I 30 ANNI DELLA FONDAZIONE ORLANDO ARLOTTI

Sabato 09 Novembre 2019

L'Interleukina-6 come marker biumorale di fragilità nel soggetto anziano. Risultati di uno studio epidemiologico longitudinale

Stefano Volpato

UO Ortogeriatria

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
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Cosa mi ha permesso di fare il supporto della Fondazione Orlando Arlotti?

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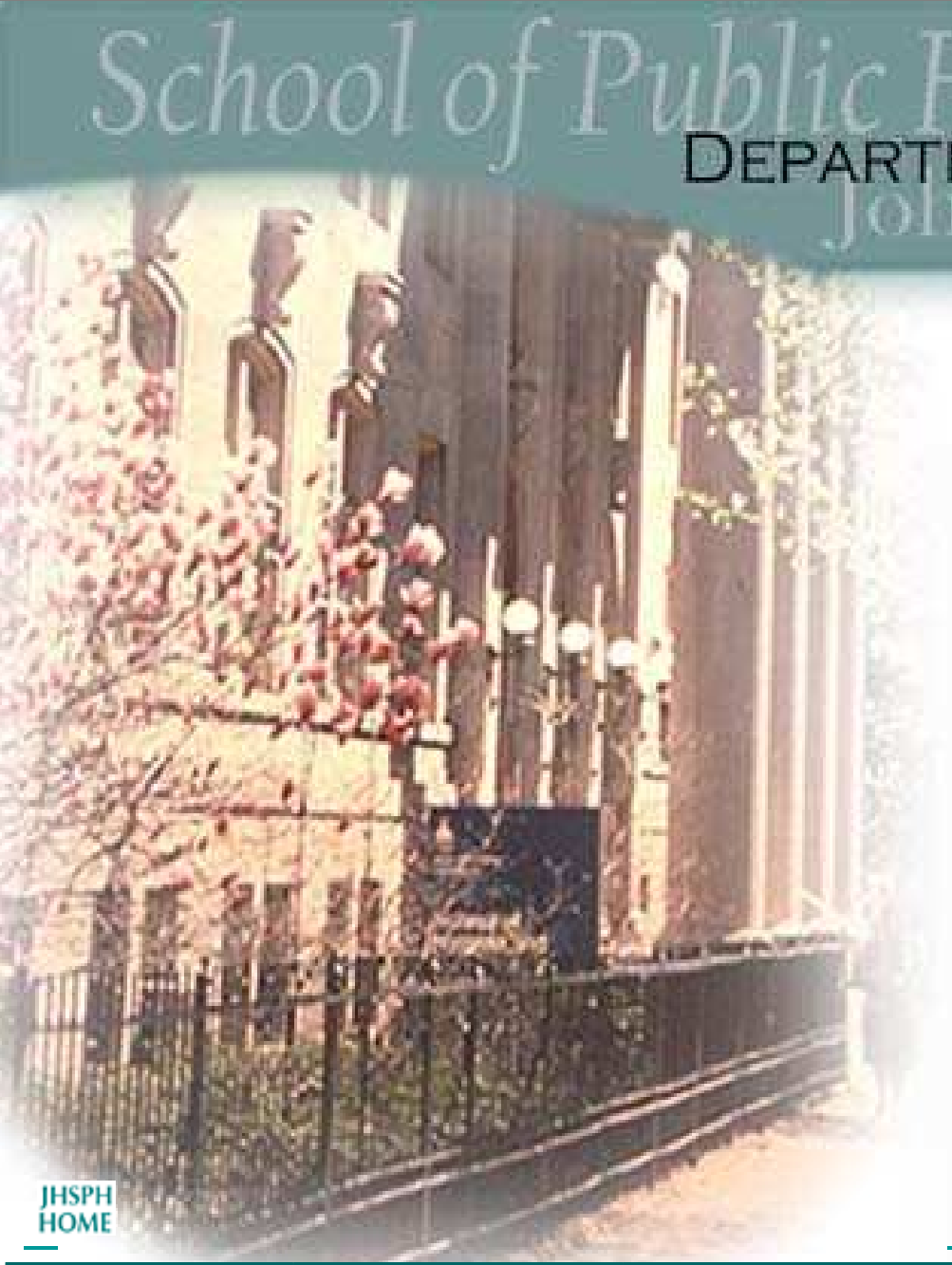

Welcome from the Chair

Academics

Faculty

Department Resources

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Welcome | Overview | Why Hopkins | Tuition and Fees

Cosa ho fatto con quello che ho imparato grazie al supporto della Fondazione Orlando Arlotti?

Laboratory of Epidemiology, Demography, and Biometry

Overview:

The **Laboratory of Epidemiology, Demography, and Biometry (LEDB)** plans, conducts, and directs epidemiology, demography, and biometry programs relevant to the mission of the NIA; collects and analyzes data regarding the distribution of the aged by such categories as sex, race, socioeconomic, and demographic characteristics and serves as a focal point for these data; and plans, initiates, coordinates, and analyzes national and international epidemiologic longitudinal studies and studies of special populations. In collaboration with NIA staff and that of other Institutes, Federal agencies and scientific organizations, the LEDB recommends priorities and develops epidemiologic studies of specific diseases and conditions affecting the aged. The LEDB also provides consultation and service to NIH program areas and private organizations on epidemiology, demography, and biometry studies on aging; recommends mechanisms to be used or develops mechanisms to accomplish Program objectives; and plans and directs research and training in the areas of epidemiology, demography, and biometry, and serves as the primary federal source of information regarding research and training in these areas.

More Information

Programs
Information on programs for Epidemiology and Demography, Neuroepidemiology, Geriatric Epidemiology, and Biometry Sections.

Resources
Papers and other resources on the epidemiology, demography, and biometry of aging.

Short Physical Performance Battery (SPPB)
Training CD "Assessing Physical Peformance in the Older Patient."

Health ABC
Study of the Dynamics of Health, Aging and Body Composition (Health ABC).

Requests for Additional Information
Contact the NIA for more information on the Laboratory of Epidemiology, Demography, and Biometry:

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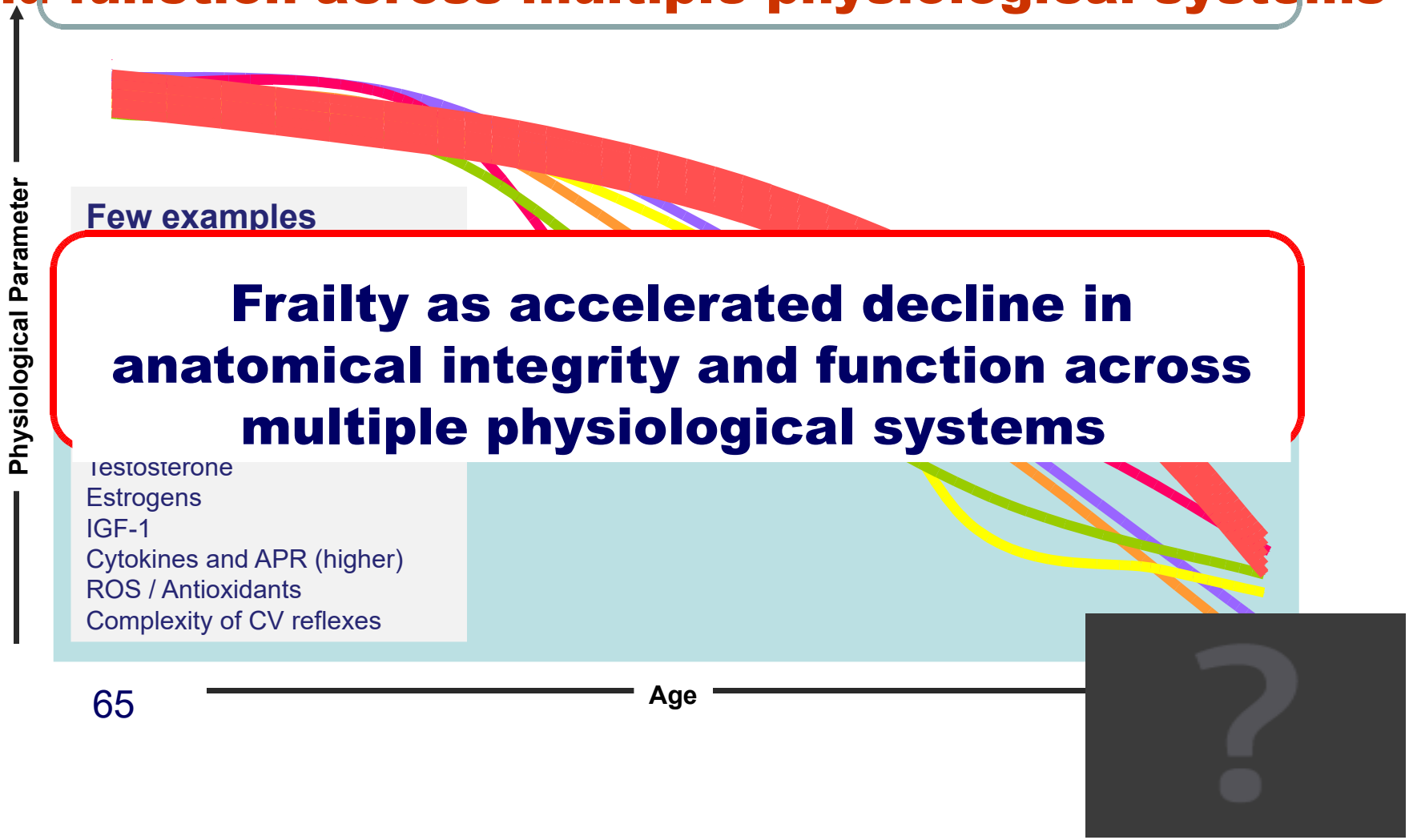
Progressive decline in anatomical integrity and function across multiple physiological systems

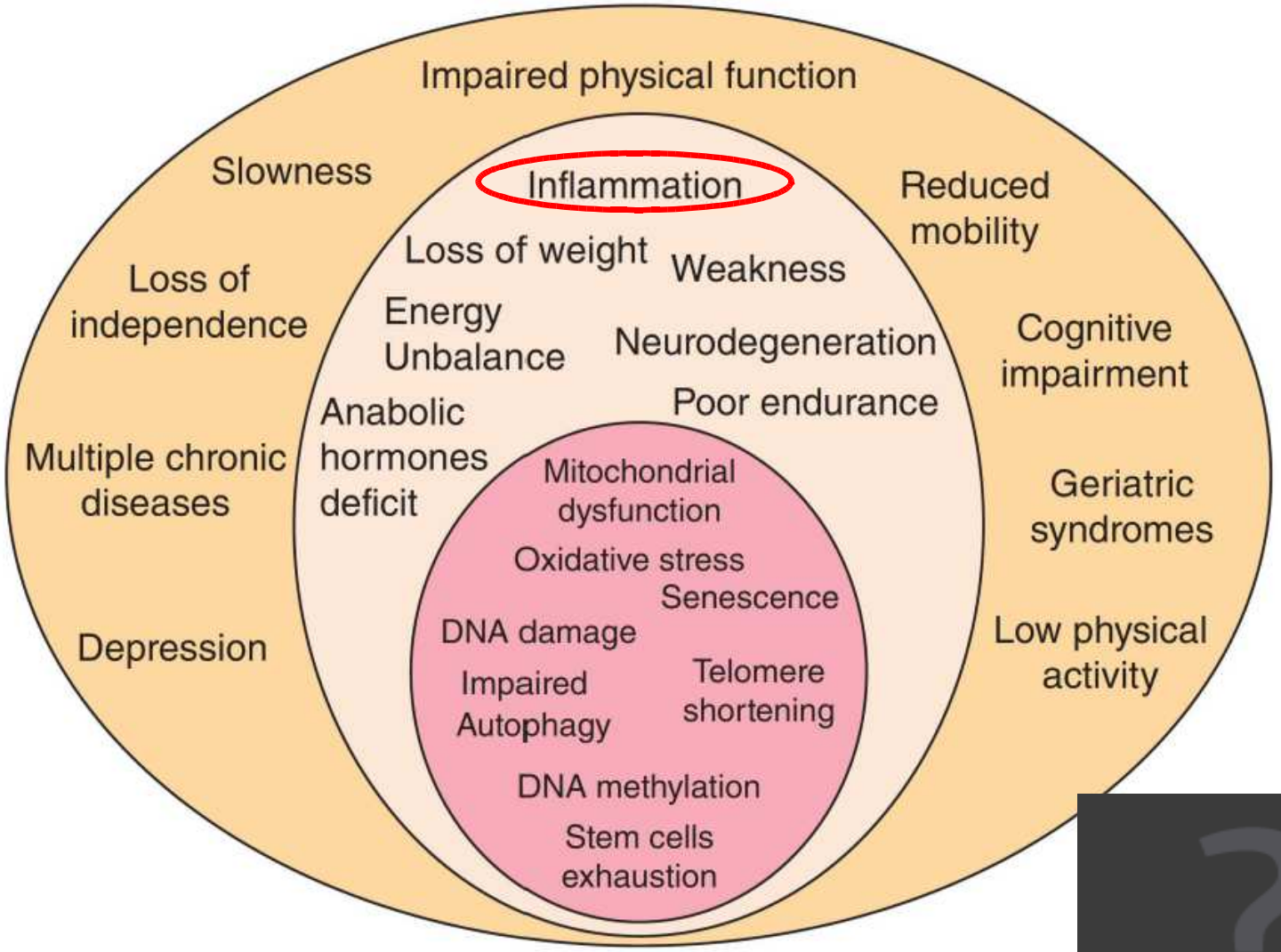


Frailty as accelerated decline in anatomical integrity and function across multiple physiological systems

- Research agenda for frailty in older adults: toward a better understanding of physiology and etiology: summary from the American Geriatrics Society/NIA Research Conference on Frailty in Older Adults

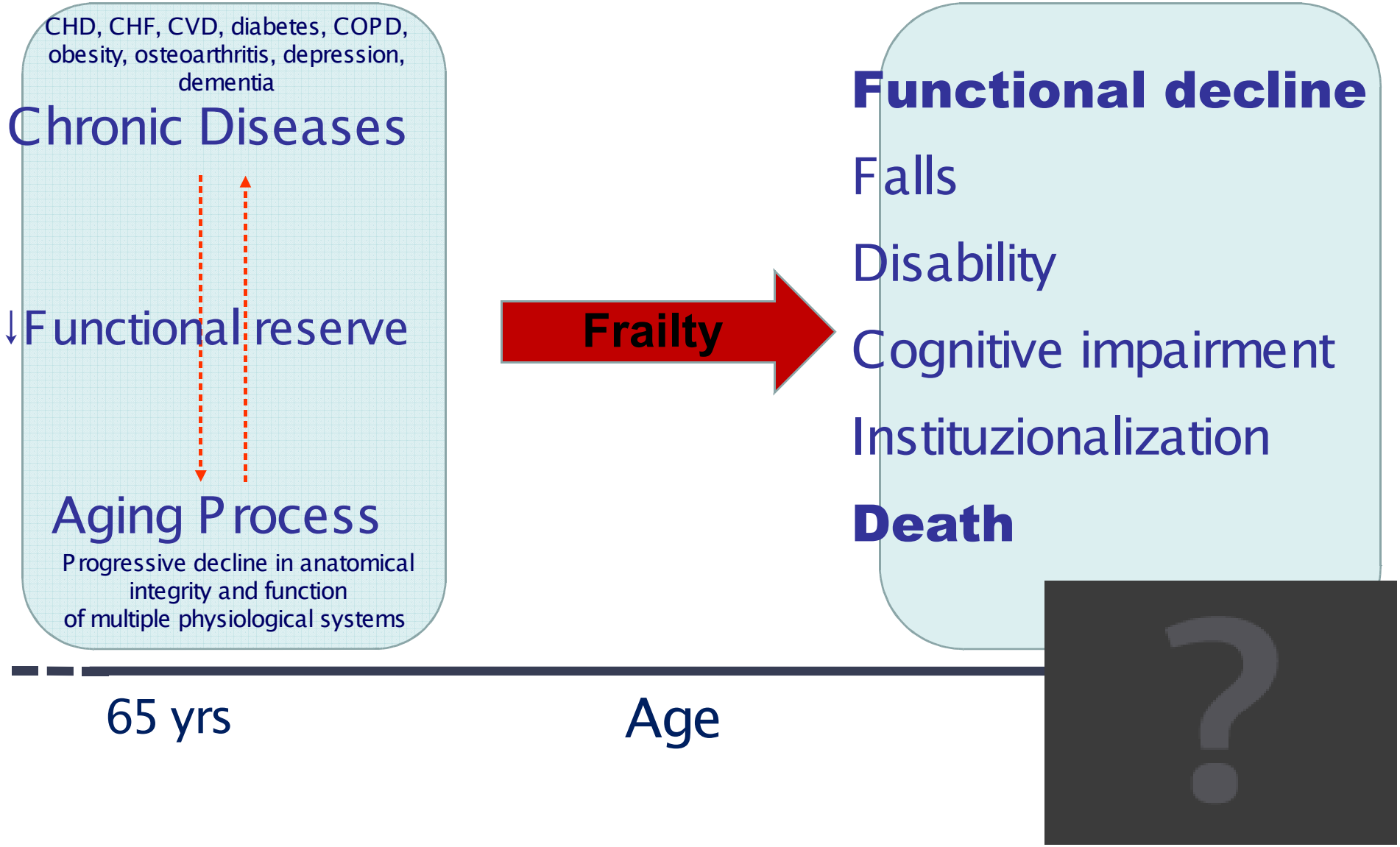
- **"A state of *increased vulnerability to stress* due to age-related declines in physiologic reserves across neuromuscular, metabolic, and immune systems"**

Watson J et al JAGS 2006



errucci L. Hazzard's Geriatric Medicine and Gerontology, 7 th Edition

Interactions between age-related changes and chronic diseases



The Women's Health and Aging Study

Obiettivi principali:

Determinare:

- **La storia naturale della disabilità fisica**
- **Le principali malattie e condizioni croniche responsabili dello sviluppo di disabilità fisica**
- **La relazione tra la presenza e gravità della malattie e la presenza di disabilità**
- **I fattori di rischio e i fattori in grado di modulare il declino funzionale età-correlato**
- **Strategie e opportunità di prevenzione prim secondaria**

Popolazione dello studio dello studio

Campione:

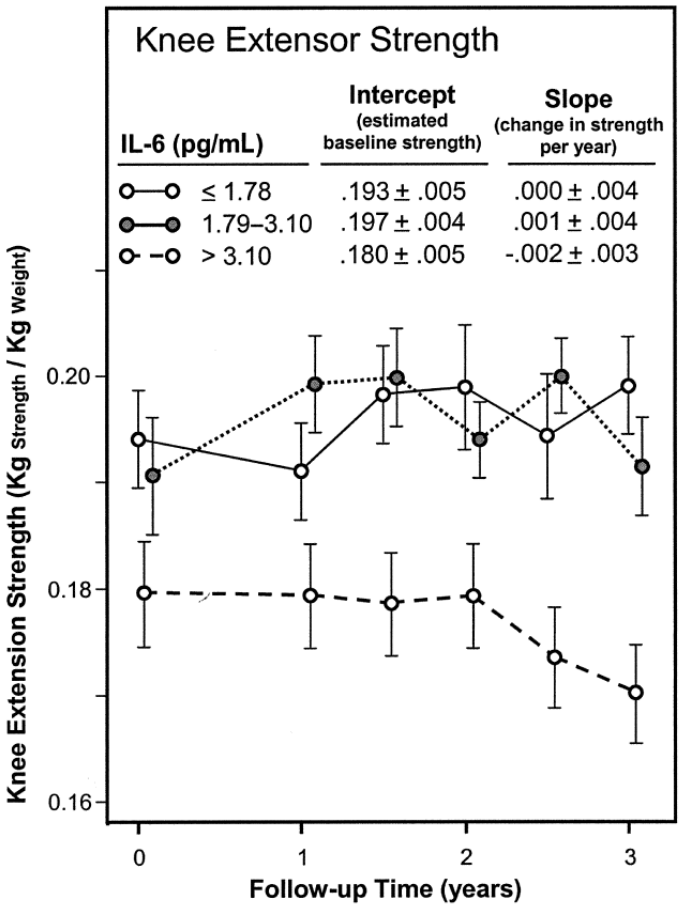
Campione random di 1002 donne anziane con limitazione fisica, non istituzionalizzate

Eleggibilità:

1) Età $\geq$ 65 anni
2) Difficulta in $\geq$ 2 aree funzionali
3) Punteggio MMSE score $\geq$ 18

Change in Muscle Strength Explains Accelerated Decline of Physical Function in Older Women With High Interleukin-6 Serum Levels

Luigi Ferrucci, MD, PhD,† Brenda W. J. H. Penninx, PhD,‡ Stefano Volpato, MD,† Tamara B. Harris, MD, PhD,† Karen Bandeen-Roche, PhD,§ Jennifer Balfour, MPH,† Suzanne G. Leveille, PhD,† Linda P. Fried, MD, PhD,‖ and Jack M. Guralnik MD, PhD†*



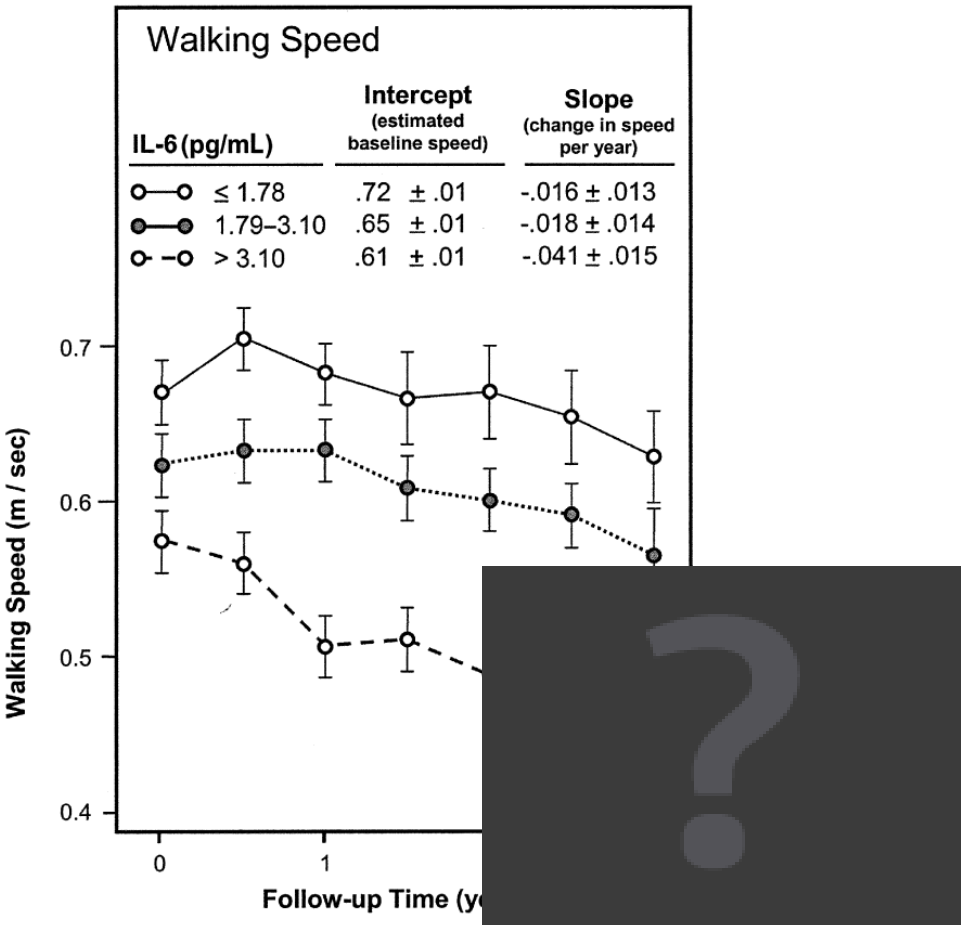


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Table 2. Cox Proportional Hazards Models Predicting Risk of Developing Mobility Disability, Activity of Daily Living (ADL) Disability, and Severe Limitation in Walking, According to Interleukin-6 (IL-6) Tertiles

	Mobility Disability* (n at Risk = 289)				ADL Disability† (n at Risk = 442)				Severe Limitation in Walking‡ (n at Risk = 445)			
	Most Parsimonious Model		Time-Dependent Knee Extensor Strength		Most Parsimonious Model		Time-Dependent Knee Extensor Strength		Most Parsimonious Model		Time-Dependent Knee Extensor Strength	
Independent Variables‖	Relative Risk (95% Confidence Interval)											
Serum IL-6 level, pg/mL												
≤1.78	—	Reference	—	Reference	—	Reference	—	Reference	—	Reference	—	Reference
1.79–3.10	1.07	(0.73–1.56)	1.09	(0.70–1.70)	1.05	(0.76–1.45)	0.98	(0.66–1.45)	0.82	(0.85–1.84)	0.97	(0.58–1.59)
>3.10	1.50	(1.01–2.27)	1.17	(0.72–1.90)	1.41	(1.01–1.98)	1.30	(0.86–1.95)	1.61	(1.09–2.38)	1.10	(0.82–1.96)
Potential confounders												
Age	1.05	(1.03–1.08)	1.05	(1.02–1.08)	1.04	(1.03–1.06)	1.05	(1.03–1.08)	1.06	(1.03–1.09)	1.08	(1.05–1.12)
Body mass index, kg/m²	‖		‖		1.03	(1.01–1.05)	1.03	(1.00–1.06)	‖		‖	
Geriatric depression score	1.05	(1.01–1.08)	1.05	(1.01–1.09)	‖		‖		‖		‖	
Level of difficulty walking 1/4 mile	1.31	(1.23–1.84)	1.48	(1.17–1.88)	1.36	(1.23–1.50)	1.38	(1.21–1.56)	1.40	(1.23–1.59)	1.24	(1.06–1.44)
Congestive heart failure	‖		‖		1.65	(1.04–2.63)	1.49	(0.84–2.63)	1.77			
Diabetes mellitus	2.01	(1.24–3.28)	2.47	(1.42–4.31)	‖		‖		1.64			
Chronic obstructive pulmonary disease	‖		‖		‖		‖		1.52			
Knee arthritis	1.43	(1.00–2.04)	1.56	(1.04–2.36)	‖		‖		‖			
Time-dependent covariate												
Knee extension strength¶			0.97	(0.94–0.99)			0.96	(0.93–0.99)				

Riassunto

- Livelli elevati di IL-6 si associano a più rapido decremento della forza muscolare degli arti inferiori e ad una più rapido declino della velocità del cammino
- Livelli elevati di IL-6 sono associati ad aumentato rischio di disabilità di movimento, disabilità nelle attività di base del vivere quotidiano e al rischio di grave limitazione nel cammino.
- Tuttavia quando il modello statistico considera anche la riduzione della forza muscolare degli arti inferiori queste associazione non sono più presenti
- Si può quindi ipotizzare che l'infiammazione acceleri la riduzione di massa e forza muscolare età correlata e questo faciliti la perdita di autonomia funzionale del soggetto anziano

Cardiovascular Disease, Interleukin-6, and Risk of Mortality in Older Women

The Women's Health and Aging Study

Stefano Volpato, MD, MPH; Jack M. Guralnik, MD, PhD; Luigi Ferrucci, MD, PhD; Jennifer Balfour, PhD; Paulo Chaves, MD; Linda P. Fried, MD, MPH; Tamara B. Harris, MD, MS

Background—Systemic chronic inflammation has been found to be related to all-cause mortality risk in older persons. We investigated whether specific chronic conditions, particularly cardiovascular disease (CVD), affect the association between high interleukin (IL)-6 level and mortality in a sample of disabled older women.

Methods and Results—IL-6 serum level was measured at baseline in 620 women ≥65 years old. The presence and severity of medical conditions was ascertained by standard criteria that used multiple sources of information. The sample was surveyed over the 3-year follow-up. After adjustment for potential confounders, compared with those in the lowest tertile, women in the highest IL-6 tertile were at higher risk of all-cause mortality. The presence of CVD, however, strongly affected the risk of mortality associated with high IL-6. Among women with prevalent CVD, those with high IL-6 levels had >4-fold risk of death (RR 4.6; 95% CI 2.0 to 10.5) compared with women in the lowest tertile, whereas the relative risk associated with high IL-6 among those without CVD was much lower and not significant (RR 1.8; 95% CI 0.7 to 4.2). Adjustment for all chronic diseases and disease severity measures, including ankle-brachial index, forced expiratory volume, and exercise tolerance, did not change the results.

Conclusions—IL-6 level is helpful in identifying a subgroup of older CVD patients with high risk of death over a period of 3 years. Systemic inflammation, as measured by IL-6, may be related to the clinical evolu
CVD. (*Circulation*. 2001;103:947-953.)

TABLE 2. Crude and Adjusted Relative Risks of All-Cause Mortality by Baseline IL-6 Tertile

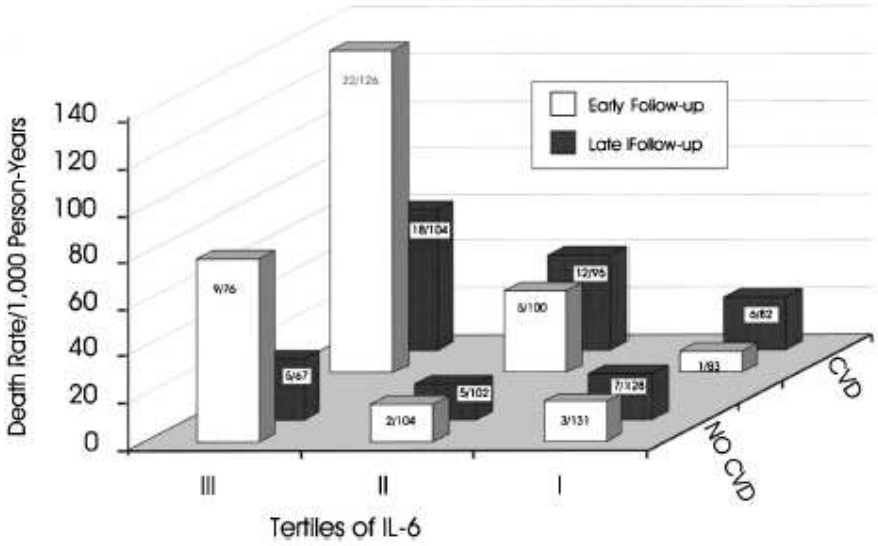
			All-Cause Mortality Relative Risk (95% CI)			
	n	Deaths	Model 1	Model 2	Model 3	Model 4
IL-6 serum level, pg/mL						
≤1.78	214	17	1	1	1	1
1.79–3.10	204	24	1.51 (0.81–2.81)	1.32 (0.70–2.47)	1.08 (0.57–3.04)	1.03 (0.55–1.95)
>3.10	202	54	3.83 (2.22–6.62)	3.54 (2.03–6.17)	2.63 (1.48–4.96)	2.03 (1.08–3.83)
Age, y				1.07 (1.04–1.10)	1.06 (1.03–1.09)	1.06 (1.03–1.10)
Smoking						
Never				1	1	1
Former				1.45 (0.93–2.28)	1.24 (0.76–1.98)	1.21 (0.75–1.94)
Current				0.95 (0.48–1.90)	0.82 (0.38–1.74)	0.81 (0.38–1.73)
BMI						
<21.45				1.72 (0.99–3.01)	1.99 (1.10–3.59)	2.03 (1.09–3.77)
21.45–31.58				1	1	1
≥31.58				1.23 (0.74–2.05)	1.09 (0.65–1.83)	1.02 (0.60–1.74)
CHF					2.35 (1.41–3.91)	2.25 (1.34–3.78)
CHD					1.25 (0.84–1.93)	1.29 (0.82–2.03)
Diabetes					1.59 (0.90–2.78)	1.49 (0.84–2.67)
ABI					0.28 (0.11–0.73)	0.30 (0.11–0.78)
FEV_1, L					0.54 (0.27–1.06)	0.58 (0.29–1.14)
Exercise tolerance (<2.5 METs)					1.94 (1.17–3.22)	1.96 (1.17–3.27)
CRP, mg/L						
≤2						
2.1–7.4						1.16 (
≥7.5						1.65 (
Albumin, g/dL						0.76 (

Relative risks and 95% CI are not displayed for race, income, COPD, PAD, orthopnea and ankle edema, chest pa
disability, and medication use because these variables were not independently associated with the risk of mortality and w
from models 3 and 4.

TABLE 4. Association Between Baseline IL-6 and Cause-Specific Mortality

	CVD Mortality Relative Risk (95% CI)			Non-CVD Mortality* Relative Risk (95% CI)		
	Deaths	Unadjusted	Adjusted†	Deaths	Unadjusted	Adjusted†
IL-6 serum level, pg/mL						
≤1.78	9	1	1	6	1	1
1.79–3.10	11	1.34	1.08	12	2.18	1.67
		(0.56–3.24)	(0.44–2.67)		(0.81–5.81)	(0.62–4.53)
>3.10	21	2.99	2.52	30	6.32	3.87
		(1.37–6.53)	(1.21–4.55)		(2.63–15.2)	(1.47–10.16)

*Malignancies, n=20; infectious diseases, n=6; other, n=22.
†Adjusted for age, BMI, smoking, and CRP.



Age-adjusted all-cause mortality rates/1000 person-years by IL-6 levels, history of CVD, and follow-up period. Figures on bars are numbers of deaths and subjects at risk.

Conclusioni

- In donne anziane con disabilità fisica iniziale, elevati valori di IL-6 si associano a:
  - più rapido decremento della forza muscolare
  - aumentato rischio di disabilità, mediato dalla perdita di forza
  - aumentato rischio di morte per CVD e per tutte le cause,
  - indipendentemente dalla presenza e gravita di patologie concomitanti
- IL-6 appare quindi associata ad alcune delle complicanze principale della sindrome da fragilità dell'anziano e può quindi essere proposta come biomarcatore di questa condizione