



Congresso Nazionale SIGG

Geriatrics e rinascita



Roma, 1 -4 dicembre 2021

Corso

Fragilità e stato nutrizionale

***La fragilità fisica e nutrizionale nel soggetto anziano:
etiopatogenesi e significato clinico***



Prof. P. Abete
Dipartimento di Scienze Mediche Traslazionali
Università di Napoli Federico II

Frail Elderly

If the question is: who is the “frail” patient?

The answer is: “...think about the older, the more sick, the most critical and the most complicated of your patients.”

*modified from: Hazzard W.R.
Principles of Geriatric Medicine and Gerontology.
McGraw-Hill, 1998.*



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***La fragilità fisica nel soggetto anziano:
etiopatogenesi e significato clinico
Il ruolo dello stato nutrizionale***



-
- **Vulnerability**
 - **Multidimensional frailty**
 - **Physical frailty**
 - **Nutritional frailty**
 - **Physical & Nutritional frailty**



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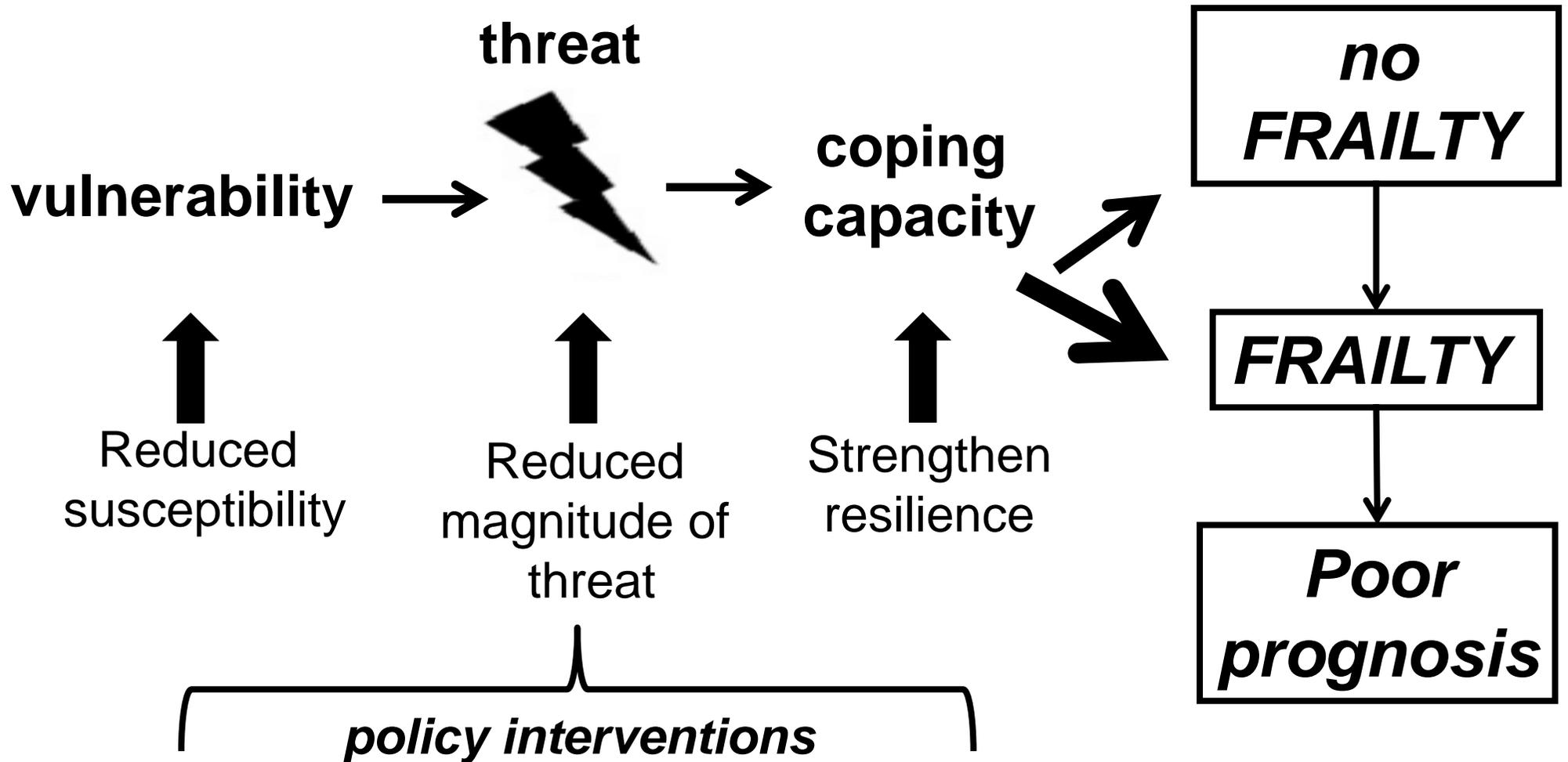
-
- **Vulnerability**
 - Multidimensional frailty
 - Physical frailty
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***VULNERABILITY* → FRAILTY**

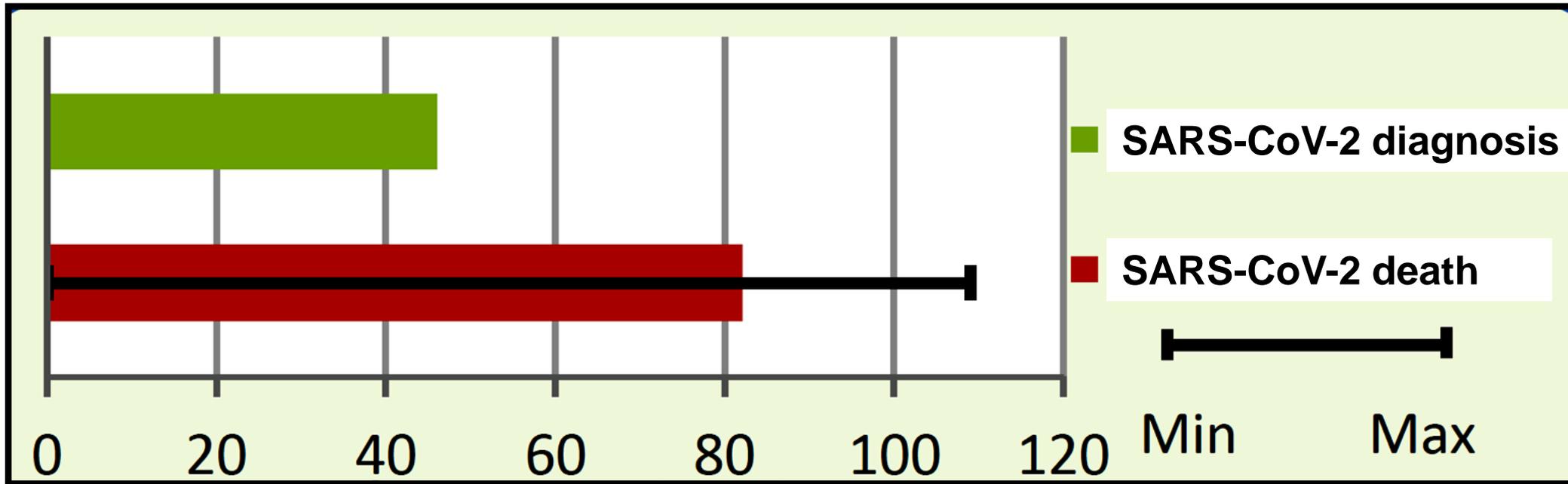
The definition of ***frailty*** remains contested, but it can be considered as a progressive age-related decline in physiological systems that results in decreased reserves of intrinsic capacity, which confers extreme ***vulnerability*** to stressors and increases the risk of a range of adverse health outcomes.

***VULNERABILITY* → FRAILTY**

VULNERABILITY* → *FRAILTY



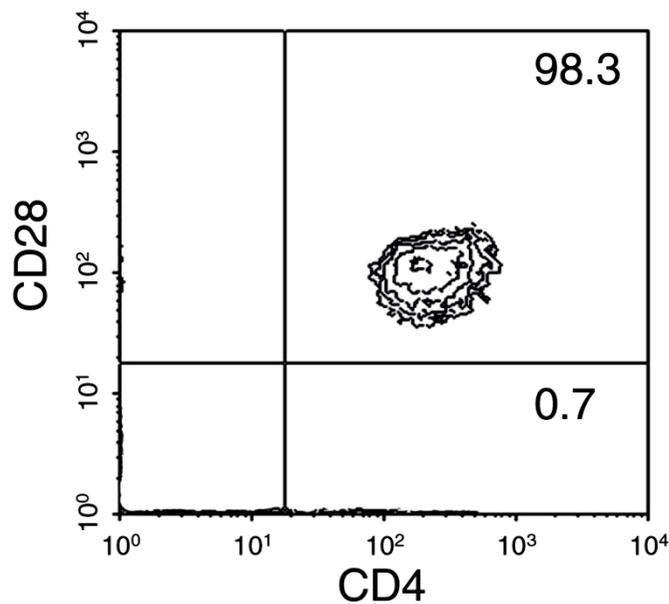
Median age of DEATH and DIAGNOSIS of SARS-CoV-2 positive subjects



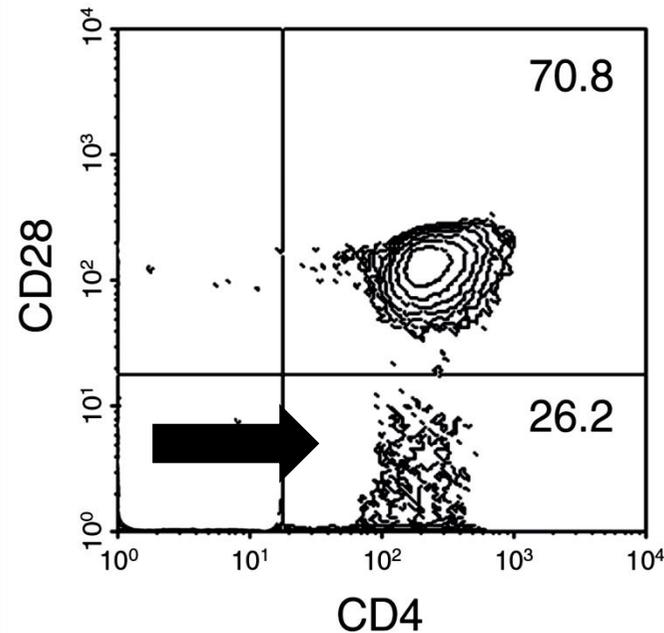
Death median age > 80 years old !

CD28null T cells is a key predictor of immune incompetence in the elderly

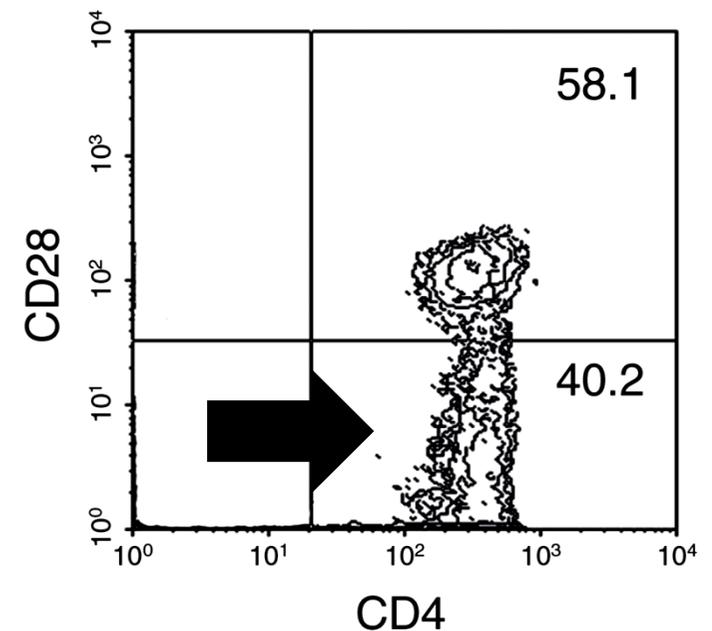
22 years
CD3+CD4+ gated



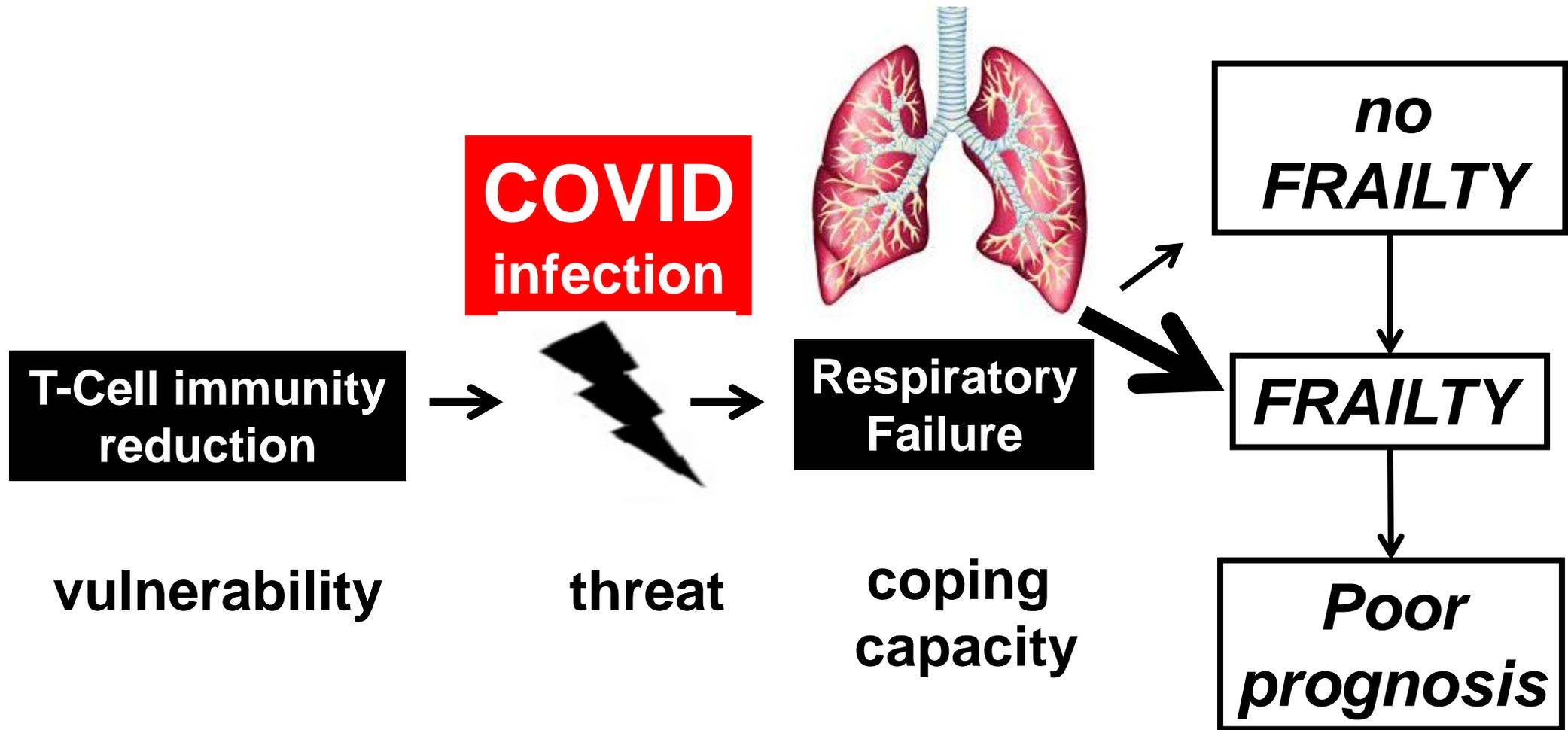
55 years
CD3+CD4+ gated



77 years
CD3+CD4+ gated

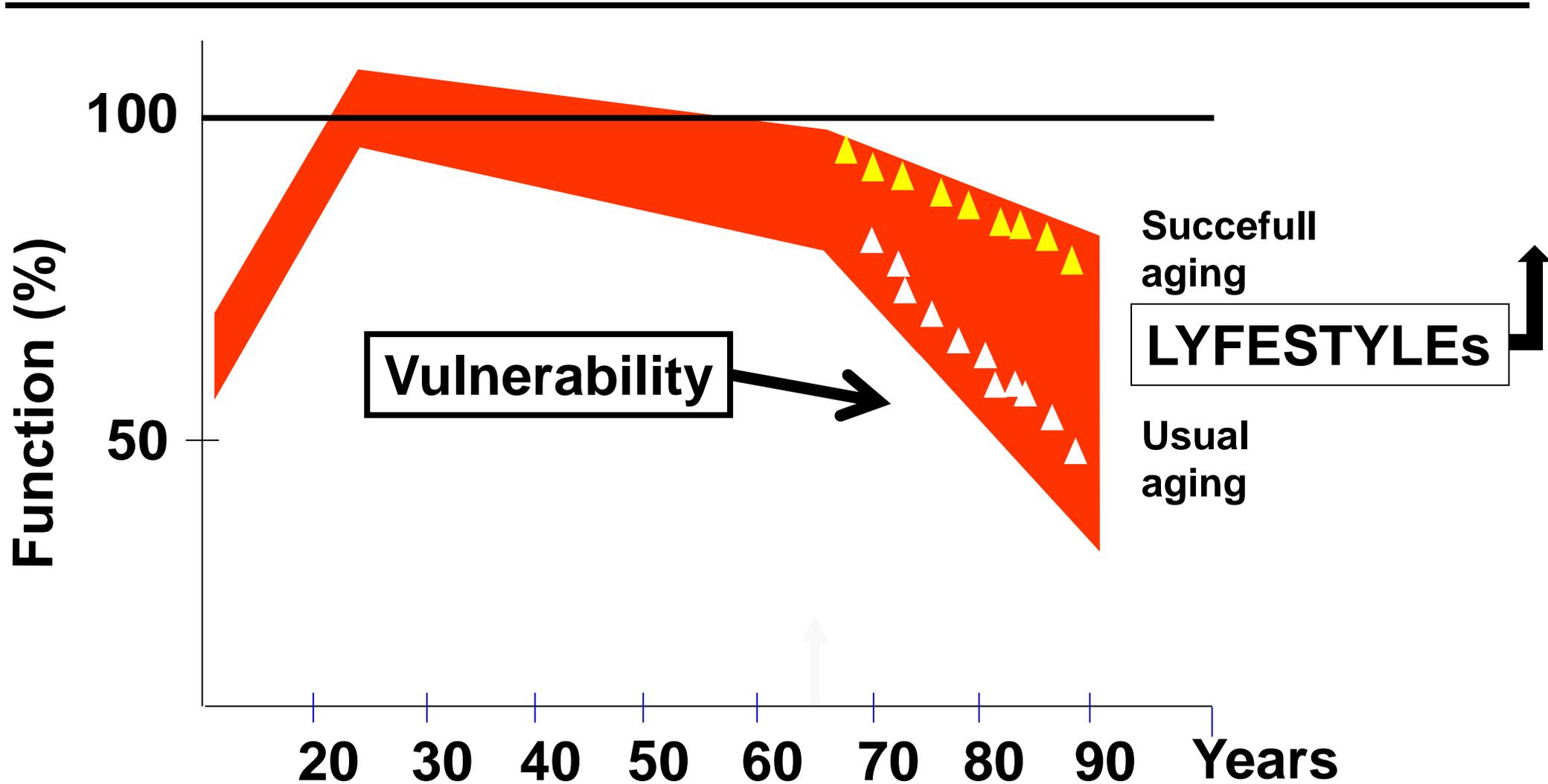


VULNERABILITY → ***FRAILTY***



Aging models

“from vulnerability to frailty”





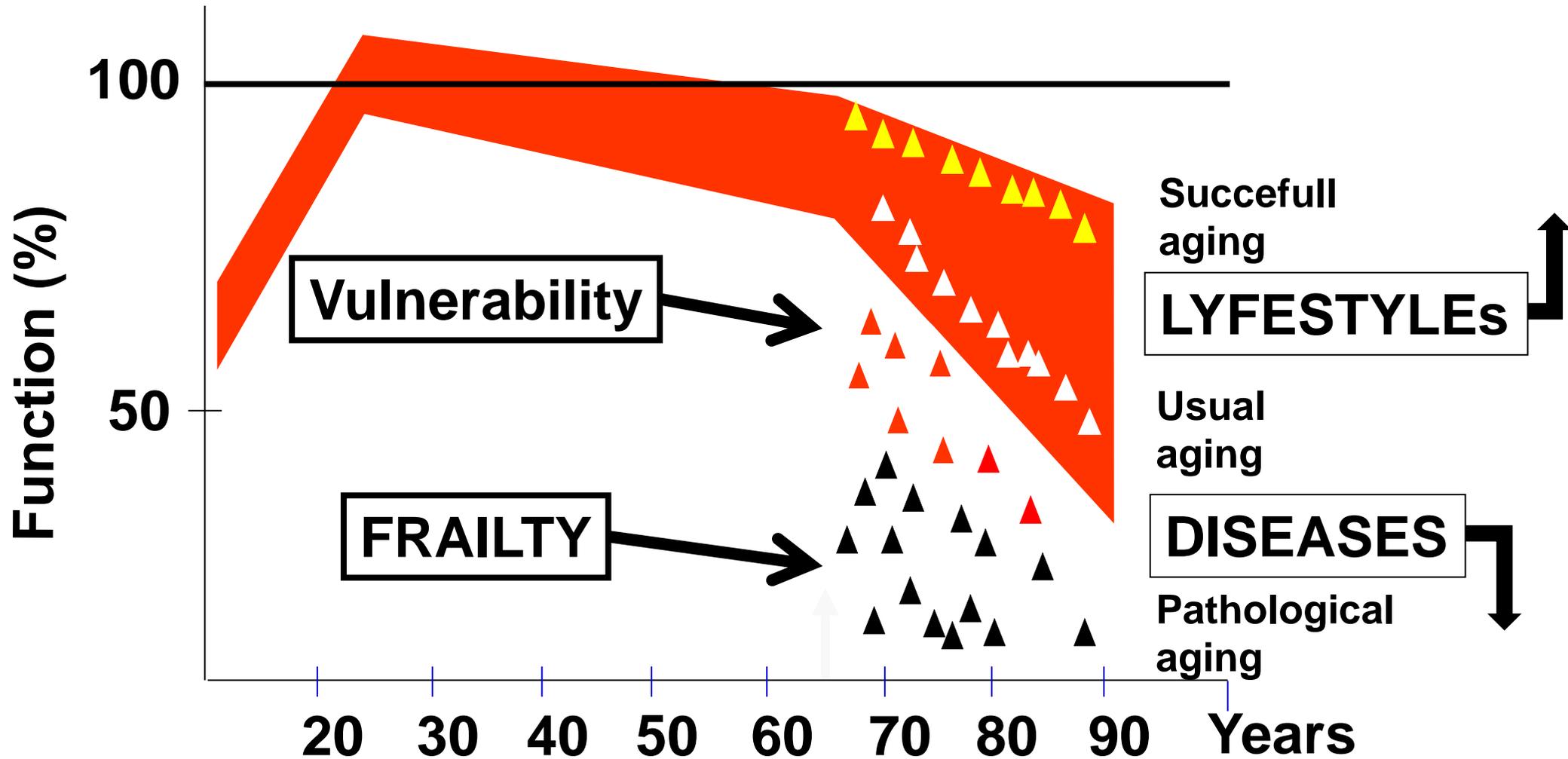
Johanna Quaas
86 years old

Very successful aging!



Aging models

“from vulnerability to frailty”



Immobility syndrome in the elderly.



...very pathological aging!



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- Vulnerability
 - **Multidimensional frailty**
 - Physical frailty
 - Nutritional frailty
 - Physical & Nutritional frailty

in 1984

“geriatric medicine”

begins.....

LAURENCE Z. RUBENSTEIN, M.D., M.P.H., KAREN R. JOSEPHSON, M.P.H., G. DARRYL WIELAND, PH.D., M.P.H.,
PATRICIA A. ENGLISH, M.S., JAMES A. SAYRE, DR.P.H., AND ROBERT L. KANE, M.D.

Abstract We randomly assigned frail elderly inpatients with a high probability of nursing-home placement to an innovative geriatric evaluation unit intended to provide improved diagnostic assessment, therapy, rehabilitation, and placement. Patients randomly assigned to the experimental (n = 63) and control (n = 60) groups were equivalent at entry.

At one year, patients who had been assigned to the geriatric unit had much lower mortality than controls (23.8 vs. 48.3 per cent, $P < 0.005$) and were less likely to have initially been discharged to a nursing home (12.7 vs. 30.0 per cent, $P < 0.05$) or to have spent any time in a nursing

home during the follow-up period (26.9 vs. 46.7 per cent, $P < 0.05$). The control-group patients had substantially more acute-care hospital days, nursing-home days, and acute-care hospital readmissions. Patients in the geriatric unit were significantly more likely to have improvement in functional status and morale than controls ($P < 0.05$). Direct costs for institutional care were lower for the experimental group, especially after adjustment for survival.

We conclude that geriatric evaluation units can provide substantial benefits at minimal cost for appropriate groups of elderly patients, over and above the benefits of traditional hospital approaches. (N Engl J Med 1984; 311:1664-70.)

Physical

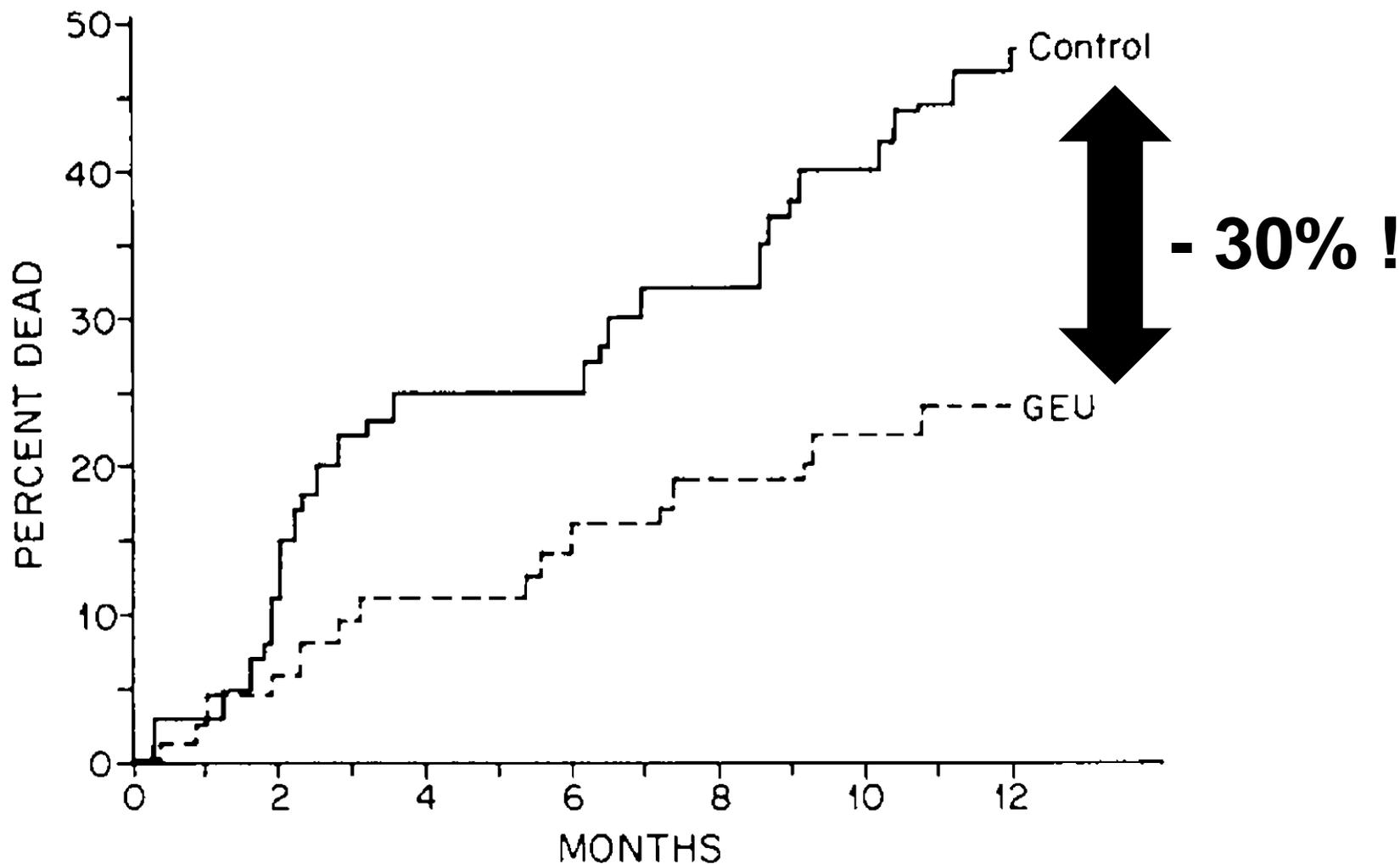
Nutritional

**Geriatric
Multidimensional
Evaluation**

Mental

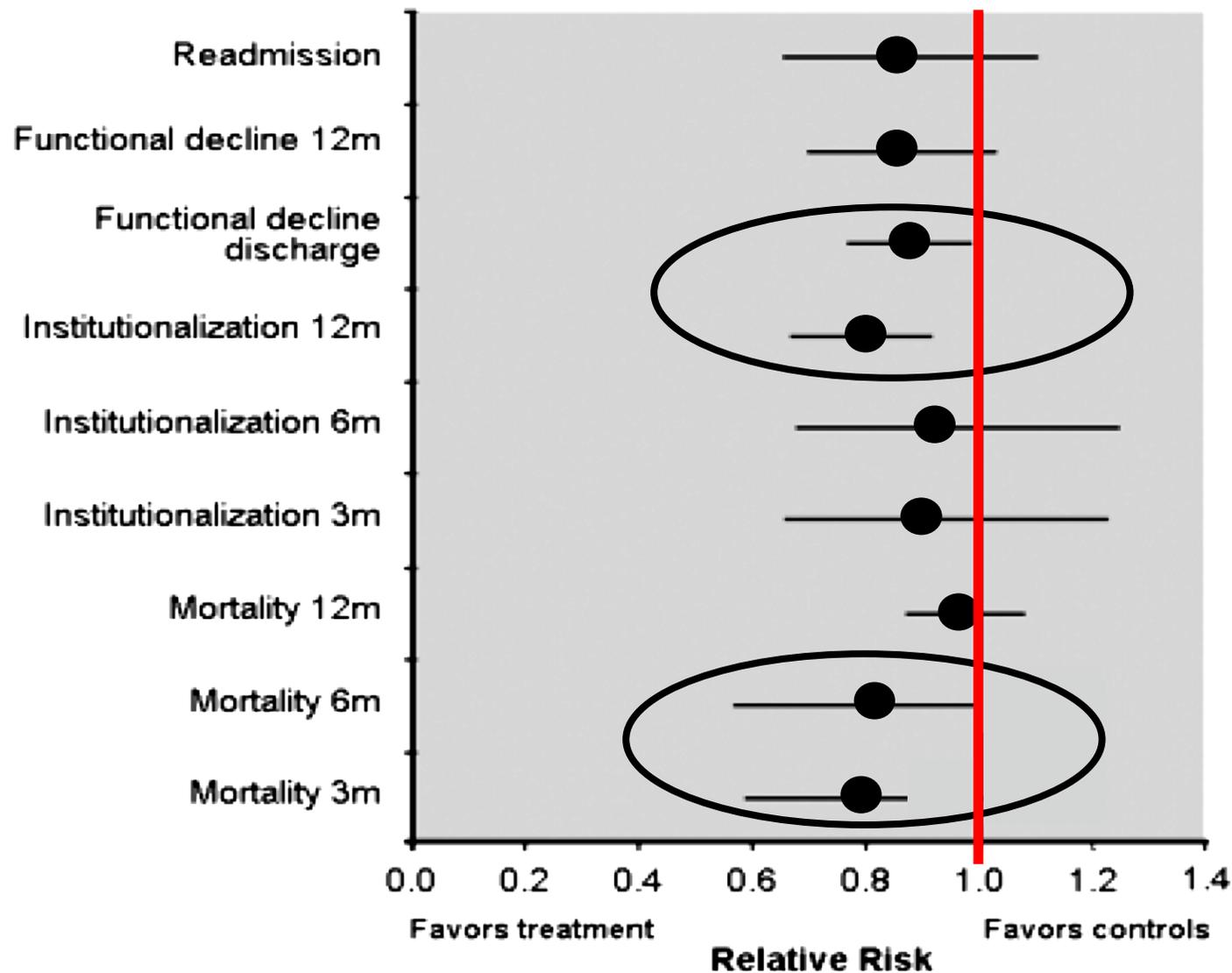
Social

One year mortality Curves for Geriatric Evaluation Unit (GEU) and control patients



Effectiveness of multidimensional geriatric evaluation

“A Systematic Review and Meta-Analysis”



Physical

Fried L et al.
2001

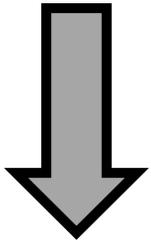
Nutritional

**Multidimensional
FRAILTY**

Rockwood K et al.
2009

Mental

Social



ADVERSE AOUTCOMES
*Disability, institutionalization,
death*

Research article

Open Access

A standard procedure for creating a frailty index

Samuel D Searle¹, Arnold Mitnitski^{1,2,3}, Evelyne A Gahbauer⁴,
Thomas M Gill⁴ and Kenneth Rockwood*^{1,2,5}

Address: ¹Geriatric Medicine Research Unit, Dalhousie University & Capital District Health Authority, Halifax, Canada, ²Department of Medicine, Dalhousie University, Halifax, Canada, ³Department of Mathematics & Statistics, Dalhousie University, Halifax, Canada, ⁴Department of Internal Medicine, Yale University School of Medicine, New Haven, CT 06504, USA and ⁵Division of Geriatric Medicine, Dalhousie University, Halifax, Canada

Email: Samuel D Searle - ssearle@dal.ca; Arnold Mitnitski - arnold.mitnitski@dal.ca; Evelyne A Gahbauer - evelyne.gahbauer@yale.edu; Thomas M Gill - thomas.gill@yale.edu; Kenneth Rockwood* - kenneth.rockwood@dal.ca

* Corresponding author

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Help Bathing
Help Dressing
Help getting in/out of Chair
Help Walking around house
Help Eating
Help Grooming
Help Using Toilet
Help up/down Stairs
Help lifting 10 lbs
Help Shopping

Yes = 1, No = 0
Yes = 1, No = 0

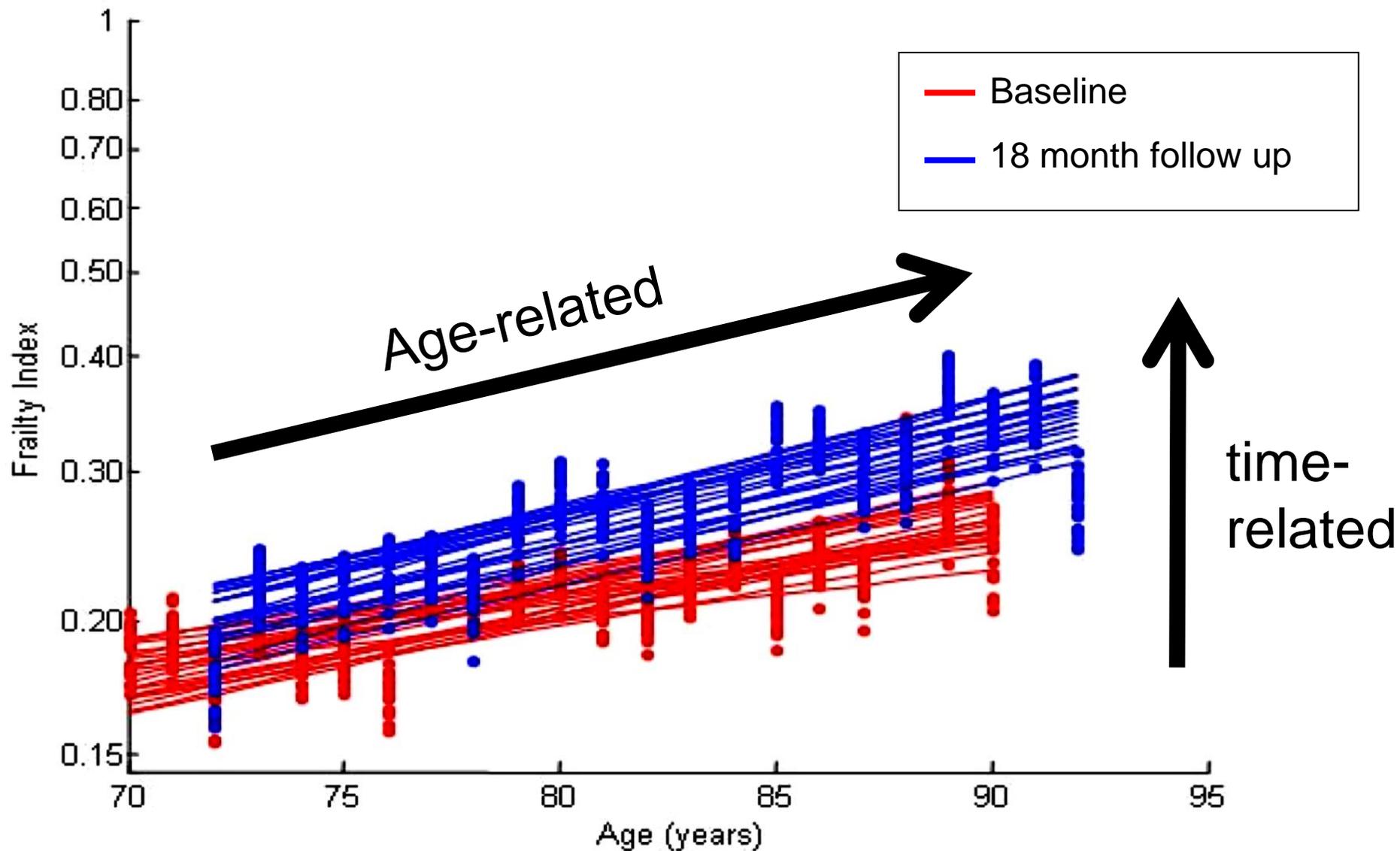
Help with H
Help with m
Help taking
Help with F
Lost more t
Self Rating o
How Health
Stayed in Be
Cut down o
Walk outsid
Feel Everyth
Feel Depres
Feel Happy
Feel Lonely
Have Troub
High blood
Heart attack

List of “40” Variables included in the “Frailty index” with related cut-point

CHF
Stroke
Cancer
Diabetes
Arthritis
Chronic Lung Disease
MMSE
Peak Flow
Shoulder Strength
BMI
Grip Strength
Usual Pace
Rapid Pace

Yes = 1, Suspect = 0.5, No = 0
Yes = 1, Suspect = 0.5, No = 0
Yes = 1, Suspect = 0.5, No = 0
Yes = 1, Suspect = 0.5, No = 0
<10 = 1, 11–17 = 0.75, 18–20 = 0.5, 20–24 = 0.25, >24 = 0
See Table 2
See Table 2

Variance in the Slope of the Frailty Index





ORIGINAL ARTICLE

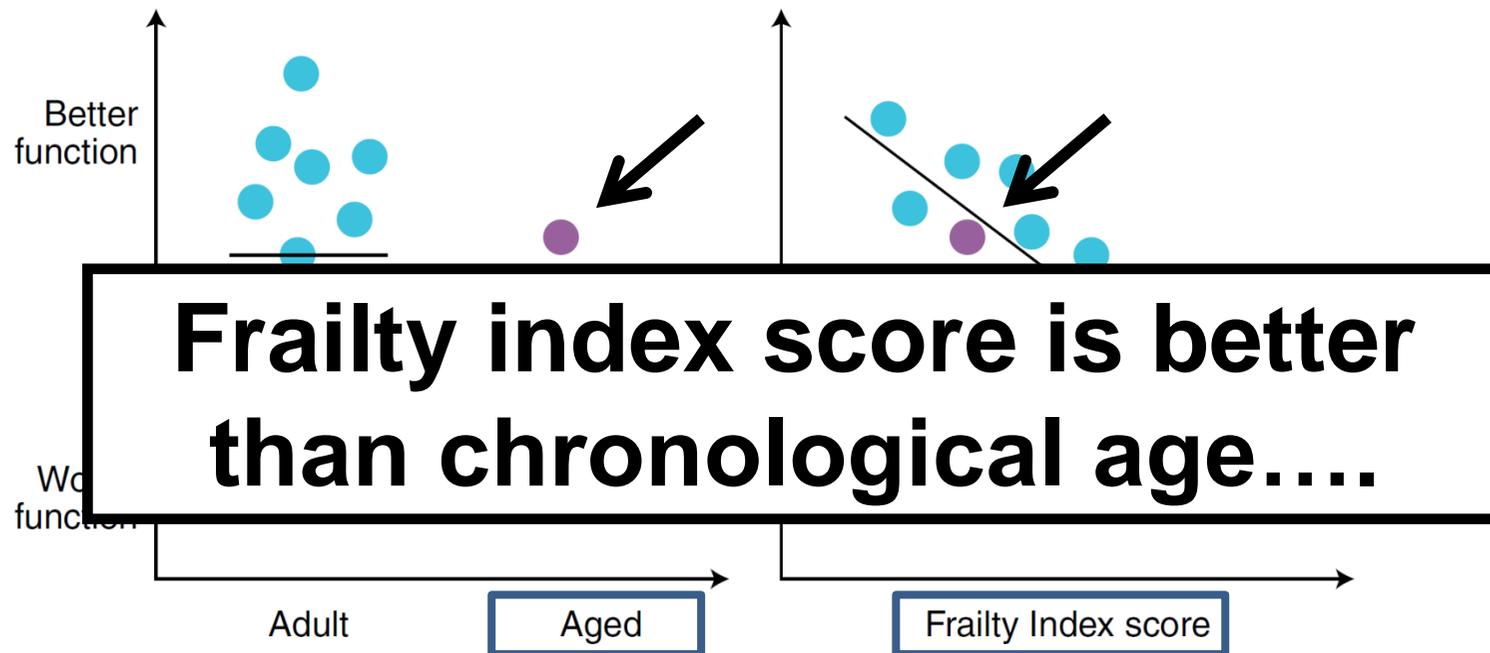
The Italian version of the “frailty index” based on deficits in health: a validation study

Pasquale Abete¹ · Claudia Basile¹ · Giulia Bulli¹ · Francesco Curcio¹ ·
Ilaria Liguori¹ · David Della-Morte^{2,3} · Gaetano Gargiulo^{1,4} · Assunta Langellotto^{1,5} ·
Gianluca Testa^{1,6} · Gianluigi Galizia^{1,7} · Domenico Bonaduce¹ · Francesco Cacciatore¹



The degree of frailty as a translational measure of health in aging

Age-dependent deterioration is heterogeneous and is graded by frailty index scores.





Corso
Fragilità e stato nutrizionale

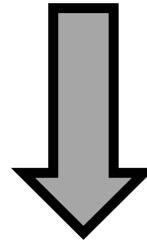
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Physical

FRAILTY



ADVERSE AOUTCOMES
*Disability, institutionalization,
death*

Frailty in older adults: evidence for a phenotype

| Frailty criteria | Parameters |
|-------------------------|---|
| Weight loss | Loss of ≥ 5 kg in prior 12 months, unintentional |
| Exhaustion | Response of "a moderate amount of the time (3–4 days)" or "most of the time" to the CES-D scale item: "I felt that everything I did was an effort" during the past week |

| | |
|------------------|---|
| Frail | = 3 of the following findings |
| Pre-frail | = 1 or 2 of the following findings |

provided by Fried et al. (2001) were adopted

| | |
|------------------------------|--|
| Slowness | Time in seconds to complete a 4-m walk at usual pace. Gender- and height-specific cutoff points provided by Fried et al. (2001) were adopted |
| Low physical activity levels | Physical Activity Scale for the Elderly (PASE); cut-points: Men < 64, women < 52 (Rothman et al., 2008) |

**A PROGRAM TO PREVENT FUNCTIONAL DECLINE IN PHYSICALLY FRAIL,
ELDERLY PERSONS WHO LIVE AT HOME**

THOMAS M. GILL, M.D., DOROTHY I. BAKER, PH.D., R.N.-C.S., MARGARET GOTTSCHALK, P.T., M.S.,
PETER N. PEDUZZI, PH.D., HEATHER ALLORE, PH.D., AND AMY BYERS, M.P.H.

Persons were considered PHYSICALLY FRAIL if

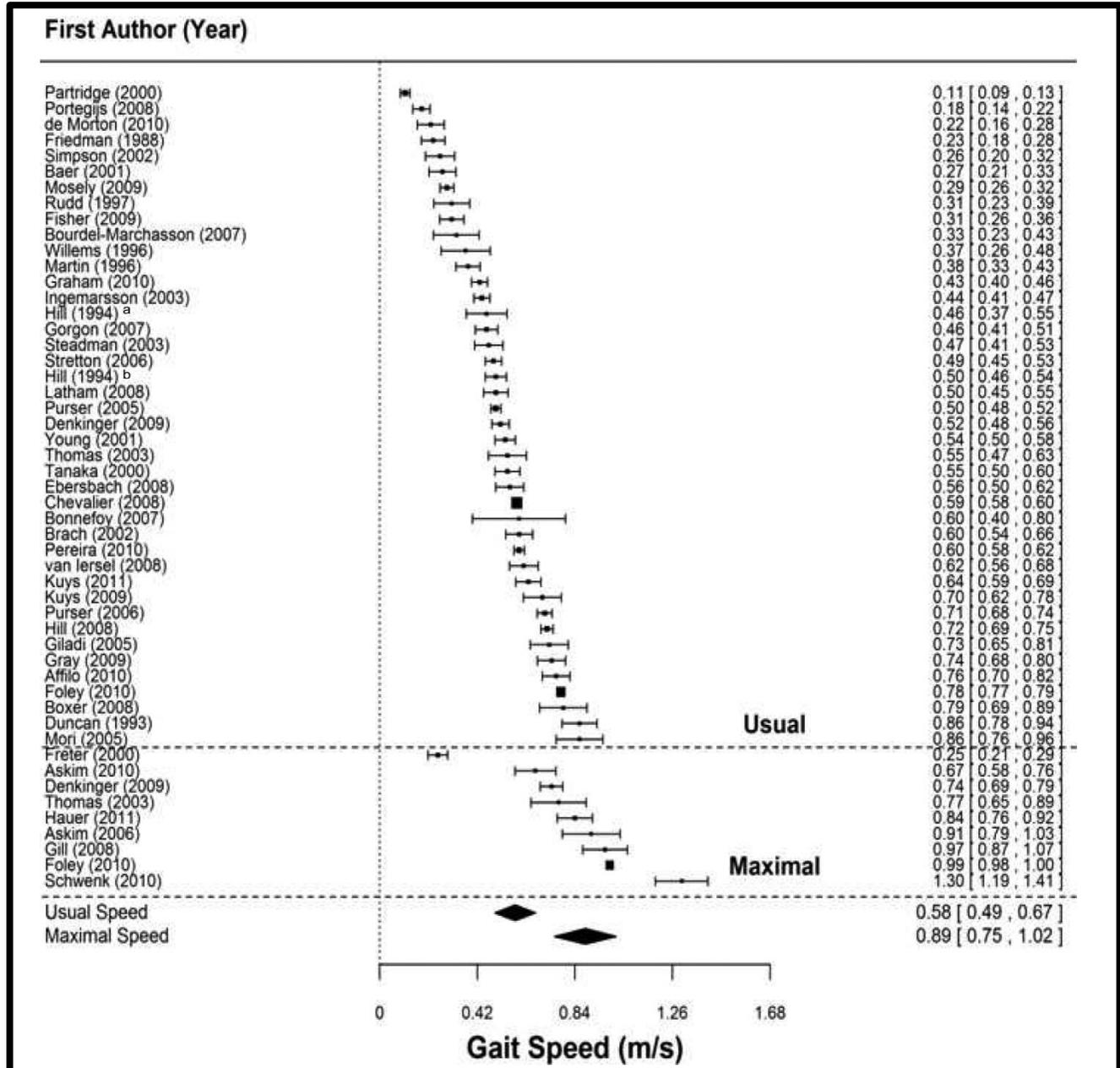
**they required more than 10 seconds to perform a
rapid-gait test (i.e., to walk along a 10-ft [3.0-m]
course and back as quickly as possible)**

or

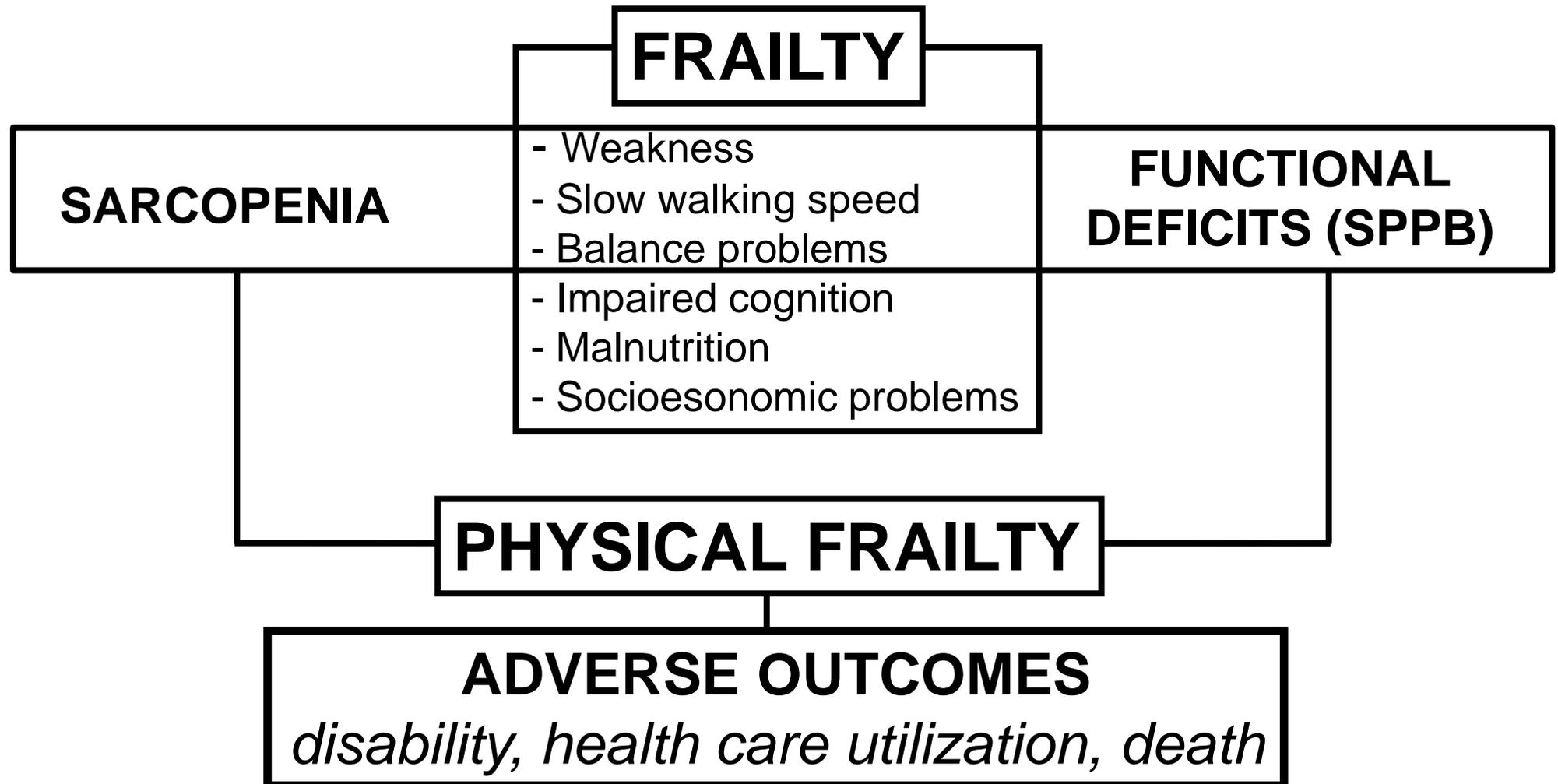
**if they could not stand up from a seated position
in a hardback chair with their arms folded.**

Gait speed as a predictor of poor clinical outcomes

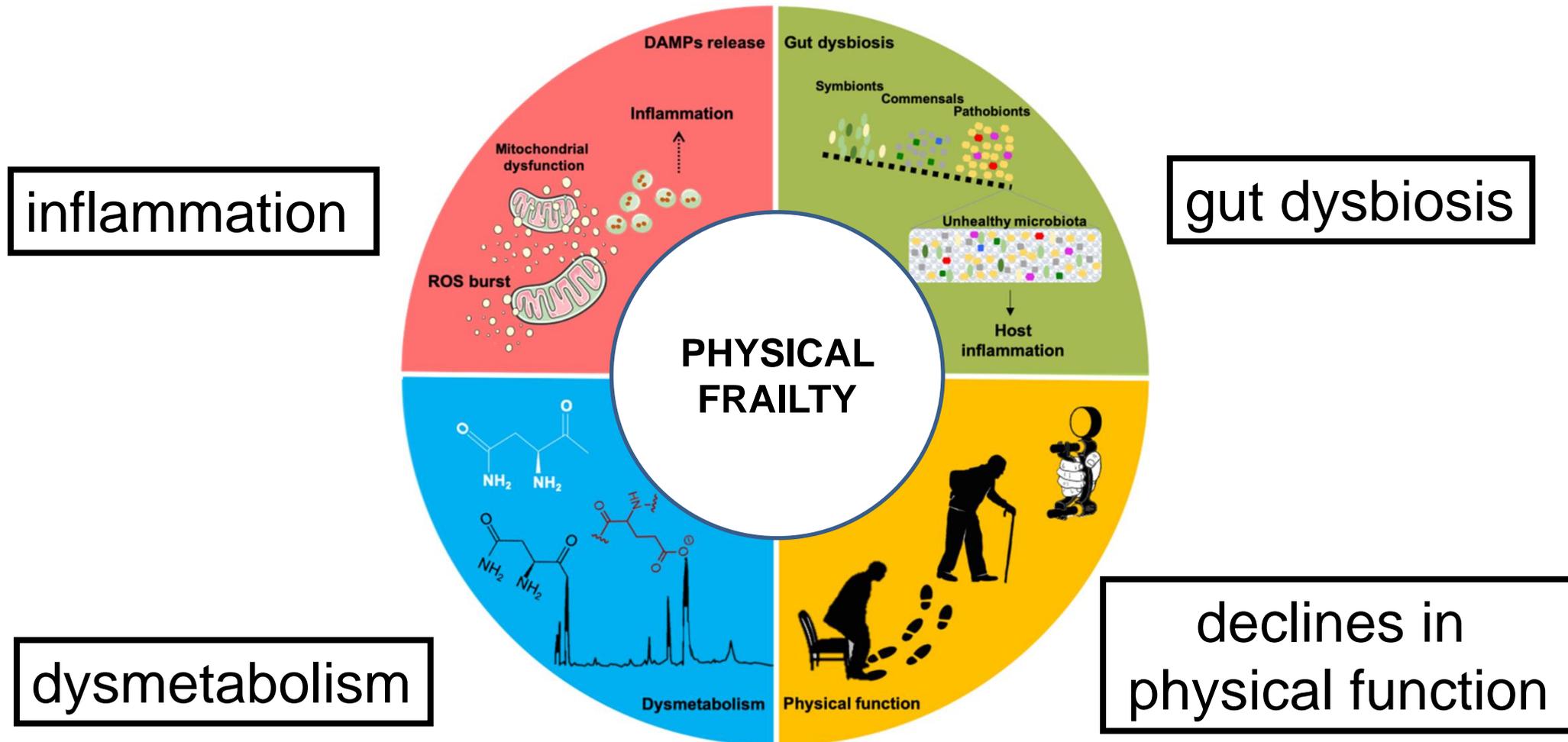
Timed over a short distance (maximum 15 m)
 Mean gait speeds for
Usual = 0.58 m/s
Maximal = 0.89 m/s



Frailty, Physical Frailty, Sarcopenia: A New Conceptual Model



Schematic representation of the main pathophysiological pathways contributing to physical frailty

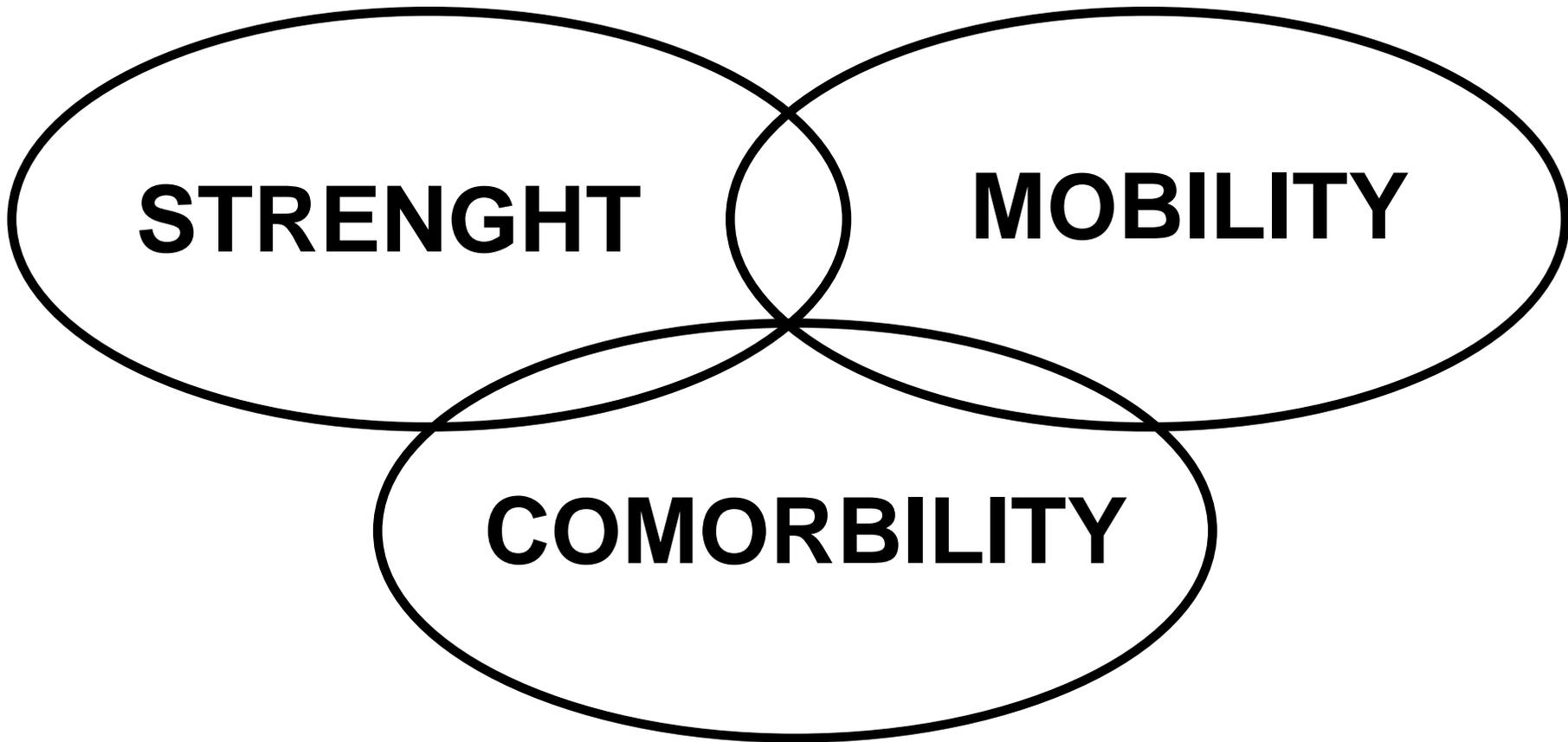


**“physical”
FRAILTY**

STRENGTH

MOBILITY

COMORBIDITY



“physical” FRAILTY - 1

STRENGTH

- Lifting an object that weighs over 5 kg
- Weakness in arms and/or legs
- Climbing stairs
- Calf muscle circumference
- Muscle strength (grip strength)
- Muscle mass (bioimped.or DEXA)

} **SARCOPENIA**

SARCOPENIA

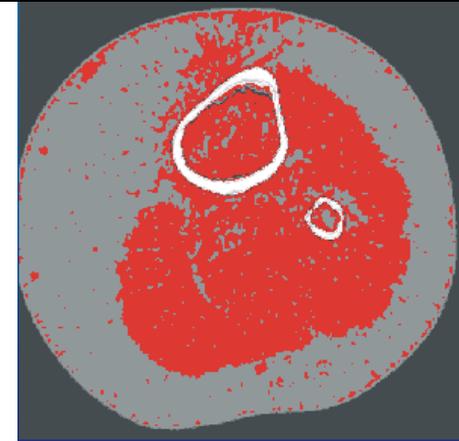
Hand-Grip = 23.7 kg

Hand-Grip = 3.75 kg

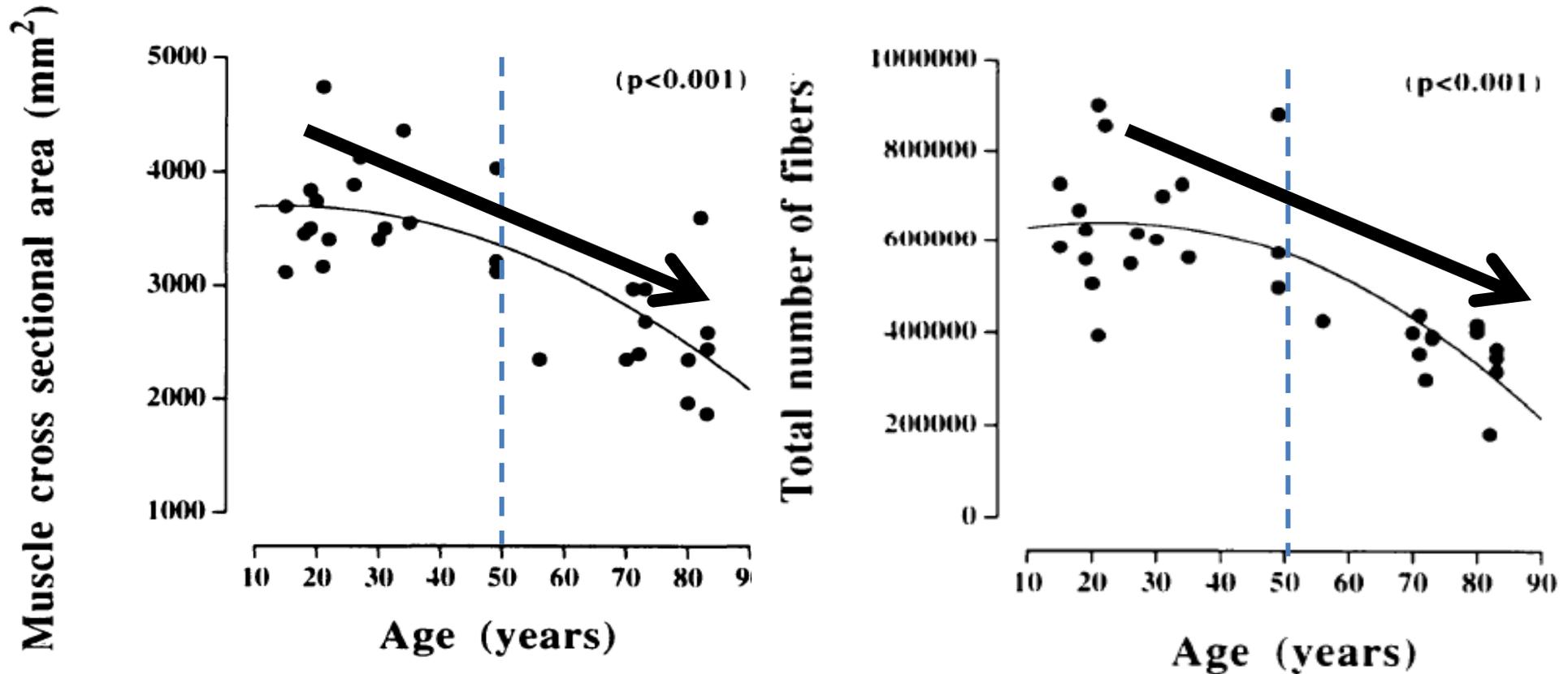


“SARCOPENIA”

Loss of skeletal muscle mass and strength that
occurs with advancing age
associated to adverse outcomes.



Age-related muscle modifications



**Age-related changes
in neuro-muscular
function**

**Age-related changes
to the systemic
environment**

↓ **PROTEIN-SYNTHESIS**

↑ **MYOCYTE LOSS**

SARCOPENIA

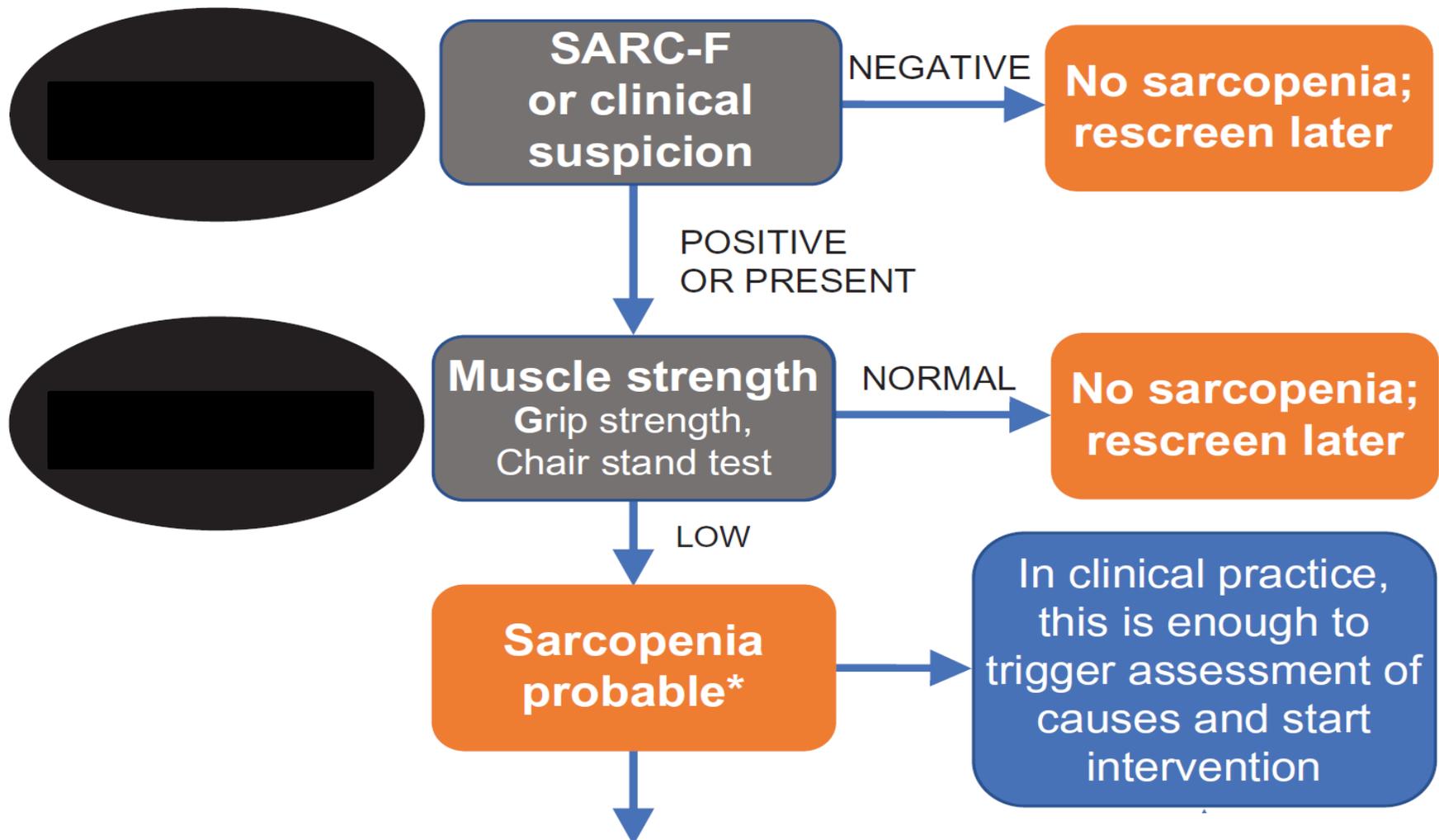
↓ **REGENERATION**

↑ **PROTEIN-LYSIS**

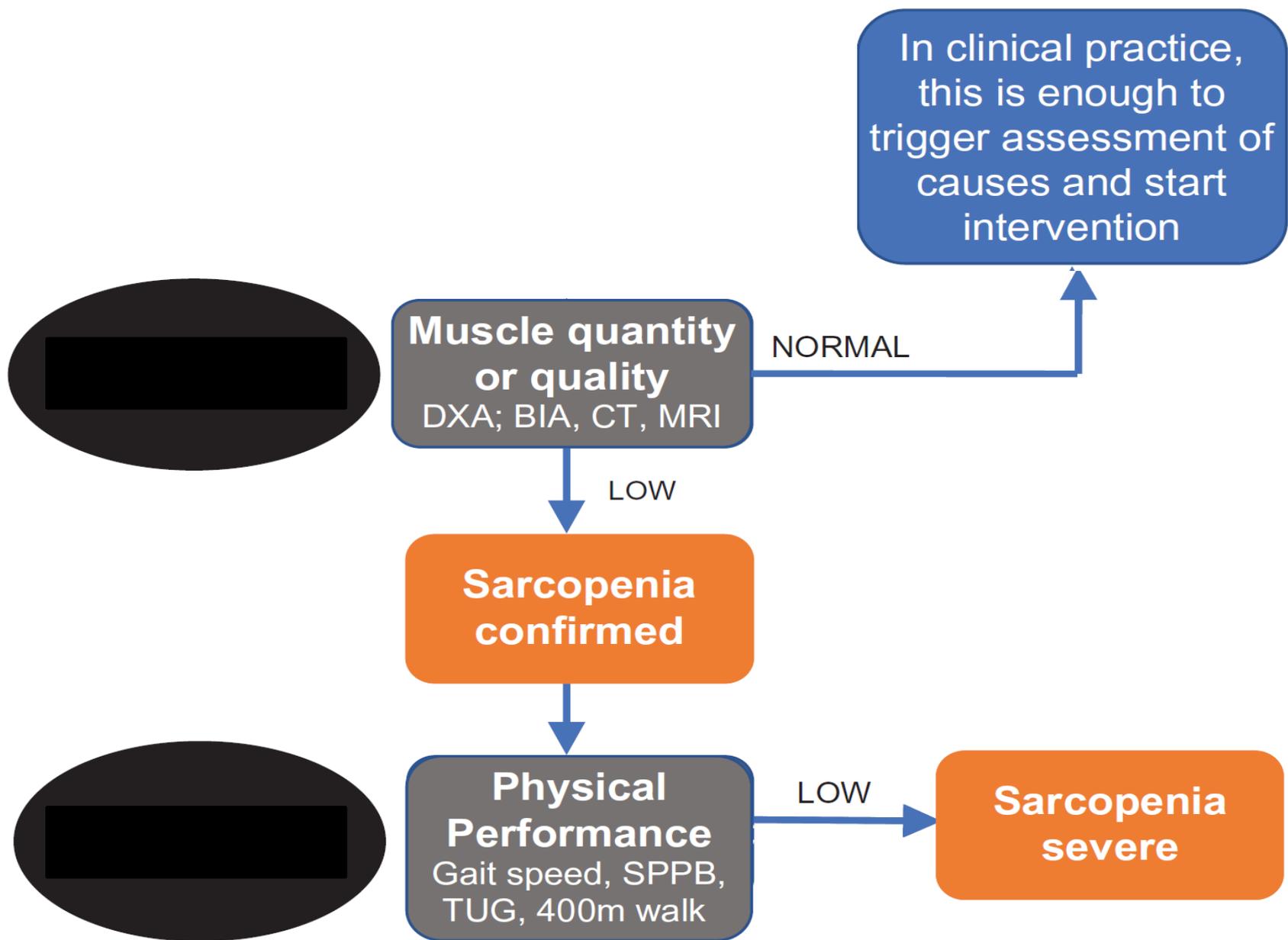
**Behavior-
mediated
pathways**

**Alterations in
muscle protein
turnover**

**Disease-
mediated
pathways**



*Sarcopenia: revised European consensus on definition and diagnosis,
Age & Ageing 2018*



Sarcopenia: revised European consensus on definition and diagnosis, Age & Ageing 2018

SARCOPENIA and clinical events in older adults InCHIANTI study

| | No Sarcopenia (<i>n</i> = 483) | Sarcopenia (<i>n</i> = 55) | | |
|--|------------------------------------|-----------------------------|----------|----------|
| | | Unadjusted | Model 1* | Model 2† |

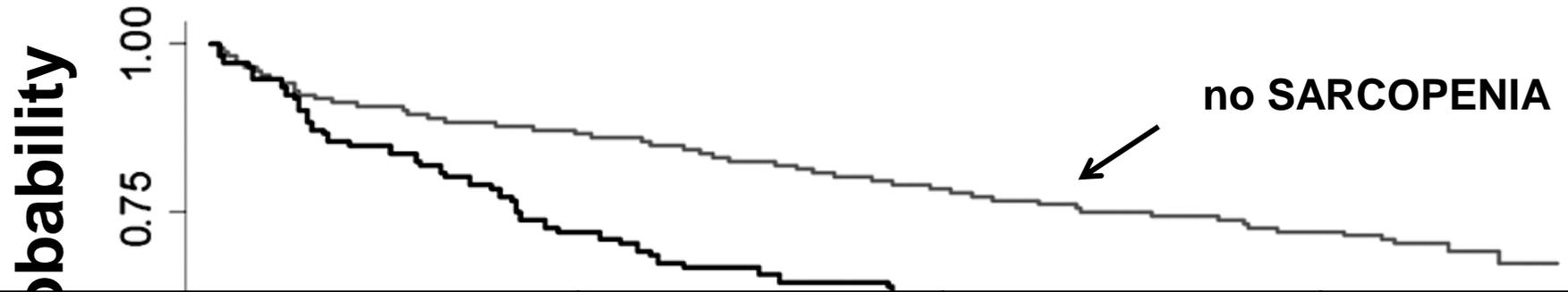
| | |
|------------------------|---------------|
| Disability | ↑ ≈ 3 times |
| Hospitalization | ↑ ≈ 1.5 times |
| Mortality | ↑ ≈ 2 times |

| Mortality | | | | |
|-----------|----|-------------|-------------|-------------|
| Events | 38 | | 17 | |
| HR | 1 | 4.28 | 2.12 | 1.88 |
| 95% CI | — | (2.42–7.59) | (1.05–4.30) | (0.91–3.91) |

Model 1: Adjusted for age, gender.

Model 2: Adjusted for age, gender, education, BMI, comorbidities, hemoglobin

3-Year Survival Prognostic Value in Older Hospitalized Adults with SARCOPENIA: The GLISTEN Study



| <i>Model</i> | 1 | 2 | 3 |
|--|----------------------------|----------------------------|--|
| <i>HR=Hazard Ratio; CI=confidence interval</i> | 2.24 (1.64–3.07) | 1.87 (1.35–2.59) | 1.84 (1.33–2.57) |
| <i>Adjusted for</i> | unadjusted | age and gender | age, gender, SPMSQ, ADL lost, comorbidity |

0

6

12

18

24

30

36

Months

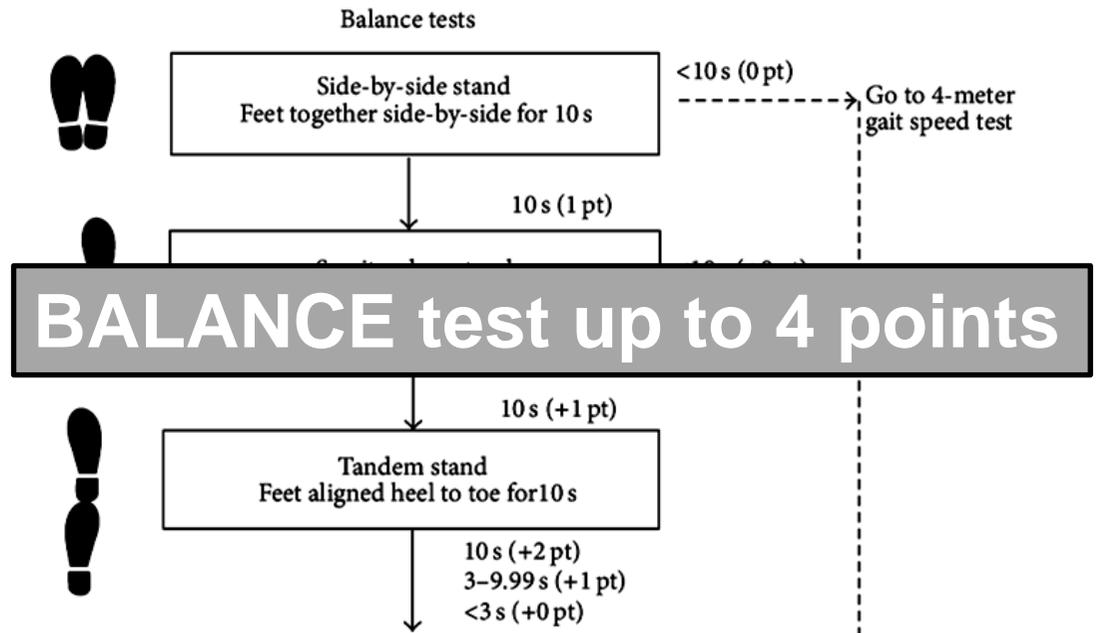
“physical” FRAILTY - 2

MOBILITY

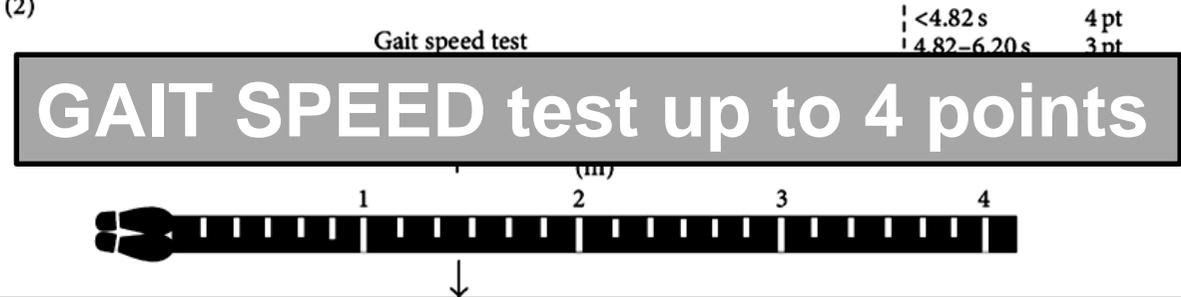
- Balance tests
 - Gait speed (4 or 3 meters)
 - Chair stand test
 - Physical Activity Scale for the Elderly (*PASE*)
- Short Physical Performance Battery (*SPPB*)**

Short Performance Physical Battery (SPPB) from 0 to 12

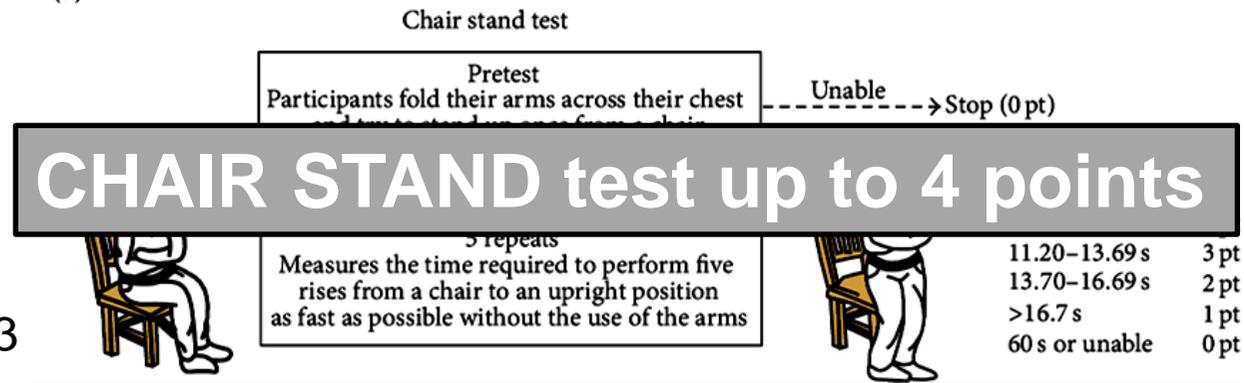
(1)



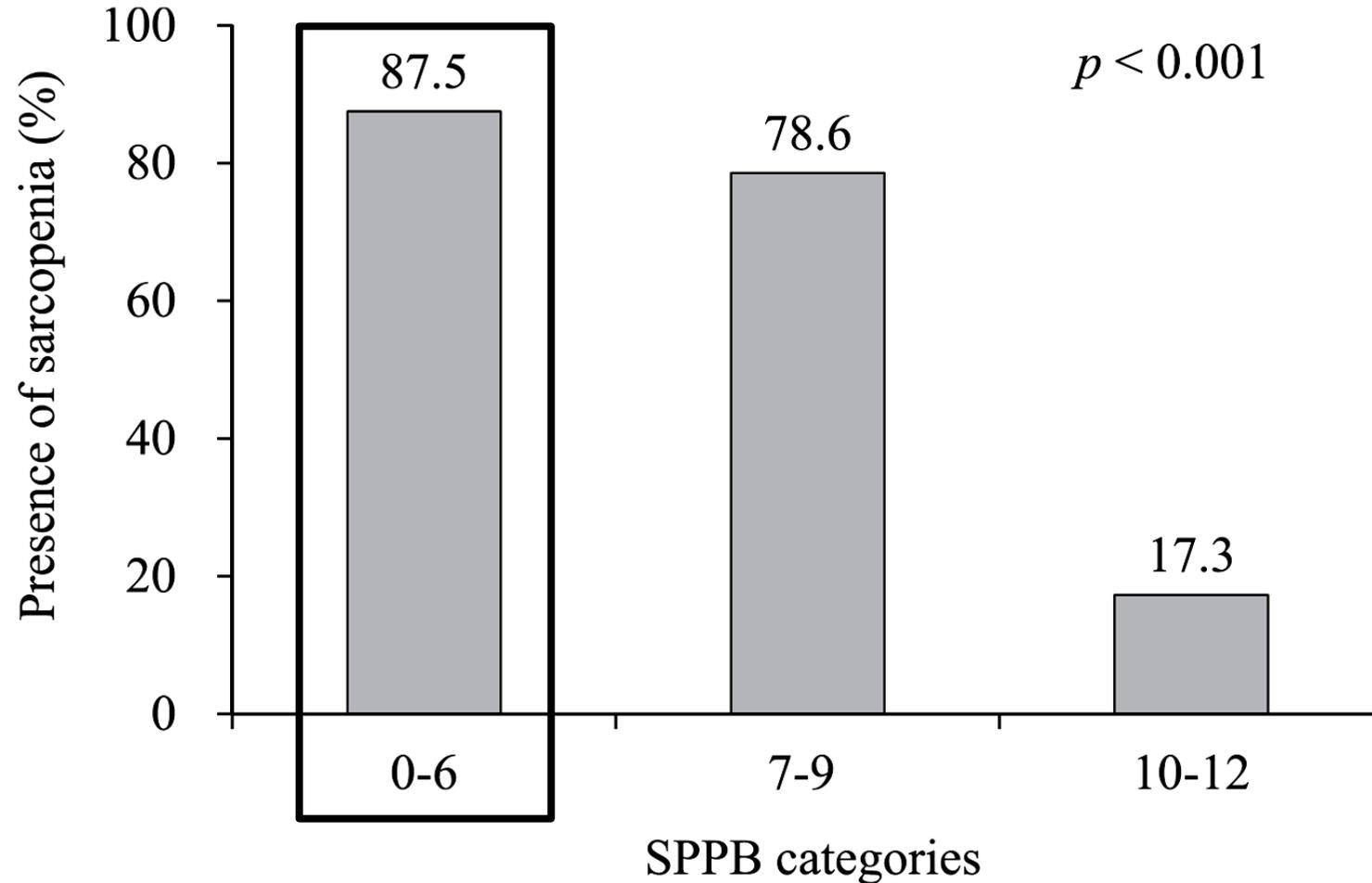
(2)



(3)



Presence of sarcopenia according short physical performance battery (SPPB) categories.



Main characteristics of study participants according to physical frailty and sarcopenia “*BIOSPHERE study*”

| Variables | PHYSICAL FRAILITY | |
|---|-------------------|---------------|
| | Yes (n=100) | No (n=100) |
| Age, years | 77.6 ± 5.1 | 74.8 ± 3.9 |
| BMI, kg/m ² | 30.0 ± 5.0* | 27.4 ± 2.9 |
| SPPB summary score | 7.2 ± 1.2* | 11.4 ± 0.8 |
| aLM, kg | 16.2 ± 3.0* | 20.1 ± 4.1 |
| aLM _{BMI} | 0.54 ± 0.11* | * 0.76 ± 0.19 |
| Number of disease conditions [§] | 2.3 ± 1.8 | 2.1 ± 1.6 |
| Number of medications | 3.6 ± 2.1 | 3.2 ± 2.0 |

§ Includes hypertension, coronary artery disease, prior stroke, peripheral vascular disease, diabetes, chronic obstructive pulmonary disease, and osteoarthritis

aLM, appendicular lean mass; aLMBMI, appendicular lean mass adjusted by body mass index (BMI); SPPB, Short Physical Performance Battery

Risk of Developing ADL Disability during 3- and 6-year follow-up according to Short Physical Performance Battery at different time points

| | | ADL Disability at 3-Year Follow-up | | ADL Disability at 6-Year Follow-up | |
|------------------------------------|------------|---------------------------------------|-----------|---------------------------------------|-----------|
| | | OR | 95% CI | OR | 95% CI |
| Short Physical Performance Battery | | | | | |
| Model 1 | Zero-time* | 0.57 | 0.48–0.68 | 0.63 | 0.54–0.73 |
| Model 2 | Zero-time | 0.54 | 0.43–0.67 | 0.60 | 0.50–0.72 |

All models are adjusted for age, sex, education, physical activity, smoking, alcohol use, body mass index, hypertension, coronary heart disease, stroke, peripheral arterial disease, diabetes, pulmonary disease, lower extremity osteoarthritis, depressive symptoms, and MMSE score.

Odds ratio for SPPB for an increment of 1 point. ADL = activities of daily living; CI = confidence interval; OR = odds ratio.

Short Physical Performance Battery and MORTALITY: meta-analysis

| | | Odds ratio | 95% CI |
|--------------------------|--------------------|------------|-----------|
| 0-3 vs 10-12 | Overall | 3.25 | 2.86-3.69 |
| | ≤75 years | 3.54 | 2.81-4.46 |
| | >75 years | 3.12 | 2.67-3.65 |
| | General population | 3.27 | 2.86-3.75 |
| | Hospitalized | 4.93 | 2.18-11.4 |
| 4-6 vs 10-12 | Overall | 2.34 | 1.92-2.39 |
| | ≤75 years | 2.40 | 1.97-2.93 |
| | >75 years | 2.04 | 1.79-2.33 |
| | General population | 2.22 | 1.98-2.49 |
| | Hospitalized | 1.94 | 0.85-4.41 |
| 7-9 vs. 10-12 | Overall | 1.50 | 1.32-1.71 |
| | ≤75 years | 1.65 | 1.27-2.16 |
| | >75 years | 1.38 | 1.22-1.57 |
| | General population | 1.48 | 1.32-1.65 |
| | Hospitalized | 1.23 | 0.53-2.85 |



Corso
Fragilità e stato nutrizionale

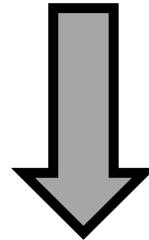
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Nutritional

**Multidimensional
FRAILTY**



ADVERSE AOUTCOMES
*Disability, institutionalization,
death*

SARCOPENIA, WEIGHT LOSS, AND NUTRITIONAL FRAILITY IN THE ELDERLY*

Connie W. Bales¹ and Christine S. Ritchie²

¹*Geriatric Research, Education and Clinical Center, Durham VA Medical Center and Department of Medicine, Duke University Medical Center, Durham, North Carolina 27710* and ²*Department of Medicine, University of Louisville School of Medicine, Louisville, Kentucky*

Key Words

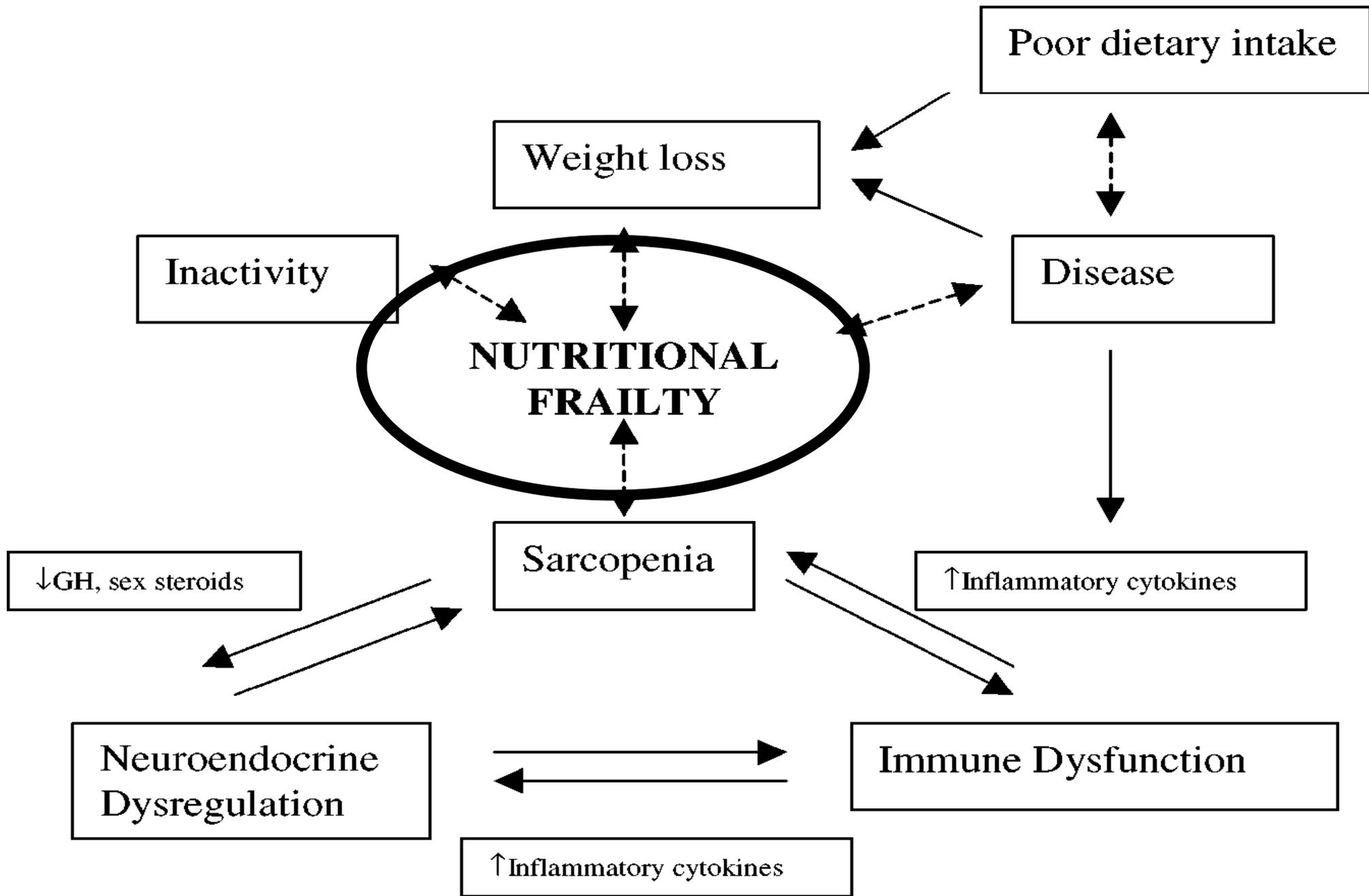
■ **Abstract**
homeostasis
cluding
age owing

**NUTRITIONAL
FRAILITY !**

(sarcopenia). Sarcopenia, a loss of muscle mass and strength, contributes to functional impairment. Weight loss is commonly due to a reduction in food intake; its possible etiology includes a host of physiological and nonphysiological causes. The release of cytokines during chronic disease may also be an important determinant of frailty. In addition to being anorectic, cytokines also contribute to lipolysis, muscle protein breakdown, and nitrogen loss. Whereas the multiple causes of nutritional frailty are not completely understood, clinical interventions for weight loss, sarcopenia, and cytokine alterations have been used with modest success.

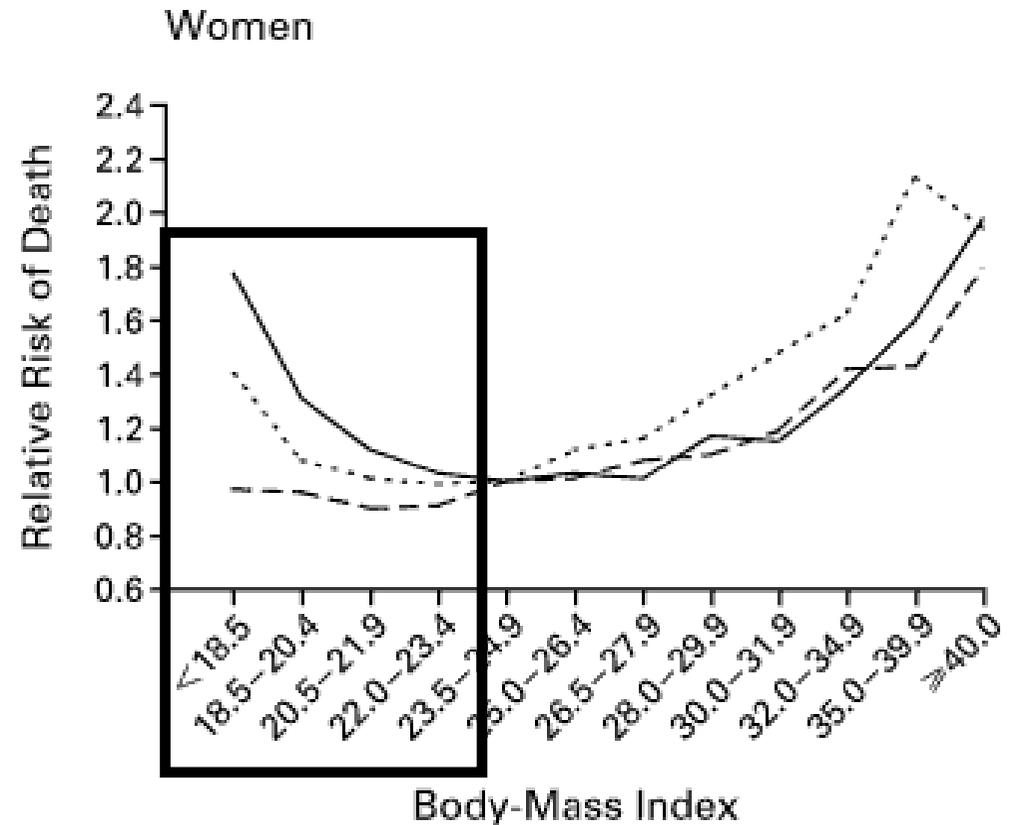
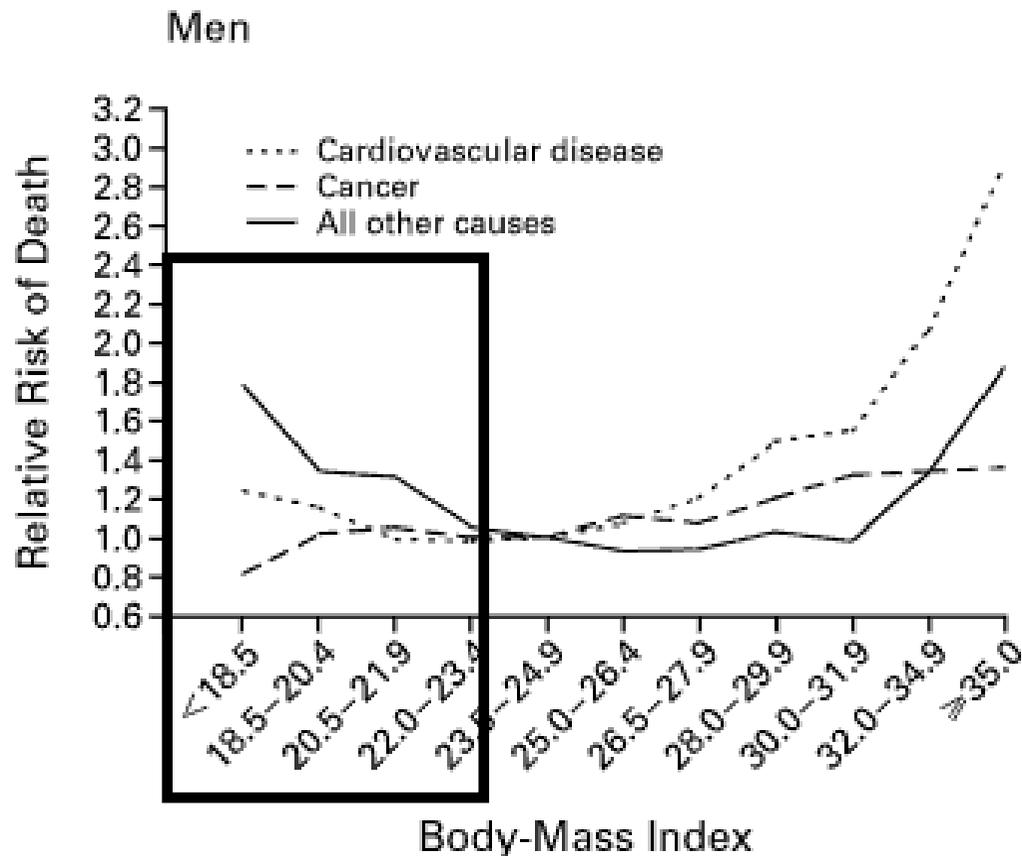
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argin of
ges, in-
s in old
y mass



Body-mass index and mortality in a prospective cohort of U.S. adult

“U” shape

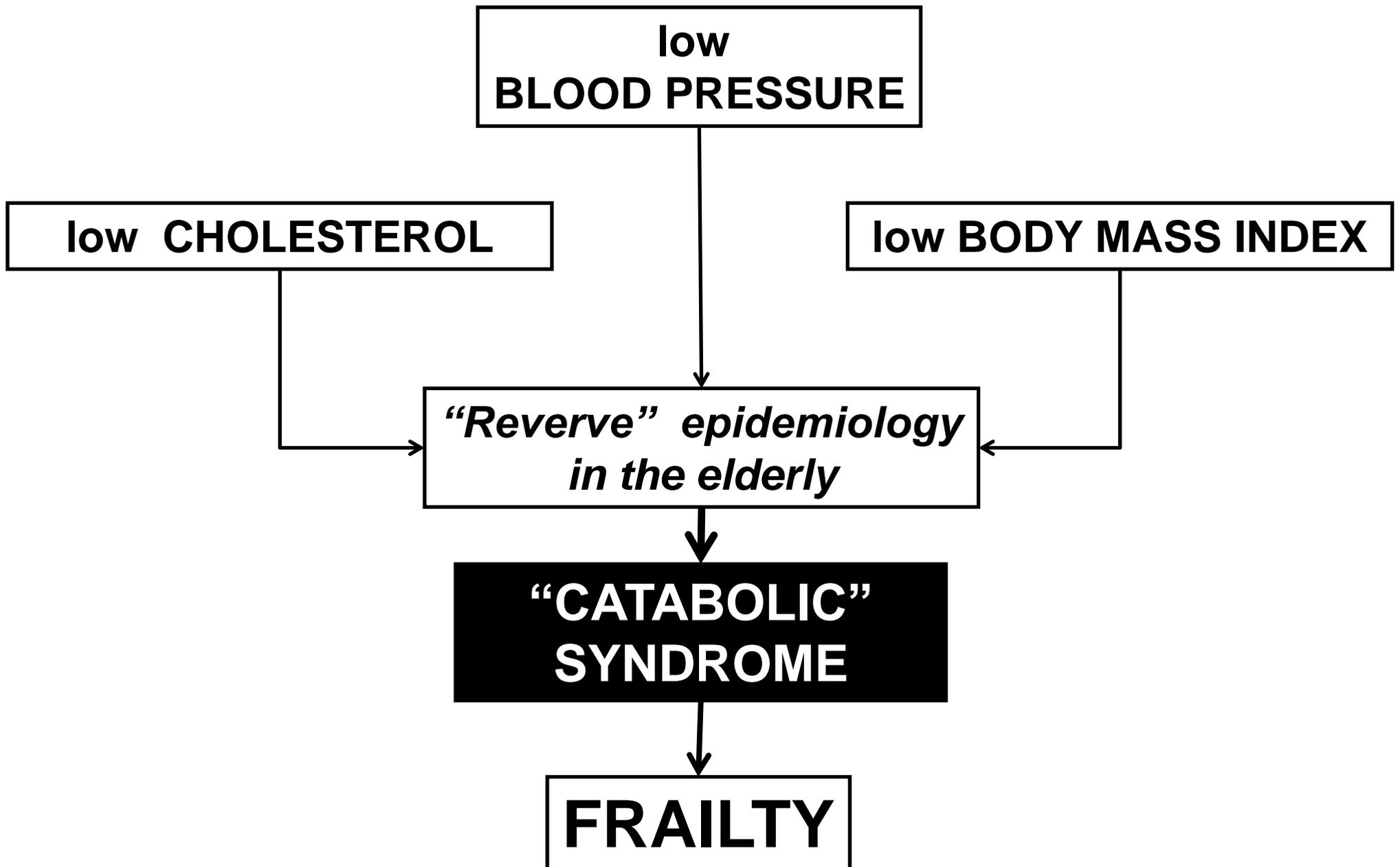


REVIEW

The reverse metabolic syndrome in the elderly: Is it a “catabolic” syndrome?

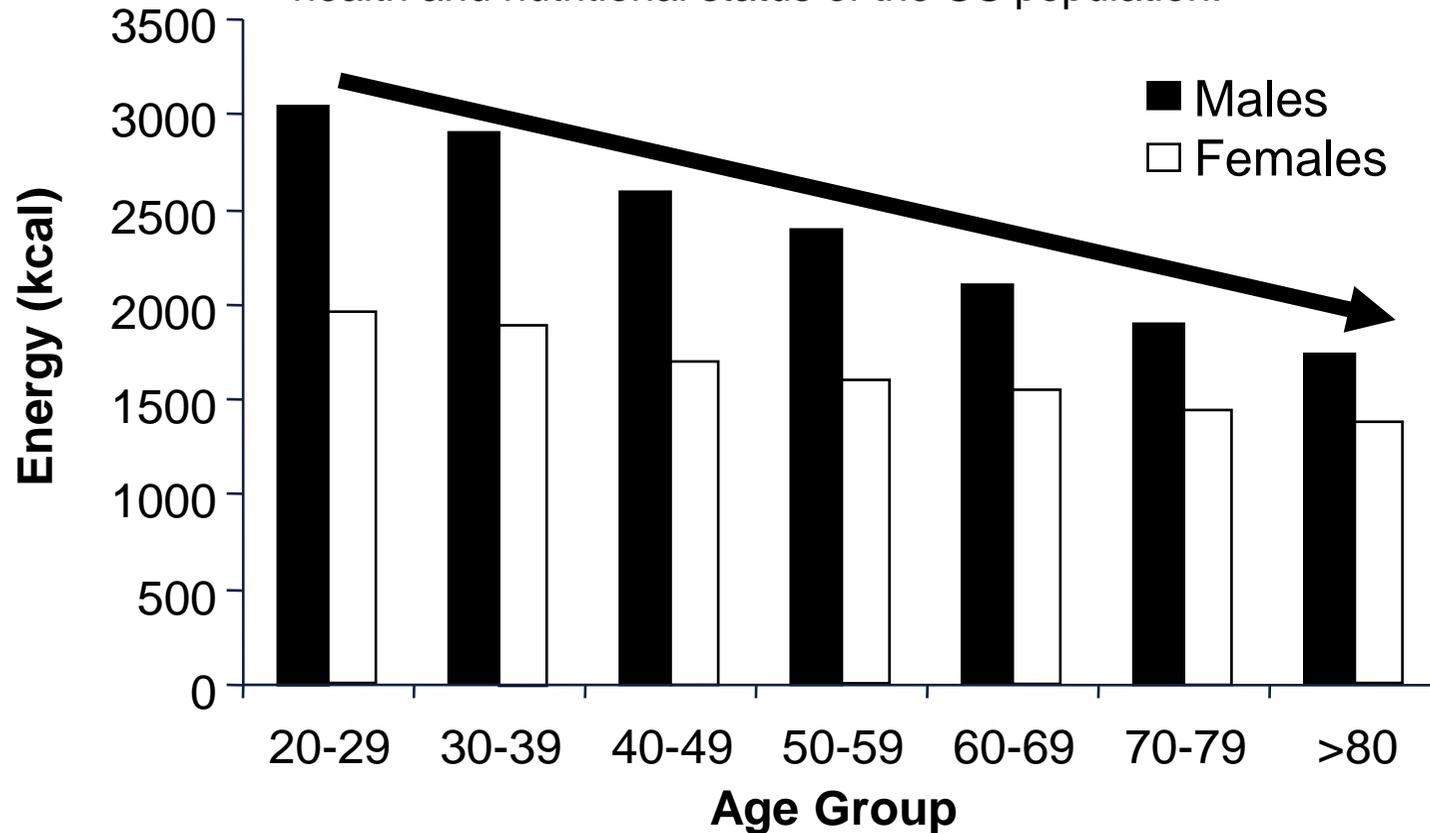
**Francesco Curcio¹ · Giuseppe Sasso¹ · Ilaria Liguori¹ · Gaetana Ferro² ·
Gennaro Russo¹ · Michele Cellurale¹ · David Della-Morte^{3,4} · Gaetano Gargiulo⁵ ·
Gianluca Testa^{1,6} · Francesco Cacciatore^{1,7} · Domenico Bonaduce¹ · Pasquale Abete¹**





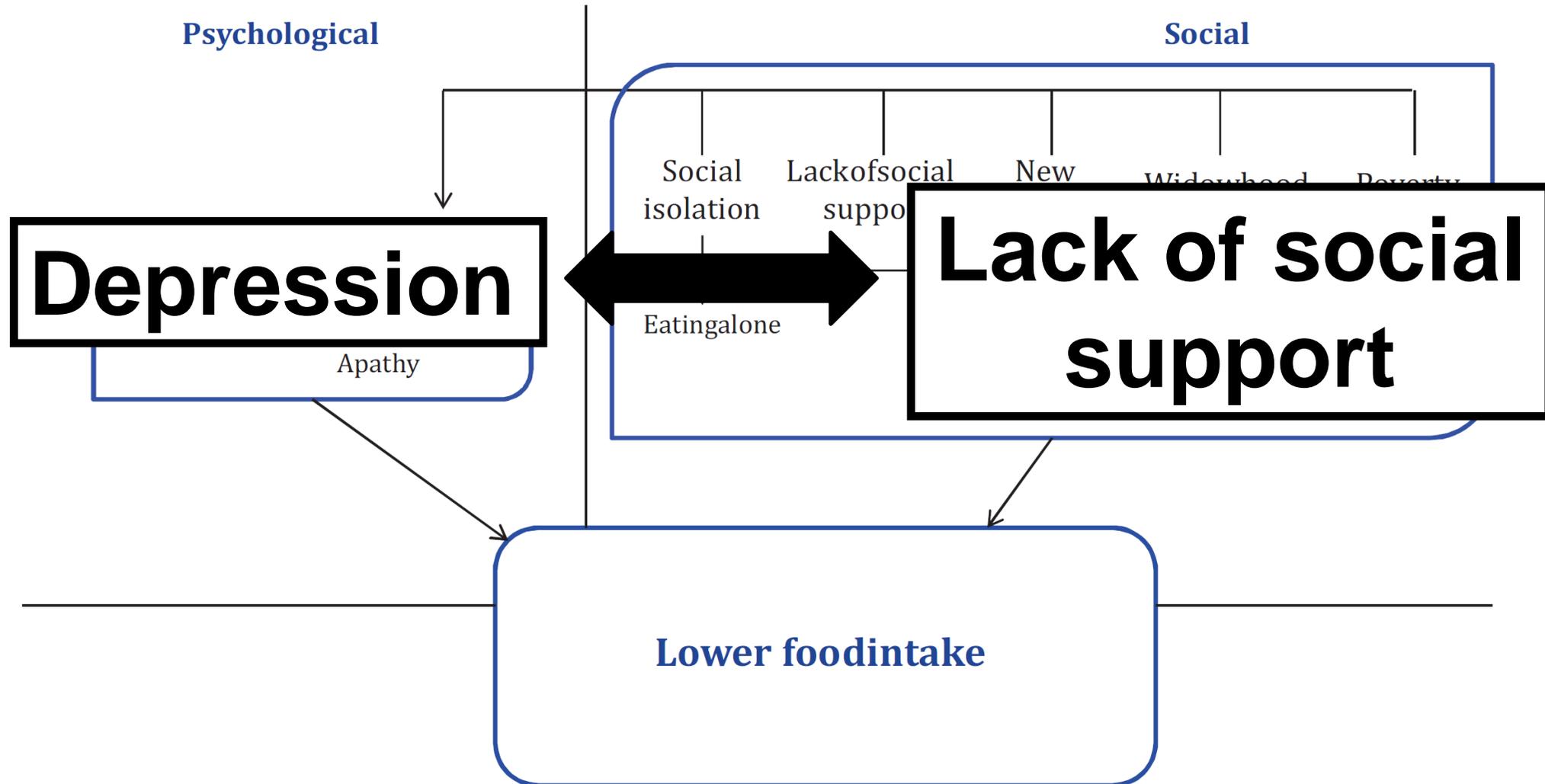
Changes in Food Intake Over Life Span

The third National Health and Nutrition Examination Survey (NHANES III) was conducted to assess the health and nutritional status of the US population.



A decrease in over 1000 calories per day for males and females

“Social” and “psychological” factors influencing food intake in older persons



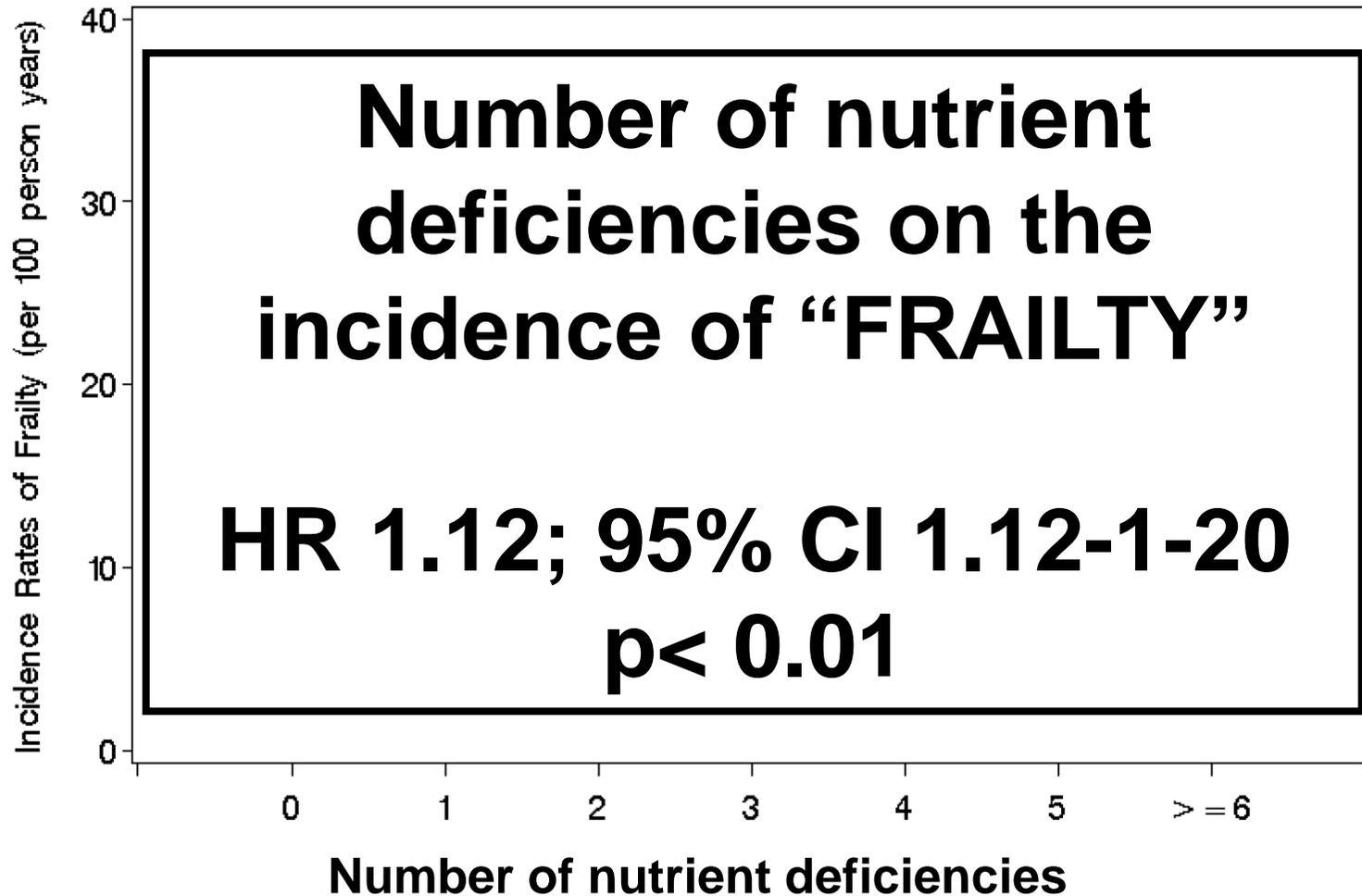
Macro- and Micronutrients.

Food includes of macro- and micro-nutrients.

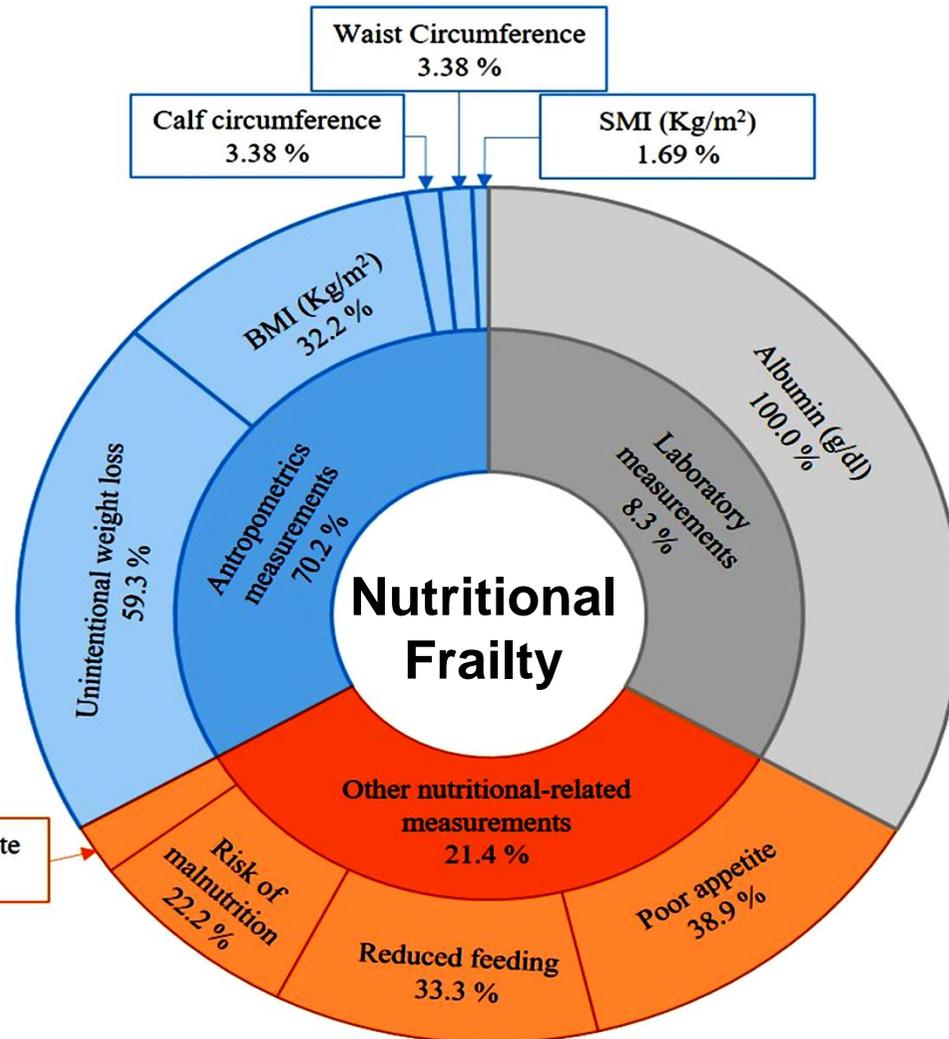
Macro-nutrients include carbohydrates , lipids and proteins. They are affected by digestion and represent the principal source of energy.

Micro-nutrients include vitamins and so-called essential minerals; they are unaffected by the digestion or absorption and is essential to life processes (for example, of enzymatic reactions)

Low serum “micronutrient” concentrations predict frailty among older women living in the community



All nutritional items extracted from different frailty tools



Anthropometric measurements 70.23%

- unintentional weight loss
- body mass index (BMI)
- calf circumference
- waist circumference
- skeletal Muscle Index (SMI)

Laboratory measurements 8.33%

- serum albumin concentration

Other nutritional measurements 21.42%

- poor appetite
- reduced feeding
- Mini Nutritional Assessment (MNA),

Mini Nutritional Assessment (MNA)

Assessment

G Lives independently (not in nursing home or hospital)

1 = yes 0 = no

H Takes more than 3 prescription drugs per day

0 = yes 1 = no

I Pressure sores or skin ulcers

0 = yes 1 = no

J How many full meals does the patient eat daily?

0 = 1 meal
1 = 2 meals
2 = 3 meals

K Selected consumption markers for protein intake

- At least one serving of dairy products (milk, cheese, yoghurt) per day yes no
 - Two or more servings of legumes or eggs per week yes no
 - Meat, fish or poultry every day yes no
- 0.0 = if 0 or 1 yes
0.5 = if 2 yes
1.0 = if 3 yes

L Consumes two or more servings of fruit or vegetables per day?

0 = no 1 = yes

M How much fluid (water, juice, coffee, tea, milk...) is consumed per day?

0.0 = less than 3 cups
0.5 = 3 to 5 cups
1.0 = more than 5 cups

N Mode of feeding

0 = unable to eat without assistance
1 = self-fed with some difficulty
2 = self-fed without any problem

O Self view of nutritional status

0 = views self as being malnourished
1 = is uncertain of nutritional state
2 = views self as having no nutritional problem

P In comparison with other people of the same age, how does the patient consider his / her health status?

0.0 = not as good
0.5 = does not know
1.0 = as good
2.0 = better

Q Mid-arm circumference (MAC) in cm

0.0 = MAC less than 21
0.5 = MAC 21 to 22
1.0 = MAC greater than 22

R Calf circumference (CC) in cm

0 = CC less than 31
1 = CC 31 or greater

Assessment (max. 16 points)

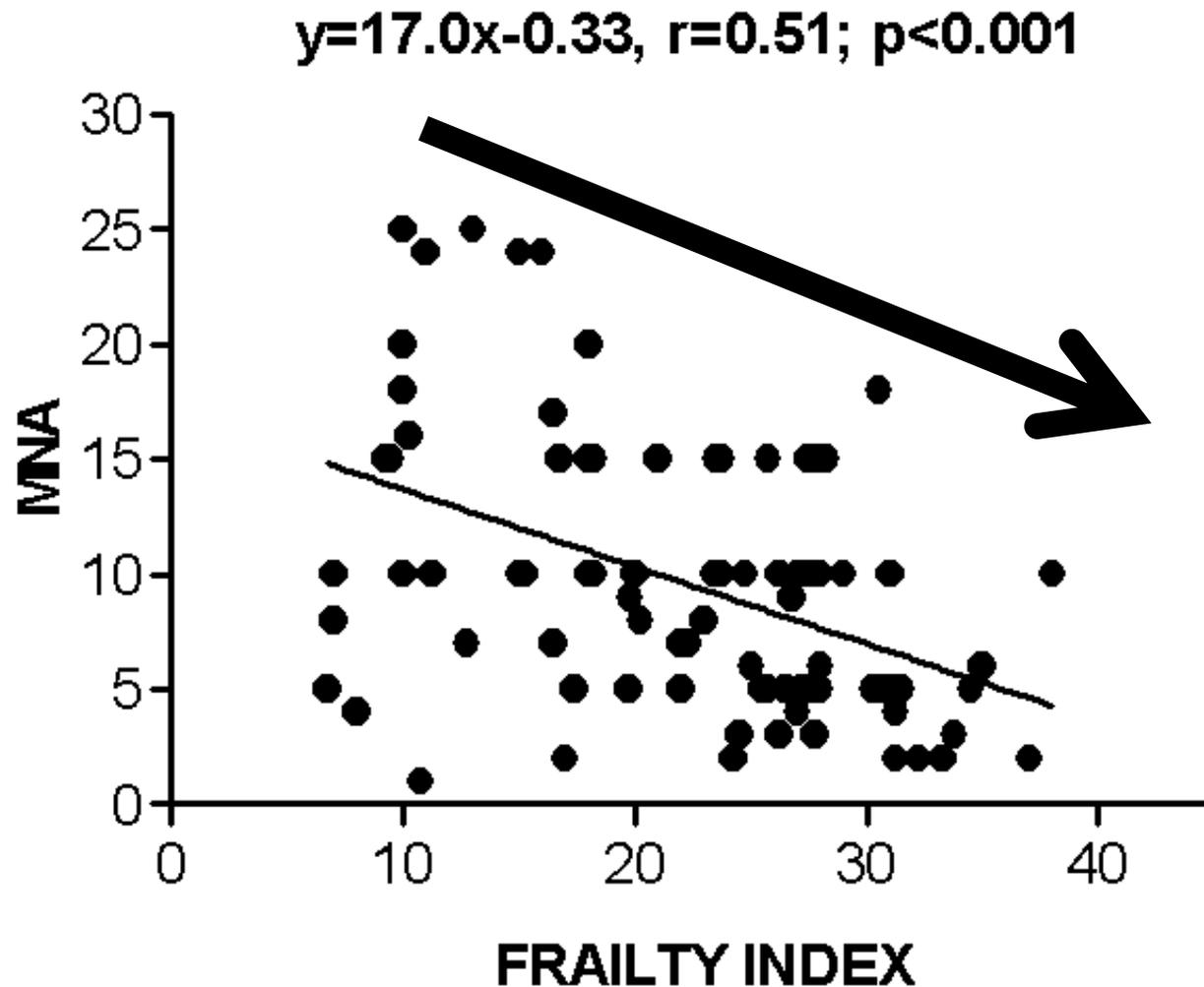
Screening score

Total Assessment (max. 30 points)

Malnutrition Indicator Score

| | | |
|---------------------|--------------------------|---------------------------|
| 24 to 30 points | <input type="checkbox"/> | Normal nutritional status |
| 17 to 23.5 points | <input type="checkbox"/> | At risk of malnutrition |
| Less than 17 points | <input type="checkbox"/> | Malnourished |

Frailty is inversely related to Mini nutritional Assessment (MNA) in the elderly





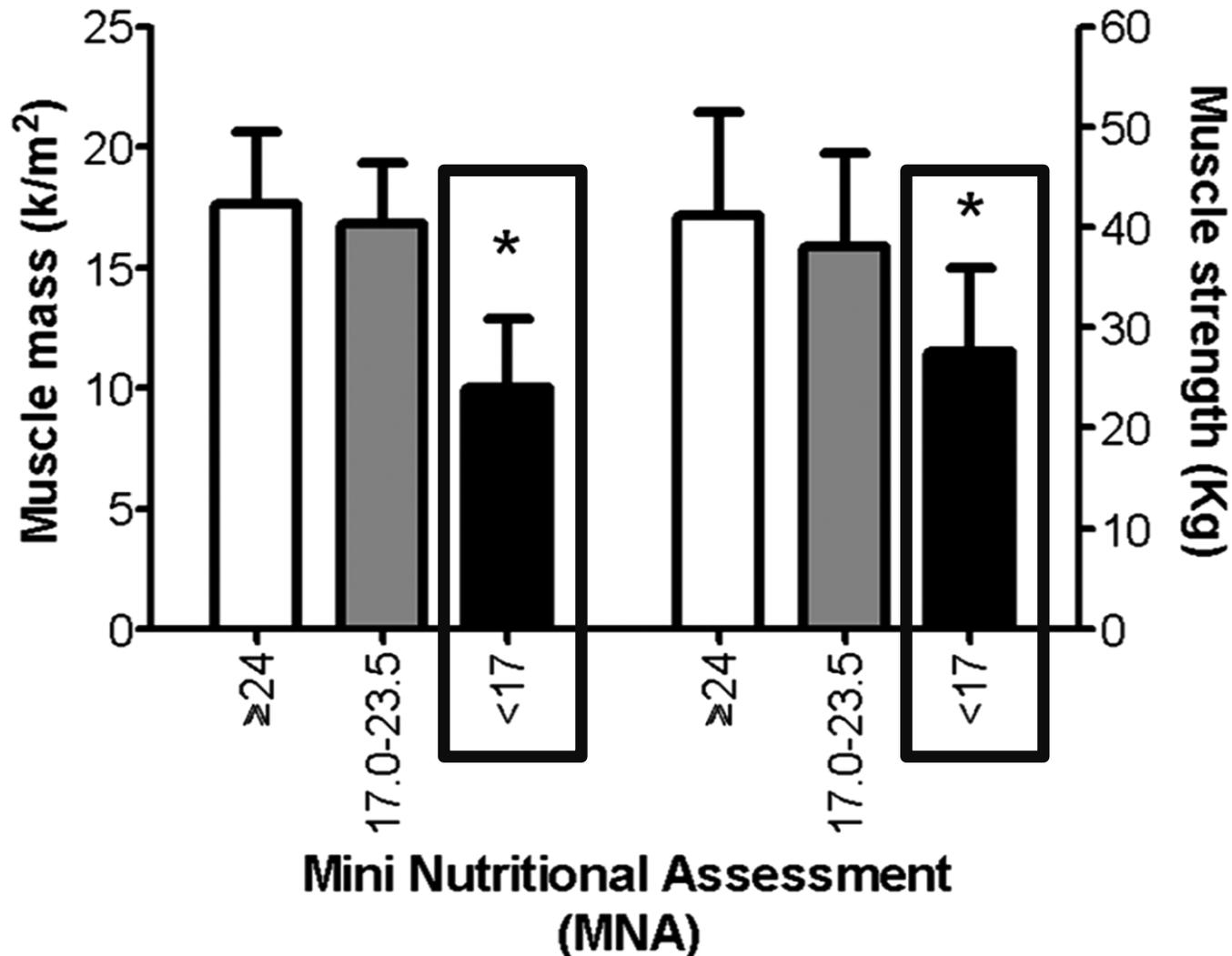
Corso
Fragilità e stato nutrizionale

***La fragilità fisica nel soggetto anziano:
etiopatogenesi e significato clinico
Il ruolo dello stato nutrizionale***



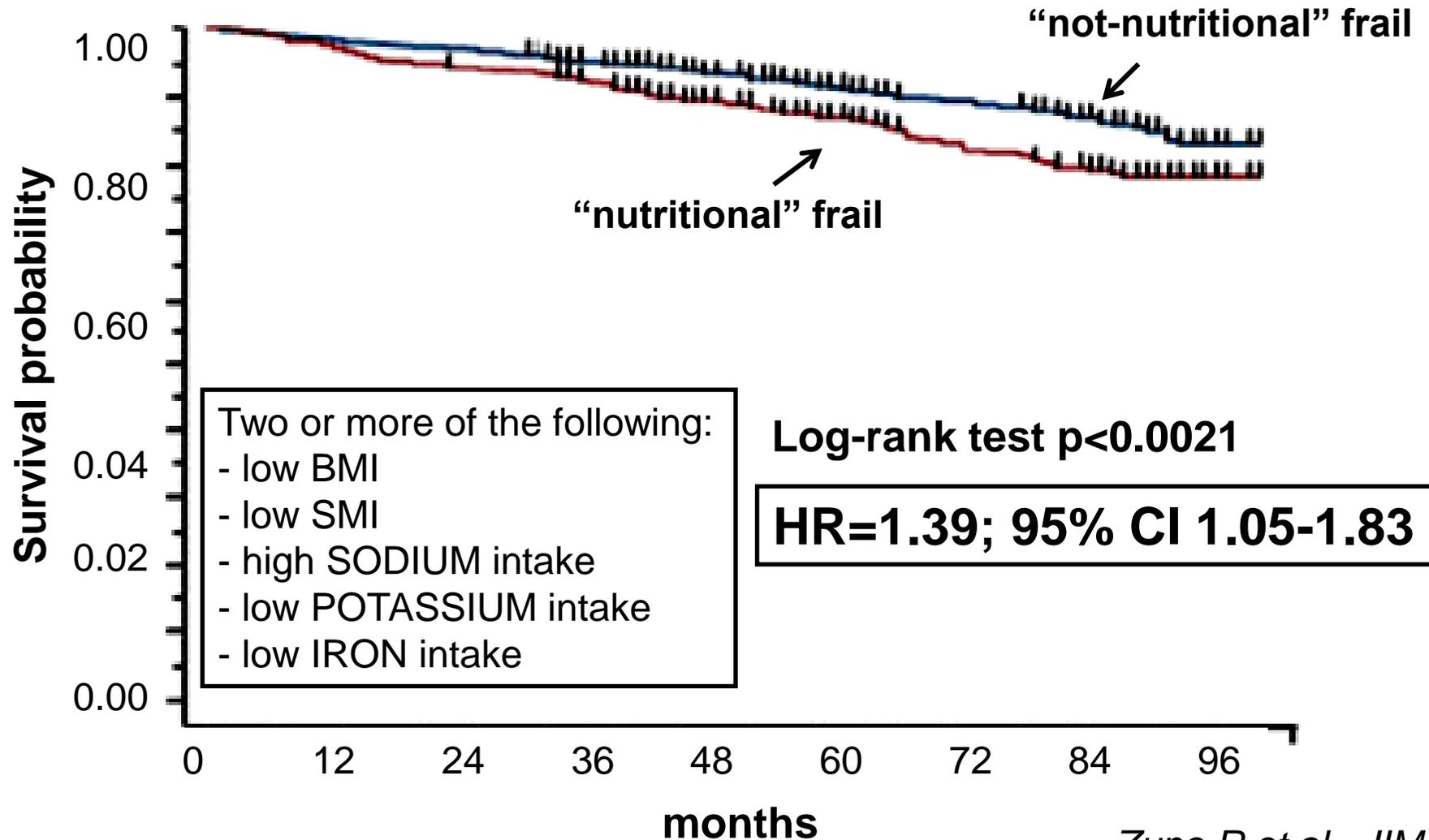
-
- Vulnerability
 - Multidimensional frailty
 - Physical frailty
 - Nutritional frailty
 - **Physical & Nutritional frailty**

Mini Nutritional Assessment (MNA) and SARCOPENIA in older adults outpatients

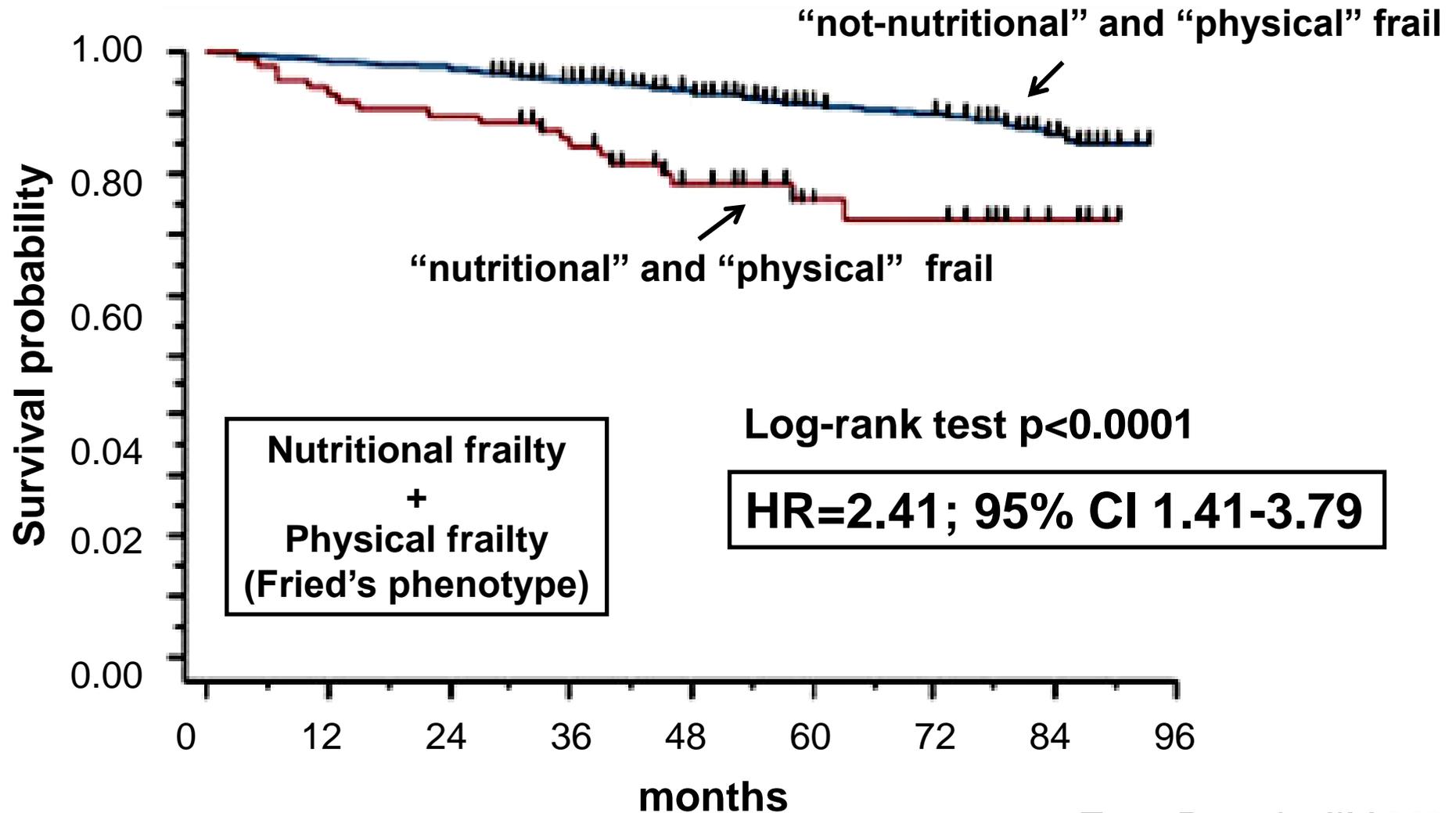


* $p < 0.05$ for <17 vs 17–23.5 and 24

NUTRITIONAL FRAILITY and 8-year cause mortality in older adults. *The Salus in Apulia Study*



NUTRITIONAL and PHYSICAL FRAILTY and 8-year cause mortality in older adults. *The Salus in Apulia Study*



Overlap among nutritional frailty, sarcopenia, and physical frailty.

Nutritional Frailty

- Unintentional weight loss
- BMI decrease

- Presence of physical frailty and/or sarcopenia

Possible Etiologic Criteria

- Low energy intake
- Low protein intake
- Micronutrient deficiency

- Anorexia of aging
- Loss appetite
- Impaired taste

- Malnutrition
- Environmental / social factors

- Multimorbidity

Sarcopenia

Low SMI

- Low muscle quantity
- Low muscle quality

Low muscle strength

Low physical performance

In black, the potentially modifiable factors

In red, the non modifiable/hardly modifiable factors

Physical frailty

Unintentional weight loss

Exhaustion

Weak grip strength

Low physical activity
Slow walking

Take home messages

- **Vulnerability** (age-related reduction of intrinsic capacity to defend against stressors) represents the **trigger to precipitate into clinical frailty**.
- Frailty is characterized by four domains (physical, mental, nutritional and social) and is actually defined **multidimensional frailty**.
- **Physical frailty** is its main component, characterized by **sarcopenia and functional deficits** and associated to **several adverse events**.
- **Nutritional frailty** is a very important domain of frailty and determined by several factors including **depression** and **lack of social support**.
- Finally, **physical and nutritional frailty are synergistic** in determining a poor prognosis in frail elderly patient.