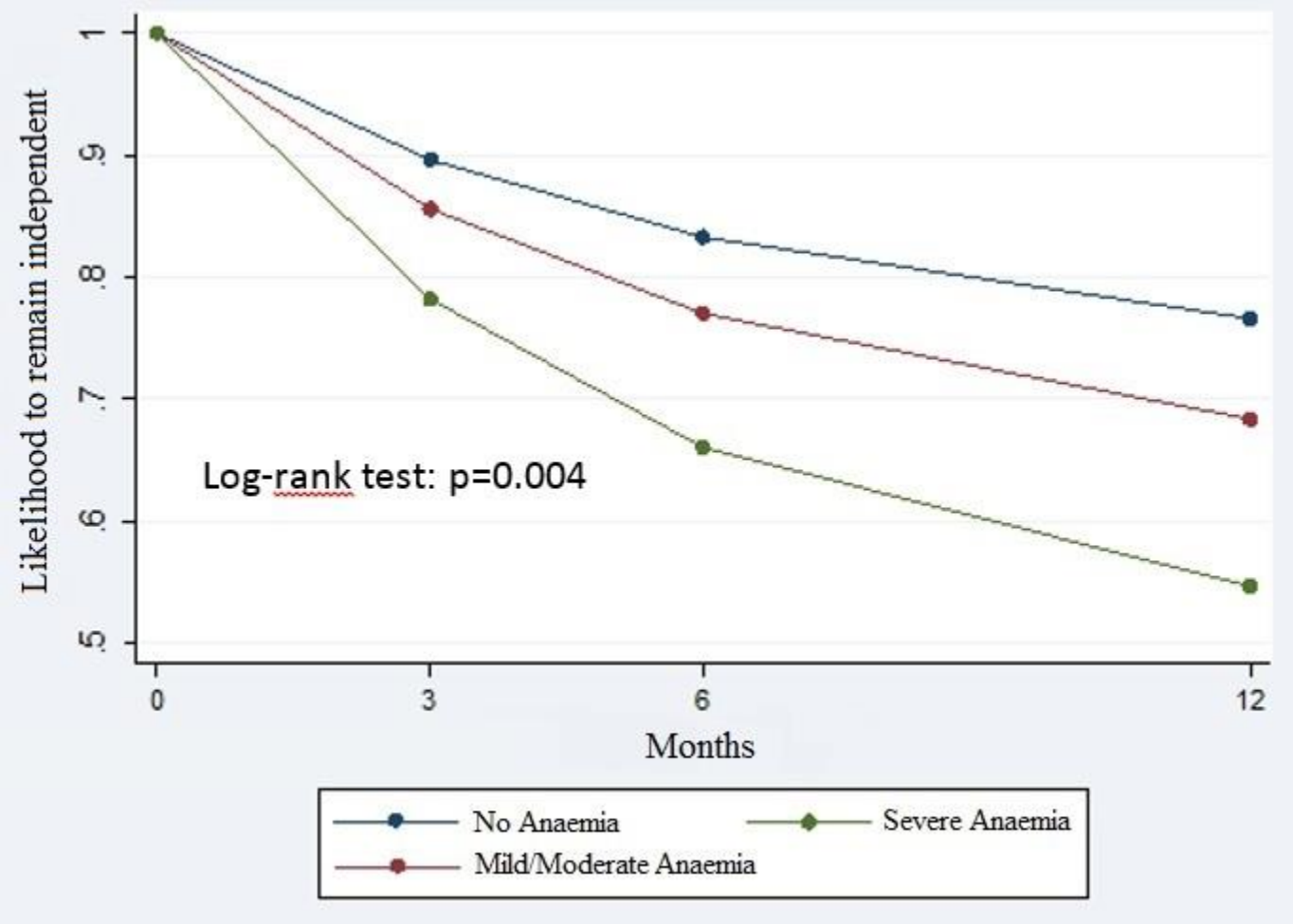
Anemia and Recovery from ADL Disability in Older Hospitalized Patients



Adjusted for age, sex, education, smoking, marital status, cognitive status, BMI, albumin, cholesterol, creatinine clearance, stroke, CVD, CHF, COPD, pneumonia, Parkinson's disease, depression, cancer, hip fracture, Charlson Comorbidity Index, number of impaired ADL at admission

Maraldi C, Volpato S et al. J Am Geriatr Soc. 2006;54:632-6

Likelihood to remain independent at 12 months in relation to anemia severity



EDITORIAL

Editorials represent the opinions of the authors and JAMA and not those of the American Medical Association.

The Central Role of Prognosis in Clinical Decision Making

Thomas M. Gill, MD

JAMA 2012;307:199–200

Prognostic Indices for Older Adults

A Systematic Review

Lindsey C. Yourman, MD
Sei J. Lee, MD, MAS
Mara A. Schonberg, MD, MPH
Eric W. Widera, MD
Alexander K. Smith, MD, MS, MPH

FAILURE TO CONSIDER PROGNOsis in the context of clinical decision making can lead to poor care. Hospice is underutilized for patients with nonmalignant yet life-threatening diseases.[1] Healthy older patients with good prognosis have low rates of cancer screening.[2] Older adults with advanced dementia or metastatic cancer are screened for slow-growing cancers that are unlikely to ever cause them symptoms but may lead to distress from false-positive results, invasive workups, and treatments.[3,4] In recognition of these phenomena, guidelines increasingly incorporate life expectancy as a central factor in weighing the benefits and the burdens of tests

Context To better target services to those who may benefit, many guidelines recommend incorporating life expectancy into clinical decisions.

Objective To assess the quality and limitations of prognostic indices for mortality in older adults through systematic review.

Data Sources We searched MEDLINE, EMBASE, Cochrane, and Google Scholar from their inception through November 2011.

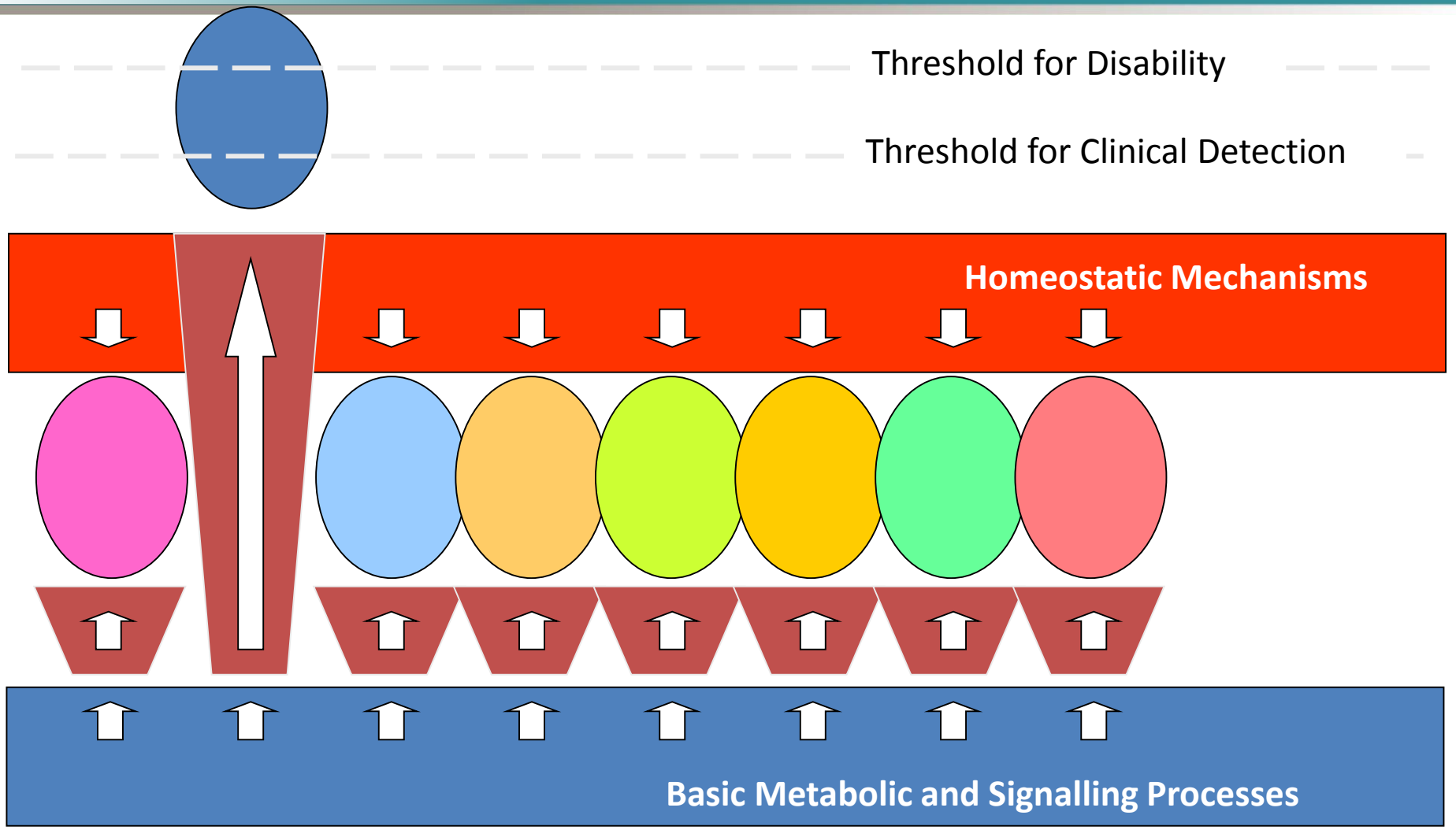
Study Selection We included indices if they were validated and predicted absolute risk of mortality in patients whose average age was 60 years or older. We excluded indices that estimated intensive care unit, disease-specific, or in-hospital mortality.

Data Extraction For each prognostic index, we extracted data on clinical setting, potential for bias, generalizability, and accuracy.

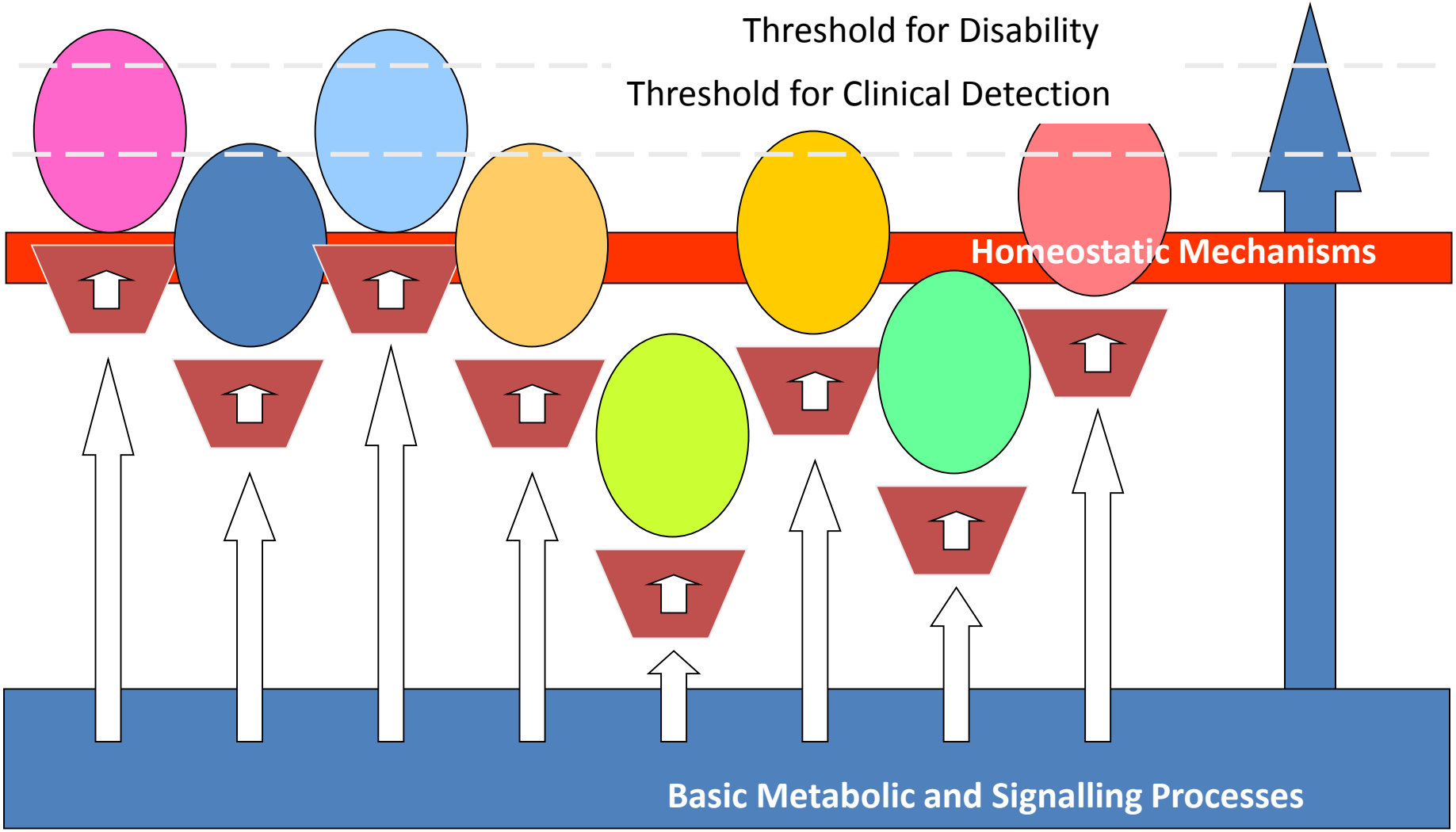
Results We reviewed 21 593 titles to identify 16 indices that predict risk of mortality from 6 months to 5 years for older adults in a variety of clinical settings: the community (6 indices), nursing home (2 indices), and hospital (8 indices). At least 1 measure of transportability (the index is accurate in more than 1 population) was tested for all but 3 indices. By our measures, no study was free from potential bias. Although 13 indices had *C* statistics of 0.70 or greater, none of the indices had *C* statistics of 0.90 or greater. Only 2 indices were independently validated by investigators who were not involved in the index's development.

Conclusion We identified several indices for predicting overall mortality in different patient groups; future studies need to independently test their accuracy in heterogeneous populations and their ability to improve clinical outcomes before their widespread use can be recommended.

JAMA. 2012;307(2):182-192 www.jama.com



SINGLE DISEASE



FRAILTY AND COMORBIDITY

Frailty Consensus: Examples of Well-Validated Frailty Models

- Cardiovascular Health Study
- Study of Osteoporotic Fractures
- Deficit Model
- FRAIL – International Academy of Nutrition and Aging
- SHARE-FI
- Vulnerable Elder Survey
- Tilburg Frailty Index
- Groningen Frailty Indicator

Morley J. et al.J Am Med Dir Assoc. 2013; 14: 392–7

Frailty in Older Adults

Frailty, commonly associated with aging, includes several characteristics (see below). Frail older adults are weak, often have many complex medical problems, have a lower ability for independent living, may have impaired mental abilities, and often require assistance for daily activities (dressing, eating, toileting, mobility). Most frail older adults are women (partly because women live longer than men), are more than 80 years old, and often receive care from an adult child. Because of the rapid rate of growth in the population aged 65 years and older, the number of frail elderly persons is increasing every year.

The November 8, 2006, issue of *JAMA* includes an article about care for frail older adults.

WHAT IS FRAILTY?

- Low physical activity
- Muscle weakness
- Slowed performance
- Fatigue or poor endurance
- Unintentional weight loss

To be considered frail, a person must have 3 or more of these characteristics. Persons who are frail are more likely to become disabled, to be admitted to the hospital, and to have health problems. Research has shown that individuals who smoke, persons with depression or long-term medical problems, and those who are underweight are more likely to become frail. Frail older adults are more likely to develop infections because their immune systems do not work as well as in healthy older adults. Simple infections may cause more harm, even death, for a frail elderly person, than for for an individual of the same age who is healthy. Malnutrition is also common among frail older adults. Loss of muscle mass (more than with healthy aging) may result from a diet low in protein. Because of inability to plan and prepare their own meals, frail elderly individuals may not consume enough protein and calories to maintain their body weight and health.

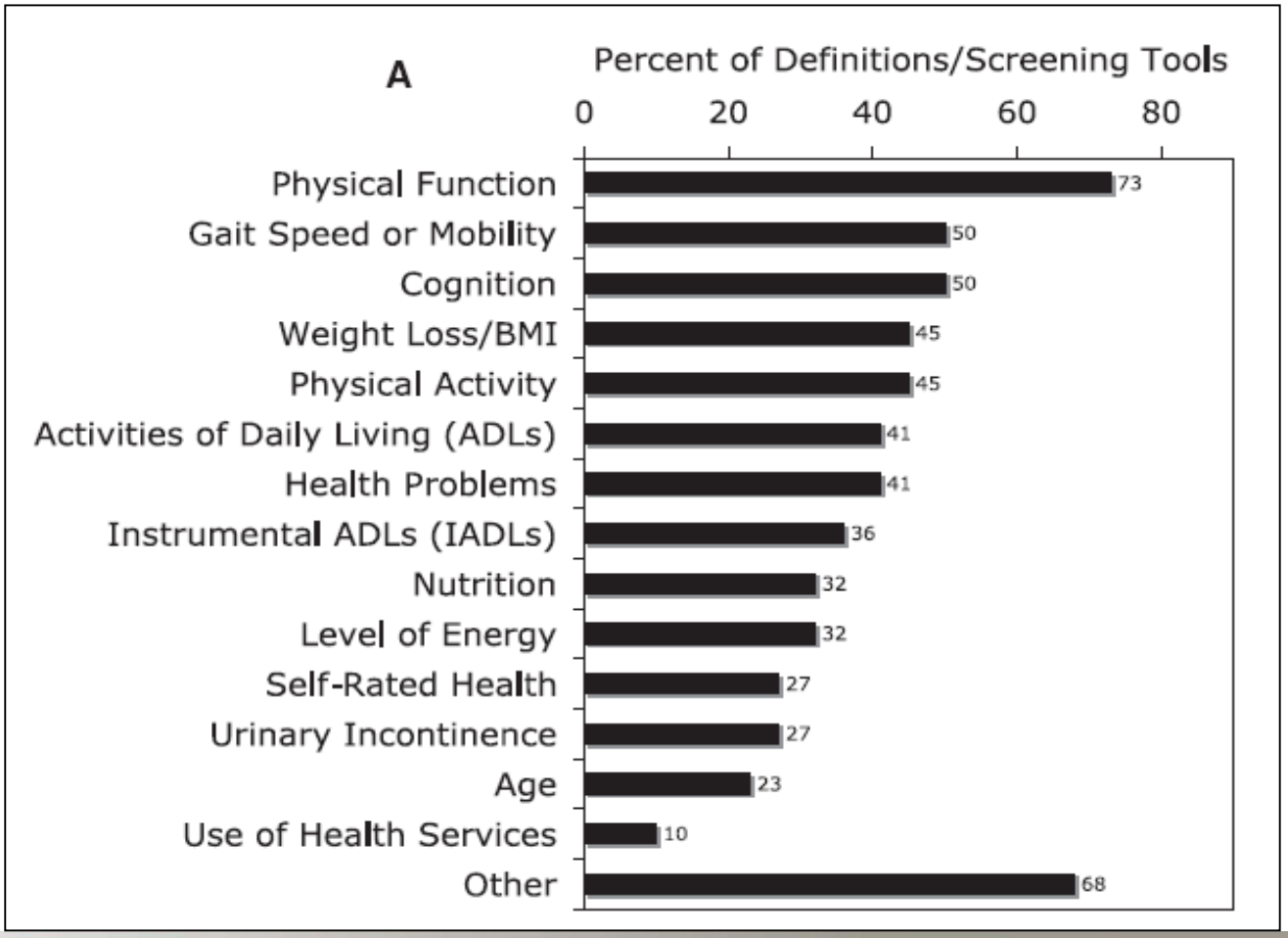
FOR MORE INFORMATION

- National Institute on Aging
  www.nia.nih.gov
- American Geriatrics Society Foundation for Health in Aging
  www.healthinaging.org
- National Council on Aging
  www.ncoa.org

INFORM YOURSELF

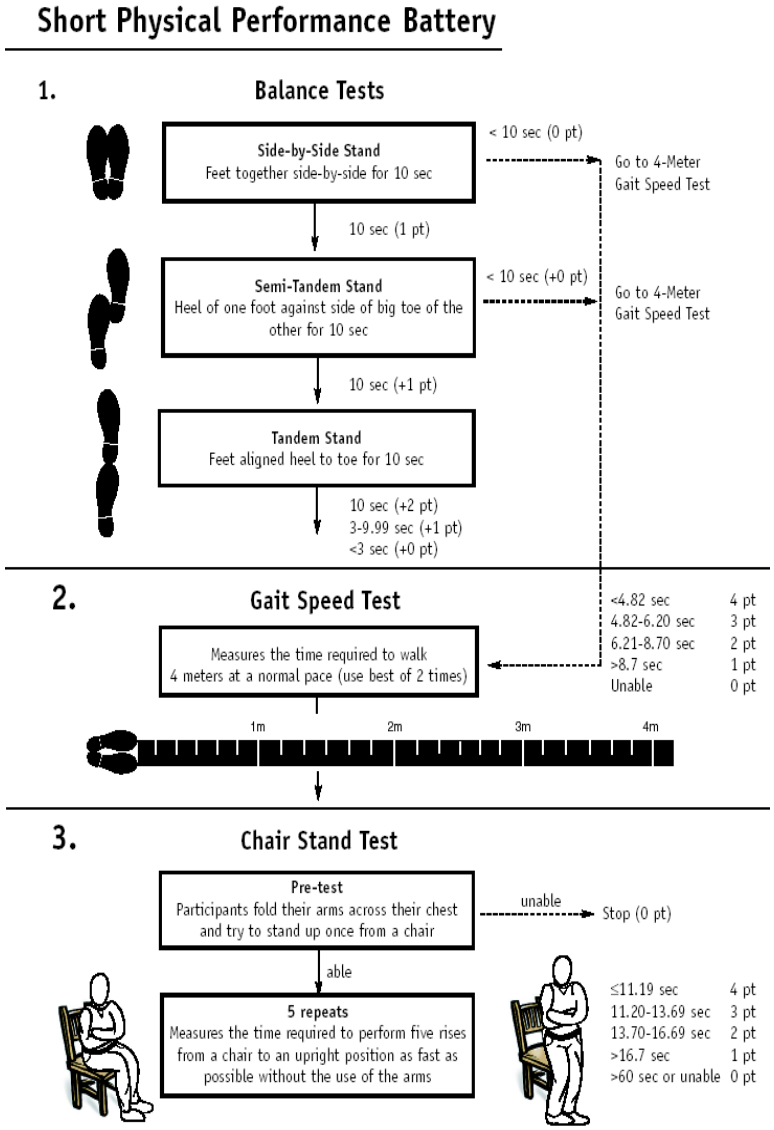
To find this and previous JAMA Patient Pages, go to the Patient Page Index on *JAMA*'s Web site at www.jama.com. Many are available in English and Spanish. A Patient Page on fitness for older adults was published in the July 12, 2006, issue; and one on psychiatric illness in older adults was published in the June 7, 2000, issue.

Prevalence of identifying factors for frailty in definitions and screening tools

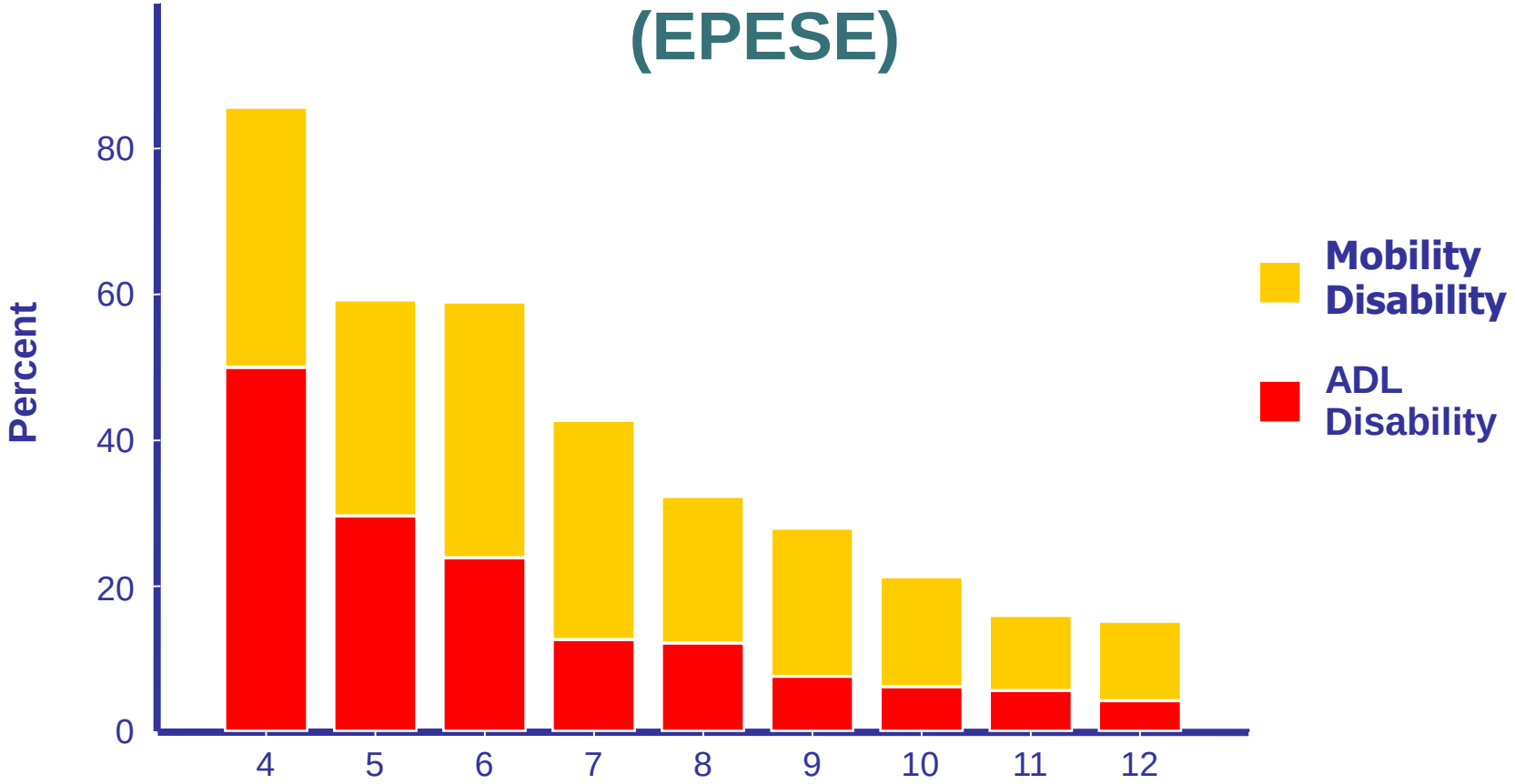


Sternberg et al. JAGS 2011;59:2129-38

Lower Extremity performance test



Absolute Risk of Disability after 4 years according to SPPB score in older non disabled people (EPESE)



Guralnik et al. *N Engl J Med* 1995;332:556-561

Short Physical Performance Battery e Length of hospital stay in older geriatric patients

		Model 1		Model 2		Model 3	
		β coef.(SE)	p	β coef.(SE)	p	β coef.(SE)	p
SBBP							
0-4	**(n.25)**	reference*	-	reference*	-	reference*	-
5-7	**(n.37)**	-2.2 (1.5)	0.151	-1.9(1.6)	.240	-1.3 (1.4)	.359
8-12	**(n.28)**	-3.9 (1.4)	0.005	-3.2(1.4)	.026	-2.5 (1.2)	.036
†SBBPscore continuous		-0.72 (0.21)	.001	-0.62(0.22)	.005	-0.54 (0.20)	.007

Model 1: adjusted for age and gender

Model 2: adjusted for age, gender, and Cumulative Illness Rating Scale (number of severe ratings)

Model 3: adjusted for age, gender, Cumulative Illness Rating Scale (number of severe ratings), and BADL disability at admission

Risk of New Hospitalization or Death During the Follow-Up According to SPPB Score at Discharge

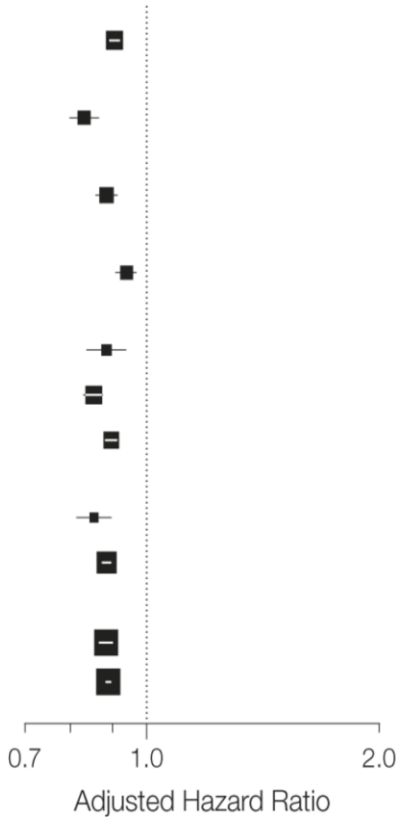
Discrete-time survival analysis with logistic regression

SPPB Categories	Outcome	Model 1		Model 2	
	%	OR	(95% C.I.)	OR	(95% C.I.)
0-4 (n. 16)	75.0	3.72	(1.52-9.08)	5.38	(1.82-15.9)
5-7 (n. 27)	65.4	2.95	(1.38-6.28)	2.63	(1.16-6.01)
8-12 (n. 44)	52.3	1.0	-	1.0	-
†SBBP (continous)		0.87	(0.78-0.97)	0.86	(0.75-0.98)

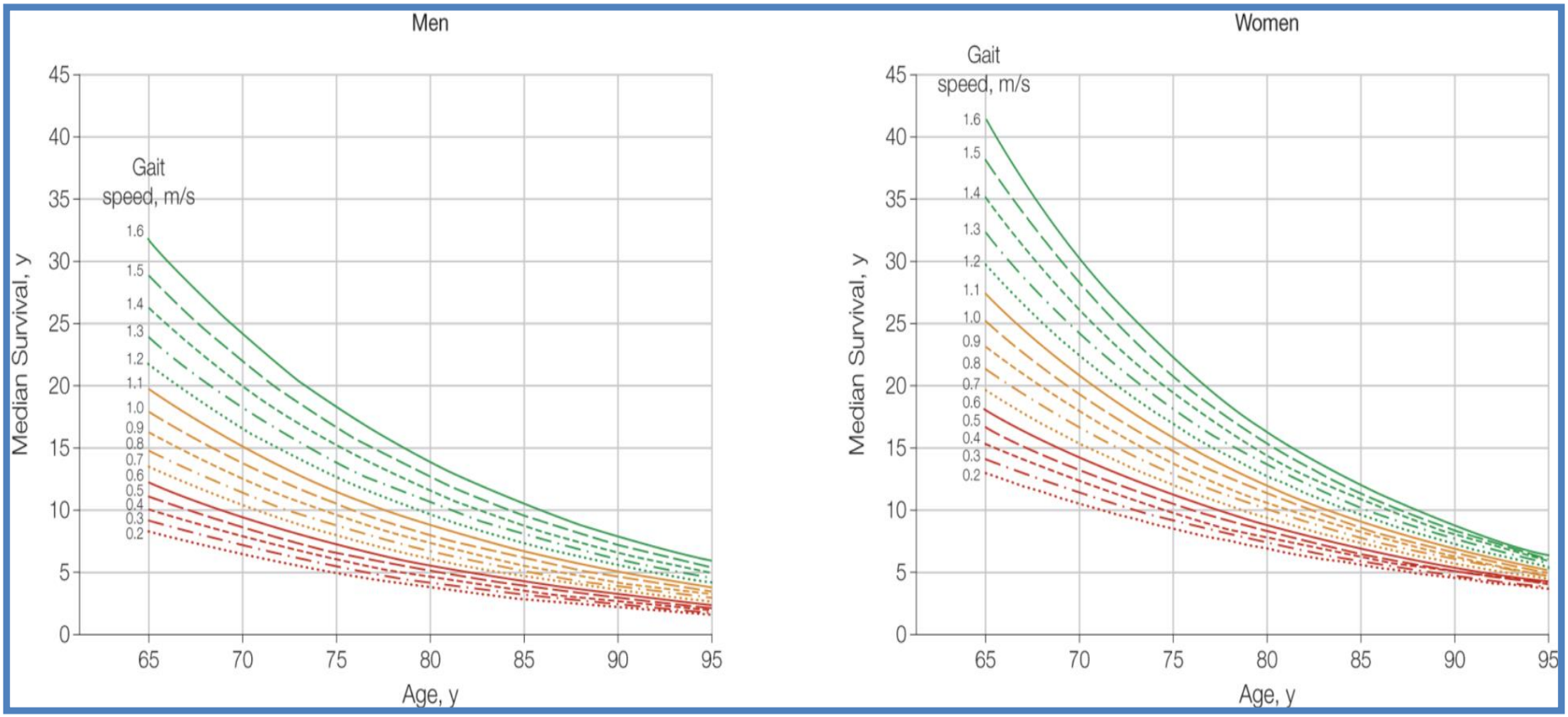
Model 2: adjusted for age, gender, education, CIRS, ADL summary scale 2 weeks before hospital admission, ADL summary scale at discharge, MMSE score at hospital admission

Gait Speed and Survival in Older Adults: Pooled analysis of 9 cohort studies

	No. of Deaths	Total Sample Size
Cardiovascular Health Study,[22] 1991	3851	5801
Established Populations for the Epidemiologies Study of the Elderly,[23] 1985	1955	2128
Health, Aging, and Body Composition Study,[11,12] 2009, 2005	848	3048
Hispanic Established Populations for Epidemiological Study of the Elderly,[13] 1999	972	1905
Invecciare in Chianti,[17] 2000	187	972
Osteoporotic Fractures in Men,[20] 2005	1073	5833
Third National Health and Nutrition Examination Study,[21] 2004	2837	3958
Predicting Elderly Performance,[28] 2003	293	491
Study of Osteoporotic Fractures,[26] 1990	5512	10349
Pooled (random effects)		
Pooled (shared frailty model)		



Gait Speed and Survival in Older Adults: Pooled analysis of 9 cohort studies



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VIEWPOINT

Incorporating Lag Time to Benefit Into Prevention Decisions for Older Adults

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Applying the Framework During an Annual Medicare Wellness Visit

The following example illustrates an approach for applying this framework. A 75-year-old man who has hypertension (blood pressure, 135/75 mm Hg), diabetes, chronic obstructive lung disease, and difficulty walking several blocks is wondering whether he should be screened for colorectal cancer.

First, determine the patient's life expectancy. Using published general mortality indexes for older adults from a systematic review, the index proposed by Lee et al[7] is identified as appropriate for this patient. Using the web calculator available at http://eprognosis.ucsf.edu, the Lee index estimates that the patient has a 4-year mortality risk of 45%, suggesting a life expectancy of approximately 5 years.

Second, determine the lag time to benefit for colorectal cancer screening and blood pressure control. A recent study quantified the lag time to benefit for screening fecal occult blood testing to be 10.3 years for an absolute risk reduction of 1 death prevented for 1000 persons screened.[6] Because the lag time to benefit exceeds the patient's life expectancy, it is unlikely that he would benefit from screening; thus, screening would not be recommended.

The ADVANCE study suggests that benefits of more intensive blood pressure control in older patients with diabetes appear at 12 to 18 months.[8] Given this patient's life expectancy of 5 years, continuing more intensive blood pressure control would be recommended.

Conclusion

Preventing illness through early detection and treatment is a central component of care for older adults. However, nearly all prevention exposes patients to immediate risks for the hope of improved future health outcomes. Thus, it is critical to the answer to the question "When will it help?" when individualizing preventive decisions in older adults. Although research will continue to improve the accuracy of life expectancy prediction and lag time to benefit, guidelines should move beyond age and explicitly encourage clinicians to juxtapose these 2 elements to improve the targeting of prevention.

Conclusions

- Frailty and multimorbidity are common conditions in older people
- Frailty and multimorbidity have a negative sinergistic effect increasing the risk for several negative outocomes
- Several Frailty models have been validated and proposed, but the utilization in clinical practice may be difficult
- Simple performance-based test of physical function may be used to identify older people at high risk of health status deterioration


Frail
people