Gruppo di ricerca geriatrica

Venerdì 2 luglio 2010

La Fatigue: un indicatore di invecchiamento

Giuseppe Bellelli

Sommario

- Brevi cenni storici sul concetto di fatigue
- Definizione
- Prevalenza del sintomo “fatigue”
- Gli strumenti per misurare la “fatigue”
- Fatigue come indicatore di invecchiamento accellerato
  - Le possibili interpretazioni
- La “fatigue” può essere utilizzato come indicatore (self-reported) di frailty?
- Conclusioni

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A Brief Historical Overview of Fatigue Research

- La “fatigue” è concettualmente un’acquisizione della società industrializzata (metà 1800) e venne, inizialmente, considerata una malattia del sistema nervoso (neurastenia)
- Intorno al 1900 si pose l’accento sulla distinzione tra fatigue e depressione; fatigue divenne sinonimo di tiredness
- Il termine “fatigue” entrò a far parte del DSM I e II, per poi venirne rimosso nel 1908 (DSM III). Rimane nell’ICD-X con il termine di neurastenia
- Mosso intuì il carattere multidimensionale del termine “fatigue”, descrivendone 4 caratteristiche (comportamento, percezione, meccanismo contesto) ed osservando che il percepito non corrisponde alla performance

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Definizione di "fatigue"

- Fatigue is an ambiguous concept, which especially relates to the reaction to physical and psychological work loads, but it may also include many different experiences and states of mind, e.g., the experience of exhaustion, impaired energy and vitality, and need for sleep.
- Centrally conditioned fatigue is more complex, and entails both chemical and hormonal factors in nerve cells and their synapses, e.g., as changes in neurotransmitter levels in various brain structures, but also psychological factors such as endurance, motivation, mood, and expectation of task difficulty.
- Fatigue which cannot be relieved by rest or sleep is a frequent sign of disease.

Avlund K, Aging Clin Exp Res 2010

Fatigue: a concept analysis

- "A subjective unpleasant symptom which incorporates total body feeling ranging from tiredness to exhaustion, creating an unrelenting overall condition which interferes with individuals' ability to function to their normal capacity".

Ream E, Richardson A. Int J Nurs Stud 1996; 33: 519-29.

La prevalenza dei sintomi exhaustion e weakness è elevata negli anziani

	10 Countries	Sweden	Denmark	The Netherlands	Germany	Austria	Switzerland	France	Italy
Age 50–64 y (*n*)	9,074	1,038	877	1,261	1,146	849	470	803	958
Frailty criteria									
Exhaustion	27.3 (25.8–29.9)	31.6 (28.5–34.6)	30.8 (27.6–34.1)	23.6 (20.7–26.5)	20.4 (17.3–23.6)	20.5 (17.6–23.5)	25.4 (21.3–29.4)	30.0 (26.0–33.9)	29.8 (25.7–34.0)
Weakness	6.1 (5.3–6.8)	4.5 (3.1–5.9)	3.1 (1.9–4.4)	4.7 (3.6–5.8)	3.9 (2.6–5.2)	3.5 (2.2–4.7)	2.5 (1.1–4.0)	4.6 (3.0–6.3)	7.2 (5.2–9.3)
Slowness	6.7 (5.8–7.6)	2.9 (1.8–4.0)	5.5 (3.9–7.1)	7.3 (5.5–9.1)	5.9 (3.6–8.2)	6.5 (4.5–8.5)	3.9 (2.0–5.8)	4.3 (2.7–5.9)	8.8 (6.7–10.9)
Low activity	13.8 (12.3–15.3)	4.5 (3.1–5.8)	6.3 (4.6–8.1)	8.8 (6.7–10.8)	9.6 (7.0–12.3)	13.6 (10.7–16.5)	11.2 (8.1–14.3)	14.8 (12.1–17.5)	24.7 (19.6–29.7)
Frailty status									
Prefrailty	37.4 (35.8–39.1)	35.9 (32.8–39.1)	34.9 (31.5–38.3)	30.8 (27.1–34.5)	30.9 (27.3–34.5)	30.4 (26.7–34.2)	36.1 (31.4–40.7)	40.3 (36.6–44.0)	43.5 (39.4–47.7)
Frailty	4.1 (3.4–4.7)	1.9 (1.1–2.8)	3.0 (1.8–4.2)	3.5 (2.4–4.7)	2.6 (1.5–3.8)	3.9 (2.6–5.2)	1.3 (0.3–2.2)	3.2 (1.9–4.5)	5.9 (4.1–7.7)
Disability									
BADL* difficulty	4.5 (3.9–5.2)	4.7 (3.3–6.1)	5.8 (4.2–7.4)	3.7 (2.4–5.0)	4.3 (2.8–5.8)	4.4 (2.8–6.1)	3.4 (1.6–5.2)	5.2 (3.5–6.9)	3.9 (2.4–5.4)
Age 65+ y (*n*)	7,510	873	635	830	933	707	412	687	833
Frailty criteria									
Exhaustion	36.7 (34.7–38.7)	39.1 (35.5–42.7)	32.9 (29.0–36.8)	28.9 (24.5–33.3)	30.0 (25.5–34.4)	27.6 (23.3–31.9)	28.0 (23.6–32.5)	36.4 (32.6–40.3)	38.4 (33.3–43.6)
Weakness	26.3 (24.4–28.3)	17.9 (15.0–20.7)	16.9 (13.7–20.0)	17.8 (14.2–21.4)	15.1 (12.0–18.2)	13.6 (10.4–16.8)	16.7 (13.0–20.5)	22.7 (19.2–26.2)	38.1 (32.0–44.1)
Slowness	22.7 (20.9–24.6)	12.7 (10.2–15.2)	19.5 (16.2–22.8)	19.9 (16.7–23.0)	18.7 (15.0–22.4)	18.9 (14.7–23.1)	10.3 (7.2–13.4)	20.7 (17.1–24.3)	28.1 (23.1–33.2)
Low activity	21.3 (19.2–23.4)	10.3 (8.0–12.5)	14.1 (11.2–17.1)	16.9 (13.5–20.3)	15.7 (12.4–19.0)	24.8 (19.1–30.5)	15.5 (11.7–19.3)	22.6 (19.0–26.2)	30.1 (23.2–37.0)
Frailty status									
Prefrailty	42.3 (40.5–44.1)	45.3 (41.8–48.9)	38.4 (34.5–42.3)	38.5 (34.4–42.7)	34.6 (31.1–38.1)	40.7 (36.5–45.0)	46.5 (41.5–51.4)	43.6 (39.6–47.6)	45.6 (40.7–50.5)
Frailty	17.0 (15.3–18.7)	8.6 (6.5–10.8)	12.4 (9.6–15.1)	11.3 (9.0–13.5)	12.1 (8.8–15.3)	10.8 (8.0–13.5)	5.8 (3.5–8.1)	15.0 (12.2–17.8)	23.0 (18.0–28.0)
Disability									
BADL* difficulty	13.5 (12.2–14.7)	11.1 (8.7–13.5)	11.8 (9.1–14.5)	9.0 (7.1–10.9)	11.4 (8.6–14.1)	8.4 (6.1–10.7)	9.9 (7.0–12.7)	16.1 (13.1–19.2)	16.2 (13.0–19.3)

Note: *Basic activities of daily living: bathing or showering, dressing, eating, getting in and out of bed, using the toilet.

Santos-Eggimann B J Gerontol 2009

Proportion of 70-, 75-, 80-, and 85-year old men and women who felt fatigued in daily activities

Age	Men with fatigue	Women with fatigue	*p*
70	(n=364) 51%	(n=367) 55%	0.406
75	(n=337) 59%	(n=411) 68%	0.005
80	(n=184) 58%	(n=248) 68%	0.045
85	(n=77) 79%	(n=119) 87%	0.126

Fatigued: Measured by Mob-T Scale (See Table 3); *p*: differences between men and women, by chi-square tests.

Avlund K Aging Clin Exp Research 2010

J Epidemiol Community Health 2000;54:827–833

Fatigue in the Danish general population. Influence of sociodemographic factors and disease

Torquil Watt, Mogens Groenvold, Jakob Bue Bjorner, Vibeke Noerholm, Niels-Anton Rasmussen, Per Bech

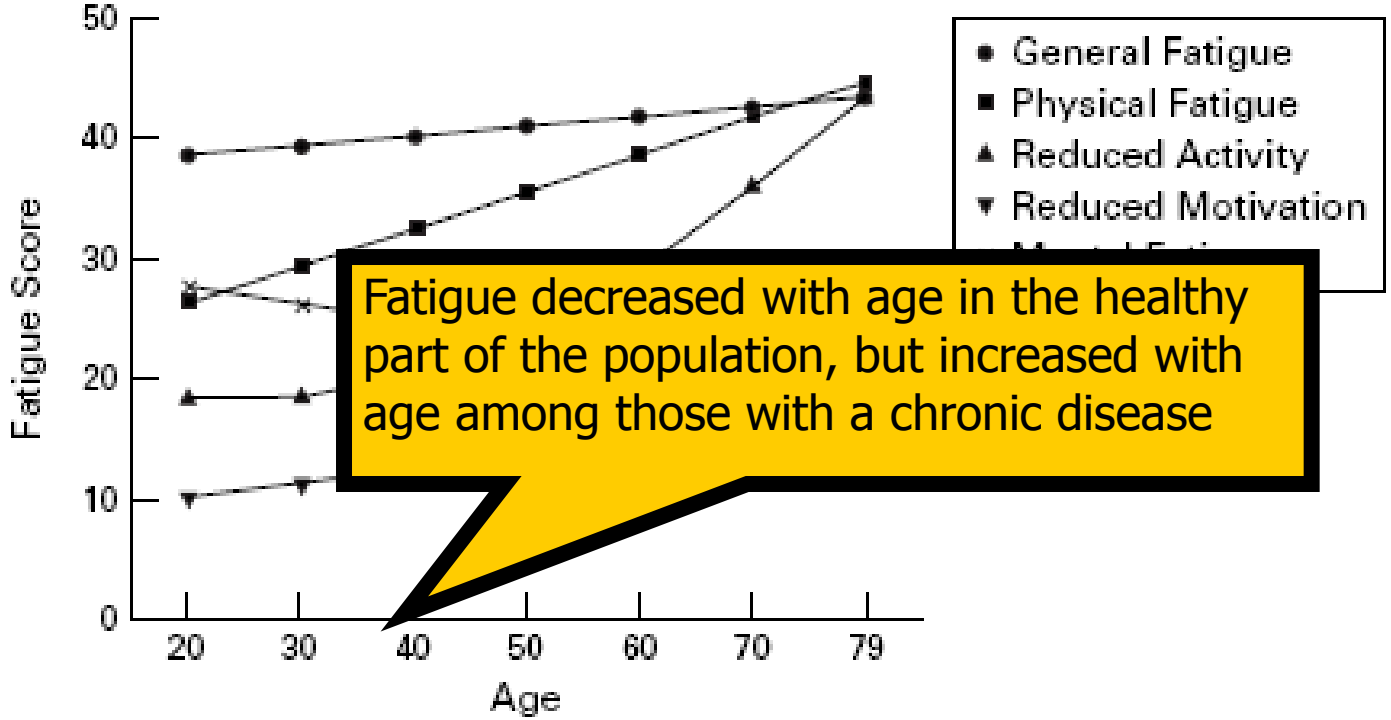

Figure 2 Association between expected fatigue scores and age among those with a chronic somatic disease. Scores are from the regression analysis—that is, controlled for gender, education, cohabitation and depression.

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Come misurare il sintomo fatigue?

Fatigue
Mob-T Scale (Mobility-Tiredness)
Transferring
Getting outdoors
Walking indoors
Walking outdoors in nice weather
Walking outdoors in poor weather
Walking on stairs to the second floor
Lower Limb-T Scale (Lower Limb-Tiredness)
Using toilet
Washing lower body
Dressing lower body
Putting on/taking off shoes/ stockings
Cutting toenails

Avlund K, Eur J Public Health 1996

Avlund K, Scand J Soc Med 1993

Multidimensional Fatigue Inventory (MFI-20) & Short Form-36 Vitality Scale

General fatigue, referring to subject's general functioning, with statements such as 'I feel tired'
Physical fatigue, bodily sensations directly referring to tiredness, e.g., 'Physically I only feel able to do a little'
Reduced activity, a potential consequence of subjective fatigue, e.g., 'I think I do very little in a day'
Reduced motivation, reflecting lack of will to start any activity, e.g., 'I dread having to do things'
Mental fatigue, referring to cognitive symptoms such as having difficulty in concentration, e.g., 'It takes a lot of effort to concentrate on things'

	All the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
Feeling full of pep	1	2	3	4	5	6
Having a lot of energy	1	2	3	4	5	6
Feeling worn out	1	2	3	4	5	6
Feeling tired	1	2	3	4	5	6

Smets E et al., Br J Cancer 1996
McHorney CA et al., Med Care 1996

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Fatigue as a predictor of new disability at 5-years follow-up

	Crude OR(95%CI)	Model 1 OR(95%CI)	Model 2 OR(95%CI)	Model 3 OR(95%CI)	Model 4 OR(95%CI)	Model 5 OR(95%CI)	Final model OR(95%CI)
Fatigue *vs* no fatigue	**3.61 (1.76-7.42)**	**3.43 (1.67-7.09)**	**2.92 (1.41-6.09)**	**3.31 (1.57-6.94)**	**2.98 (1.42-6.25)**	**2.53 (1.19-5.36)**	**2.25 (1.05-4.85)**
Income Poor *vs* higher	1.96 (0.93-4.11)	1.74 (0.81-3.71)				-	-
1-4 diseases *vs* none	**4.74 (1.42-1**					9 0-10.68)	2.90 (0.84-10.07)
Cognition Poor *vs* high	**10.35 (2.34-4**						-
Medium *vs* high	**5.73 (1.29-2**						- -
Depressive mood *vs* not	**3.61 (1.76-7.**					**4 5-5.57)**	**2.66 (1.26-6.60)**
Walking speed Slow *vs* quick	**3.30 (1.08-10.07)**						2.06 (0.64-6.60)
Medium *vs* quick	2.75 (0.87-8.68)						2.10 (0.64-6.87)

- La capacità predittiva del sintomo "fatigue" si riduce introducendo nell'analisi multivariata la comorbilità, le performances cognitive e la depressione
- L'associazione rimane significativa anche nel modello finale

Significant associations marked in bold type; Model 1. Adjusted by income; Model 2. Adjusted by number of diseases; Model 3. Adjusted by cognitive performance; Model 4. Adjusted by depressive mood; Model 5. Adjusted by the covariates which attenuated association between fatigue and onset of disability more than 20%. Final model. Further adjusted by walking speed.

Avlund K et al. J Gerontol Med Sci 2006; 61A: 1201-5.

Fatigue predicting new disability at 5 years - 2

	Onset of disability		Mortality	
5-year follow-up	**(n=564)**		**(n=705)**	
	Crude OR (95% CI)	*Adjusted OR (95% CI)²*	*Crude OR (95% CI)*	*Adjusted OR (95% CI)²*
Fatigue	**10.16 (5.39-19.12)**	**9.09 (4.71-17.54)**	**2.29 (1.51-3.49)**	**1.83 (1.17-2.85)**
Maximal power[1]				
not performed	**12.30 (4.23-35.65)**	**6.42 (2.01-20.48)**	**3.37 (1.50-7.56)**	**3.32 (1.40-7.84)**
Lowest	**5.35 (2.01-14.28)**	2.66 (0.89-8.02)	**2.29 (1.14-4.60)**	**3.23 (1.46-7.14)**
Medium	2.75 (0.99-7.61)	1.85 (0.64-5.35)	**2.02 (1.00-4.07)**	1.20 (0.97-4.13)
Highest	1.0	1.0	1.0	1.0
10-year follow-up	**(n=360)**		**(n=705)**	
	Cr			*Adjusted OR (95% CI)²*
Fatigue	**2.**			**2.16 (1.52-3.05)**
Maximal power[1]				
not performed	**4.**			**2.37 (1.21-4.64)**
Lowest	**5.**			1.37 (0.76-2.47)
Medium	**2.**			1.48 (0.89-2.46)
Highest	1.(			1.0
15-year follow-up	**(n=181)**		**(n=705)**	
	Crude OR (95% CI)	*Adjusted OR (95% CI)²*	*Crude OR (95% CI)*	*Adjusted OR (95% CI)²*
Fatigue	**2.15 (1.16-3.99)**	1.84 (0.93-3.64)	**2.61 (1.91-3.58)**	**2.31 (1.64-3.24)**
Maximal power[1]				
not performed	3.06 (0.84-11.18)	2.87 (0.75-10.97)	**2.89 (1.52-5.52)**	**2.98 (1.44-6.15)**
Lowest	**5.44 (2.16-13.74)**	**4.43 (1.45-13.56)**	**1.60 (1.02-2.53)**	**2.41 (1.34-4.35)**
Medium	2.22 (0.89-5.52)	2.06 (0.79-6.44)	1.48 (0.94-2.35)	1.63 (0.99-2.69)
Highest	1.0	1.0	1.0	1.0

- Maximal aerobic power was also related to onset of disability and mortality but did not seriously attenuate the association between fatigue and outcomes

Katrice Kurtis ONLY

Schultz-Larsen K Arch Gerontol Geriatr 2007

Fatigue in a Representative Population of Older Persons and Its Association With Functional Impairment, Functional Limitation, and Disability

Sonja Vestergaard,[1] Susan G. Nayfield,[2] Kushang V. Patel,[1] Basil Eldadah,[2] Matteo Cesari,[3] Luigi Ferrucci,[4] Graziano Ceresini,[5] and Jack M. Guralnik[1]

Background. Older persons often complain of fatigue, but the functional consequences of this symptom are unclear. The aim of the present study was to evaluate fatigue and its association with measures of physical function and disability in a representative sample of the older population.

Methods. Cross-sectional data from a population-based sample of 1,055 Italian men and women aged 65 and older were analyzed. Fatigue was defined according to two questions evaluating whether participants felt that "everything was an effort" and/or they "could not get going" on three or more days in the past week. Objective measures of physical function were handgrip strength, the Short Physical Performance Battery (SPPB), and 400-m walking speed. Disability was defined as the inability to complete the 400-m walk test and self-reported difficulty in activities of daily living (ADL) and instrumental activities of daily living (IADL).

Results. The prevalence of fatigue was higher in women (29%) than in men (15%). In age-adjusted analyses, fatigued men and women had weaker handgrip strength, lower SPPB score, slower walking speed, and higher mobility, ADL, and IADL disability than nonfatigued persons. Further adjustment for health behaviors, diseases, inflammatory markers, and thyroid function generally reduced the relationship between fatigue and functional outcomes, but fatigue remained significantly associated with SPPB score, walking speed, and mobility and IADL disability.

Conclusions. Older persons who report fatigue had significantly poorer functional status than those who did not report this symptom. The causal link between fatigue and these outcomes should be further investigated.

Journal of Gerontology: MEDICAL SCIENCES
Cite journal as: J Gerontol A Biol Sci Med Sci
2009. Vol. 64A, No. 1, 76–82
doi:10.1093/gerona/gln017

Fatigue as predictor of various outcomes

- Fatigue in daily activities at 75 is independently related to risk of hospitalizations and being users of home help 5 years later and not using regular dental services (Avlund K, J Aging Health 2001 & JAGS 2001)
- Score indicating fatigue at the Mob-T scale predict less activity with regard to physical, intellectual, cultural and social activities (Avlund K, Scand J Occupat Ther 1994)
- With a measure of fatigue which reflects feelings of exhaustion, several studies showed that fatigue in the general adult population is positively related to incident non-fatal heart disease (Prescott E Int J Epidemiol 2003), fatal myocardial infarction (Schuitemaker Psychosomatics 2004) and stroke (Schuitemaker Psychosomatics 2004).
- Low levels of fatigue independently predicted longer recurrence-free and overall survival in newly diagnosed breast cancer patients, controlling for biological factors (Groenvold, Breast Cancer Res Treat 2007).

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Possible ex

- Disease explanation
- Physiological expla
- Cognitive decline
- Biological e
- Pshychoso

The first explanation is that fatigue may be a consequence of disease; Nevertheless, when the association between fatigue and adverse outcomes was adjusted for diseases (comorbidity, specific diseases) the estimates were attenuated, but the

fatigue is a consequence of age-related physiological and biological changes which are not disease-based, such as in muscle, cardiovascular and pulmonary

It is well-documented that there is an aging related loss in cognitive reserve capacities. Studies showed that subjects with poor self-reported memory and low cognitive performance reported more fatigue in B-ADL and I-ADL

3 possible biological factors: mitochondria, telomeres, and low-grade inflammation, as they all are related to aging and all may be related to fatigue.

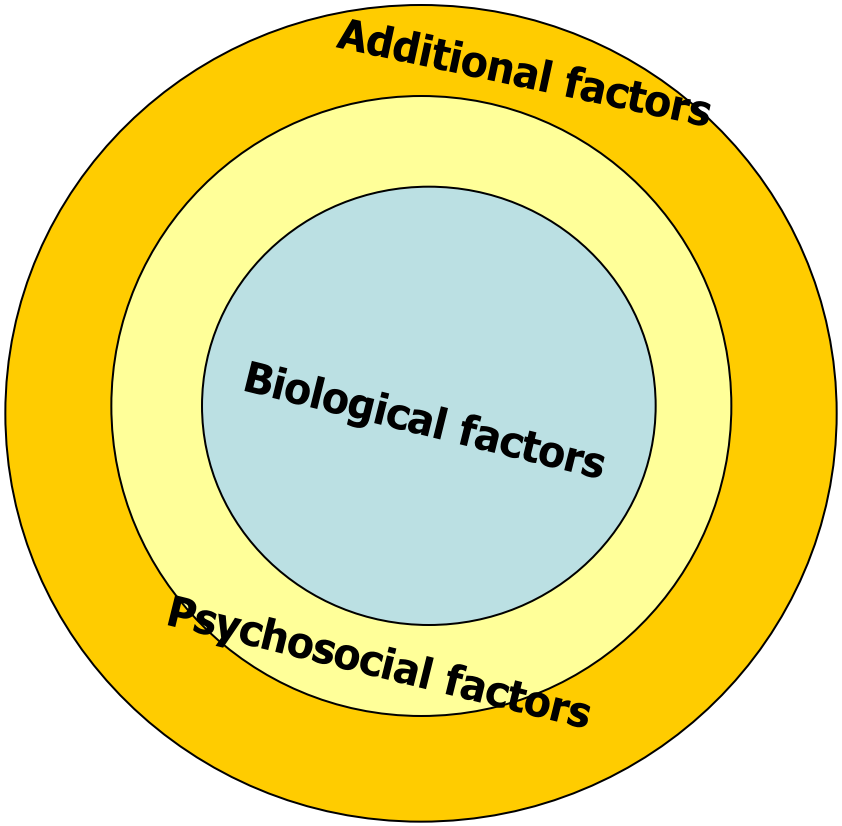
Fatigue is one symptom of depression and the feeling of fatigue is thus included in several measures of depressive symptoms. Depression is related to changes in SNC, with a bidirectional mode. A hypothetical model of fatigue in aging proposes that psychosocial factors (stress and depression) plus individual differences (personality and neuroticism) can lead to fatigue directly or indirectly through inflammation.

Importance of life-course factors

- Lack of social relation
- Social position
- Lack of partnership
- Physical performances in mid-life

Additional explanations

- Inizialmente la disregolazione del sistema avviene a livello muscolare, cardiorespiratorio e cognitivo; successivamente occorre un'interazione con fattori psico-sociali e di altra natura



Avlund, Aging Clin Experiment Research 2010

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Frailty and the Foolishness of Eos

- For the Greeks, equivalence between longevity and physical decadence is a limit only for humans. In fact, gods can age and remain fit. It is through "foolishness," or forgetfulness, rather than necessity, that living long becomes associated with frailty: Eos asked of Zeus that Tithonos may be deathless but forgets to ask for agelessness and its specific corollary, eternal youth, therefore bringing to her lover eternal aging. Interestingly, a "wise" solution to this dilemma was to transform Tithonos into a cicada (tettix). Greeks believed the cicada, being almost free from the need of food and at the same time having an extremely short life, to be a symbolic bridge between the ageless immortals and humans.

Ferrucci L. et al, Journal of Gerontology: MED SCI 2006, Vol. 61A, 260–261

The New York Times

THE NEW AGE

Old but Not Frail: A Matter of Heart and Head

Jessica Dimmock for The New York Times

Witold Bialokur is a strong runner at age 71.

By GINA KOLATA
Published: October 5, 2006

Cos'è la frailty?

- At its simplest, frailty is a state of vulnerability to adverse outcomes

Frieswijk N et al Psychol Aging 2004

Who are the frail elderly?

- Anziani ultra65enni dipendenti da altri per le ADL, spesso istituzionalizzati, che non si muovono autonomamente pur in assenza di gravi malattie cardiache, respiratorie, epatiche, renali e metaboliche che possano di per se giustificarlo ma che tuttavia richiedono continui controlli medici; la definizione non si basa solo su criteri sociali e funzionali ma deve tener conto anche d aspetti psicologici, biologici di una ridotta capacità di adattamento a modificazioni dell'ambiente interno o esterno (declino delle funzioni cognitive, alterazioni metaboliche secondarie a malnutrizione, alterazioni elettrolitiche, ridotti livelli di albumina, ridotta eliminazione dei farmaci

Woodhouse et al., Q J Med 1988

Frailty: definitions

- Condizione caratterizzata da una ridotta riserva fisiologica, associata ad un'aumentata suscettibilità, …le principali componenti della fragilità sono una ridotta capacità del sistema neurologico, cardiovascolare e respiratorio indotta dal sommarsi degli effetti dell'invecchiamento dei danni conseguenti ad uno stile di vita inadeguato (sedentarietà, fumo, abuso, alcool, ecc) ed a malattie in atto o subite nel corso della vita… la fragilità si realizza solo quando la riduzione delle riserve fisiologiche raggiunge un livello critico (critical mass)

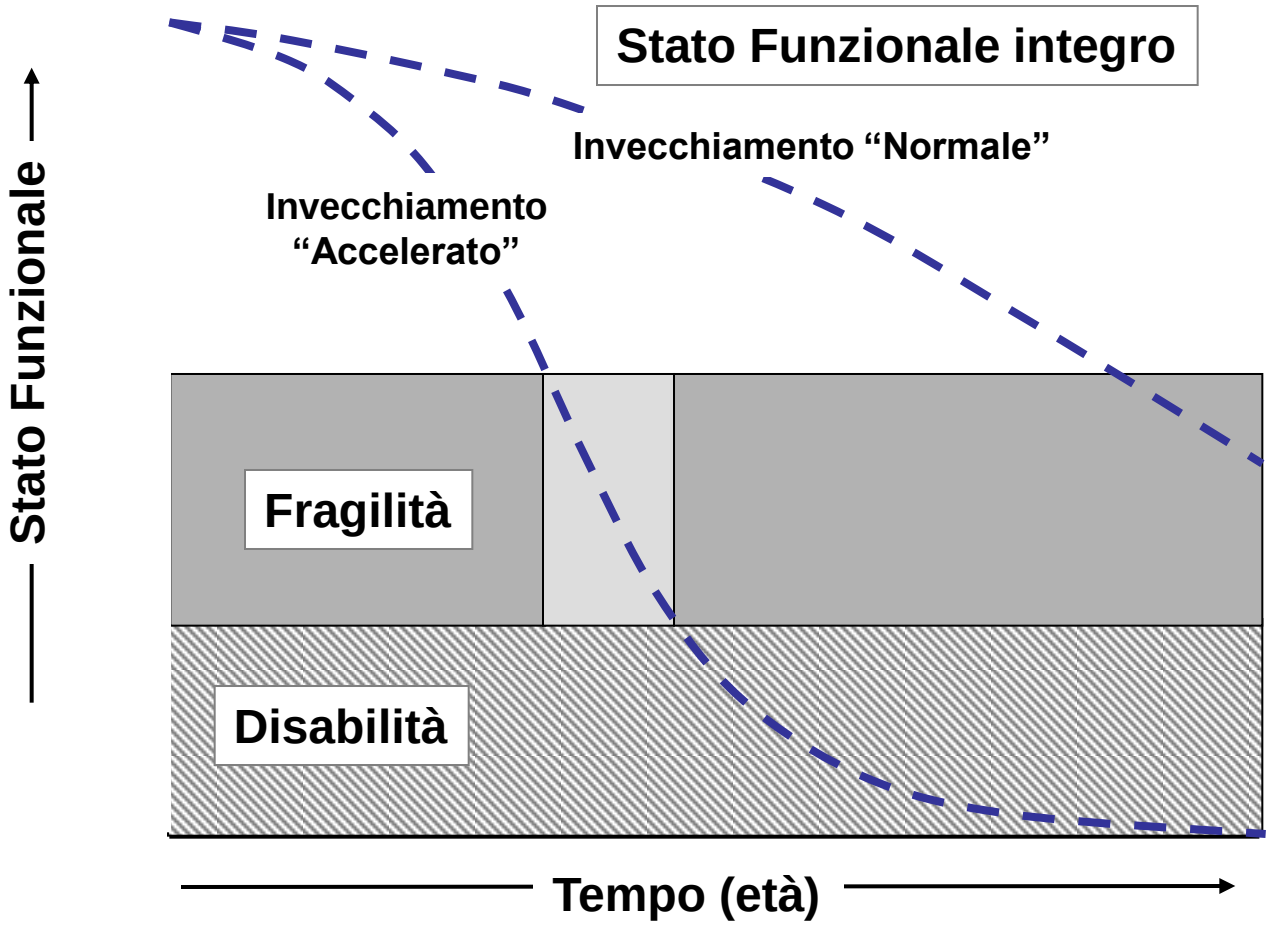
Buchner et al, Clin Geriatr Med 1992

Unstable disability and the fluctuations of frailty

- La disabilità indica perdita di funzione mentre la fragilità uno stato di instabilità e di rischio di perdita o di ulteriore perdita della funzione … espressione del numero di sistemi fisiologici vicini o al di là della soglia del compenso omeostatico. Ne deriva che la persona fragile è quella che ha un aumentato rischio di disabilità e di morte quale conseguenza di un evento stressante anche di minima entità

Campbell et al, Age Ageing 1997

Modelli di Invecchiamento: Fragilità e Disabilità



Modificato da Ferrucci L et al.

Gli strumenti per valutare la fragilità

Frailty staging system (FSS)

The FSS combines 7 core domains of functioning:

1) Disability
2) Mobility
3) Cognitive function
4) Visual function
5) Hearing function
6) Urinary continence
7) Social support

Lachs MS et al., Ann Intern Med 1990

A global clinical measure of fitness and frailty in elderly 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 proble
- Poor muscle tone in n
- Bradykinesia, facial
- Problems getting dres
- Problems with bathing
- Problems carrying out
- Urinary incontinence
- Toileting problems
- Bulk difficulties
- Rectal problems
- Gastrointestinal probl
- Problems cooking
- Sucking problems
- Problems going out al
- Impaired mobility
- Musculoskeletal probl
- Bradykinesia of the lir
- Poor muscle tone in li
- Poor limb coordination
- Poor coordination, trunk
- Poor standing posture
- Irregular gait pattern
- Falls
- Mood problems
- Postural tremor
- Intention tremor
- History of Parkinson's disease
- Family history of degenerative disease
- Seizures, partial complex
- eralized
- lackouts
- ular problems
- oke
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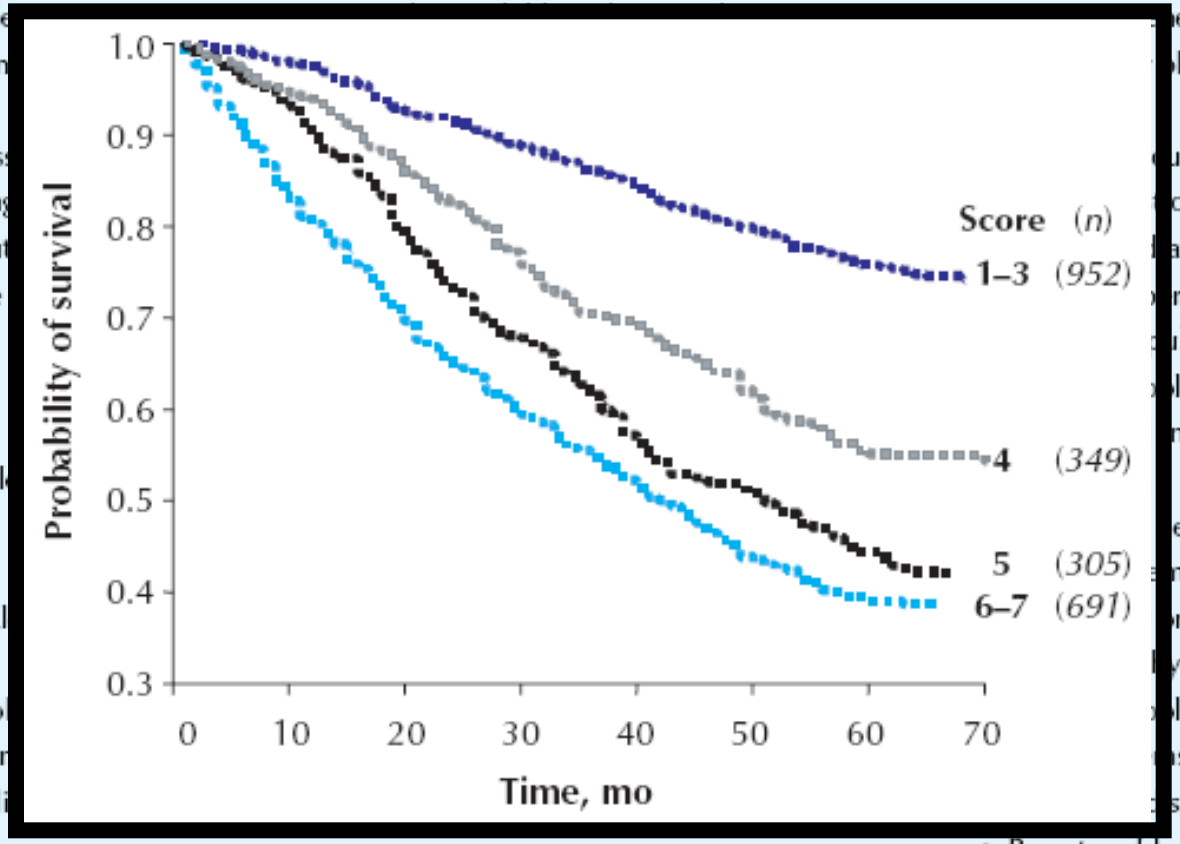
- ulses
- lems
- nfarction
- eart failure
- ns
- roblems
- yroid disease
- lems
- s
- sease
- Breast problems
- Abdominal problems
- Presence of snout reflex
- Presence of the palmomental reflex
- Other medical history



Rockwood K et al , CMAJ 2001

The Edmonton Frail Scale

Frailty domain	Item	0 point	1 point	2 points
Cognition	Please imagine that this pre-drawn circle is a clock. I would like you to place the numbers in the correct positions then place the hands to indicate a time of 'ten after eleven'	No errors	Minor spacing errors	Other errors
General health status	In the past year, how many times have you been admitted to a hospital?	0	1–2	≥2
	In general, how would you describe your health?	'Excellent', 'Very good', 'Good'	'Fair'	'Poor'
Functional independence	With how many of the following activities do you require help? (meal preparation, shopping, transportation, telephone, housekeeping, laundry, managing money, taking medications)	0–1	2–4	5–8
Social support	When you need help, can you count on someone who is willing and able to meet your needs?	Always	Sometimes	Never
Medication use	Do you use five or more different prescription medications on a regular basis?	No	Yes	
	At times, do you forget to take your prescription medications?	No	Yes	
Nutrition	Have you recently lost weight such that your clothing has become looser?	No	Yes	
Mood	Do you often feel sad or depressed?	No	Yes	
Continence	Do you have a problem with losing control of urine when you don't want to?	No	Yes	
Functional performance	I would like you to sit in this chair with your back and arms resting. Then, when I say 'GO', please stand up and walk at a safe and comfortable pace to the mark on the floor (approximately 3 m away), return to the chair and sit down'	0–10 s	11–20 s	One of >20 s patient unwilling, or requires assistance
Totals	Final score is the sum of column totals			

Rolfsonn et al, Age Ageing 2006

Age and Ageing 2008; **37:** 161–166
doi:10.1093/ageing/afm195
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Development of an easy prognostic score for frailty outcomes in the aged

Giovanni Ravaglia[1], Paola Forti[1], Anna Lucicesare[1], Nicoletta Pisacane[1], Elisa Rietti[1], Christopher Patterson[2]

Prognostic score	Subjects No.	Death No.	(%)	HR (95% CI)	*P*-value
0–2	628	32	5.1	1	
3	159	19	11.9	2.37 (1.34–4.19)	0.003
4	83	18	21.7	4.49 (2.52–8.01)	<0.001
5	61	25	41.0	8.97 (5.31–15.1)	<0.001
6	49	32	65.3	17.5 (10.73–28.70)	<0.001
≥7	27	21	77.8	30.6 (17.57–53.3)	<0.001

Hazard ratios (HR) and relative 95% confidence intervals (CI) are for a total of 1,007 participants with 147 cases of death.

Variables in the frailty score

- age ≥80 years,
- male gender,
- low physical activity
- comorbidity,
- sensory deficits,
- calf circumference < 31 cm
- IADL dependence
- Gait & performance test < 24
- Pessimism about health

Domains evaluated in different instruments

	Groningen Frailty Indicator[19]	Frailty and Autonomy Scoring Instrument of Leuven (FRAIL)[51]	Edmonton Frail Scale[23]	Frailty Staging System[53]
ADL	•	•	•	•
IADL	•	•	•	•
Activities outside	•	•	•	•
Sensory functions	•	•		•
Medication	•	•	•	
Memory	•	•	•	
Orientation		•	•	•
Behaviour	•	•	•	•
Social contacts	•	•		
Familial functioning	•	•		
Ability to plan things		•		
Finances		•		
Feeling fit/health status	•		•	
Weight loss	•		•	
Continence		•	•	•

ADL = activities of daily living. IADL = instrumental activities of daily living.

De Lepeleire et al, Br J Gen Pract 2009

Critiche mosse al modello di frailty di Rockwood

- La fragilità è considerata una variabile di stato (aggregato di malattie)
  - "the more things individuals have wrong with them, the higher the likelihood they will be frail'
  - Non possibile un miglioramento
- Coesistenza di malattie, impairments, disabilità (è un indicatore di salute più che di fragilità)
- Poca trasferibilità nella pratica clinica

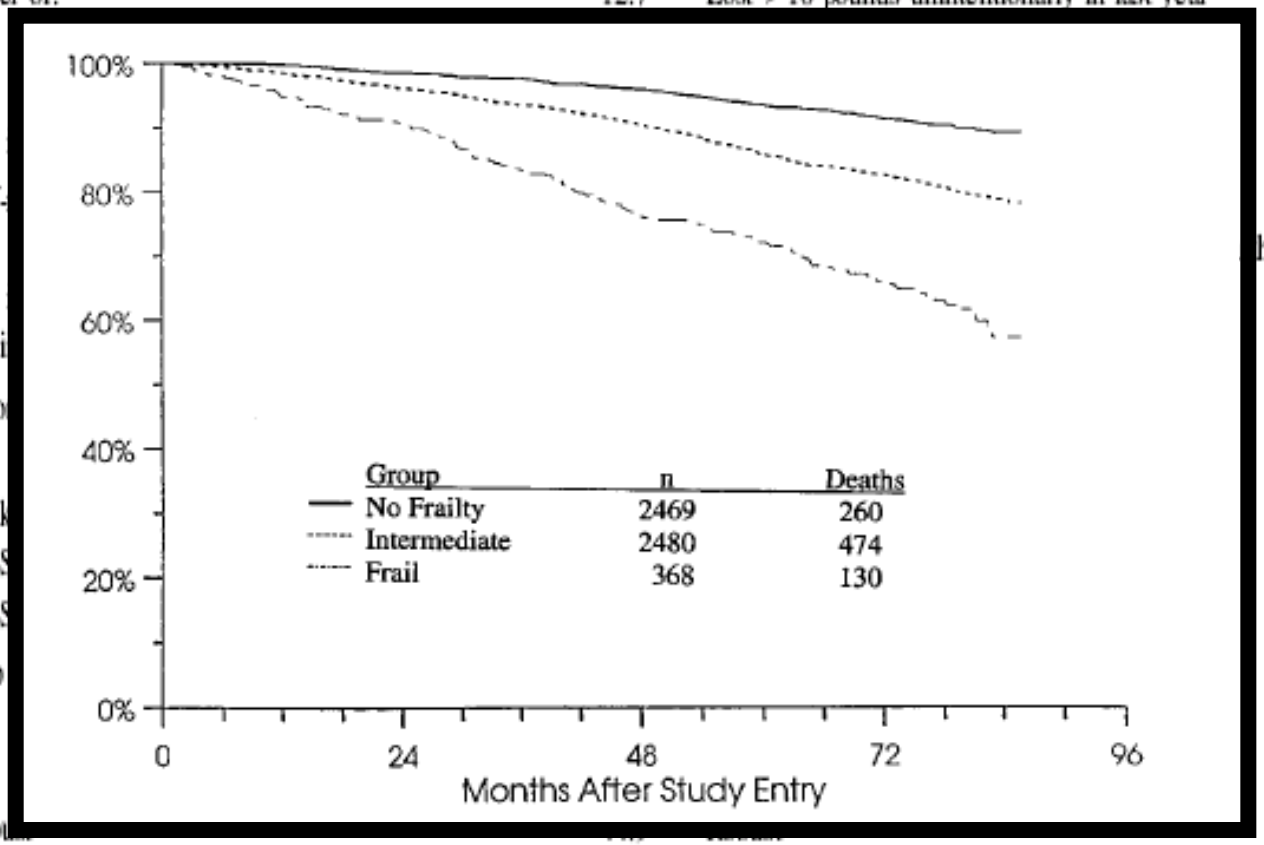
Il modello di frailty della Fried

- State of high vulnerability for adverse health outcomes, including disability, dependency, falls, need for long-term care, and mortality.
- Frailty can be defined as a physiologic state of increased vulnerability to stressors that results from **decreased physiologic reserves, and even dysregulation, of multiple physiologic systems**
- Frailty is an **aggregate expression of risk** resulting from age- or disease-associated **physiologic accumulation of subthreshold decrements affecting multiple physiologic systems**

Fried L. et al, *Journal of Gerontology, 2004*

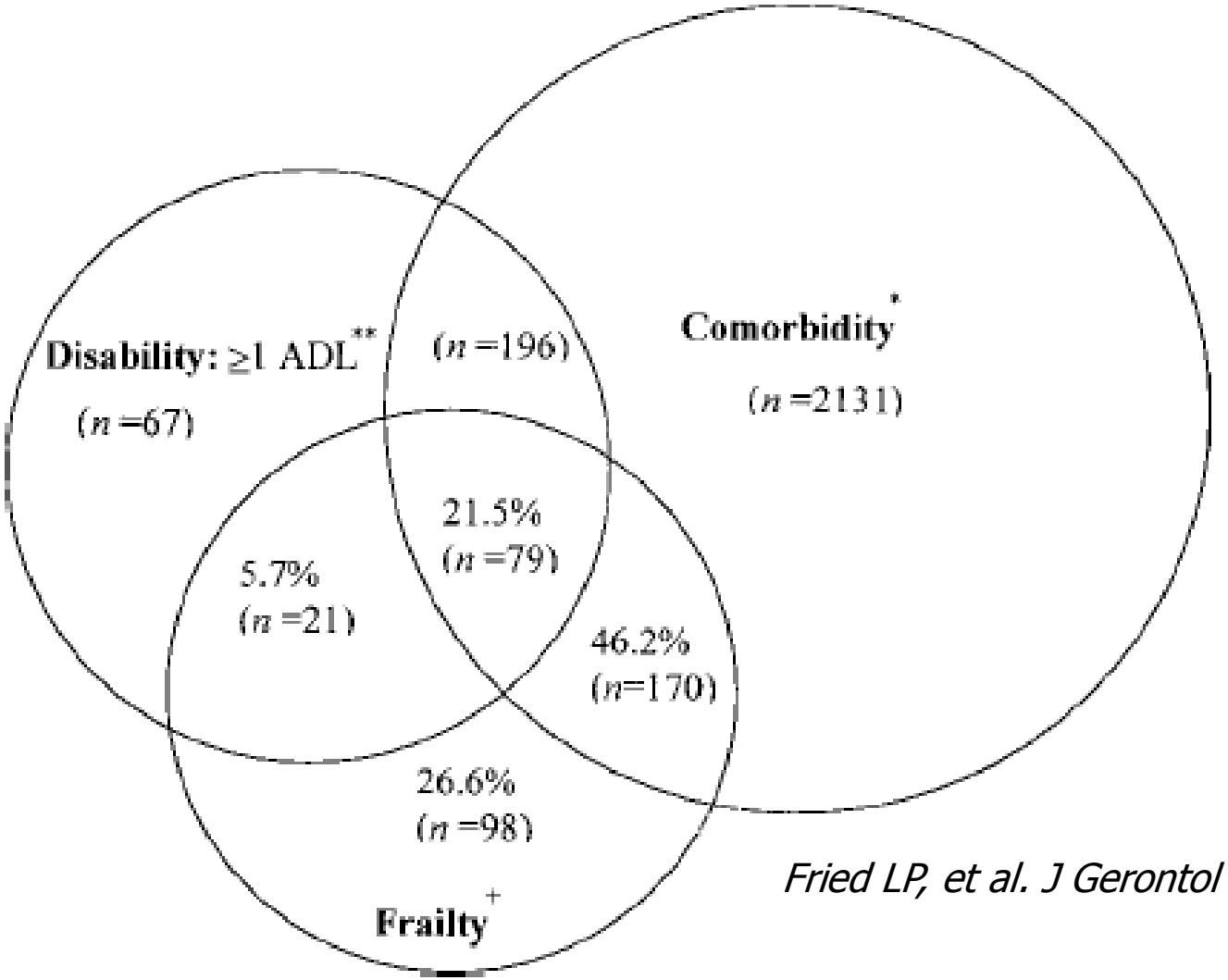
Table 1. Frailty-Defining Criteria: WHAS and CHS

Characteristics	WHAS Definition	WHAS %*	CHS Definition	CHS %*
Weight loss	Either of:	12.7	Lost >10 pounds unintentionally in last year	7.3
Exhaustion	Self-			21.3
			he last week, or	
Low energy expenditure§	90 o			24.1
Slowness§	Walk			38.0
Weakness§	Grip			26.2
Overall frailty status	Robu			33.2
	Intermediate	43.8	Intermediate	55.2
	Frail	11.3	Frail	11.6



Bandeen-Roche et al, *Journal of Gerontology, 2006*

Fragilità, comorbilità e disabilità non sono sinonimi

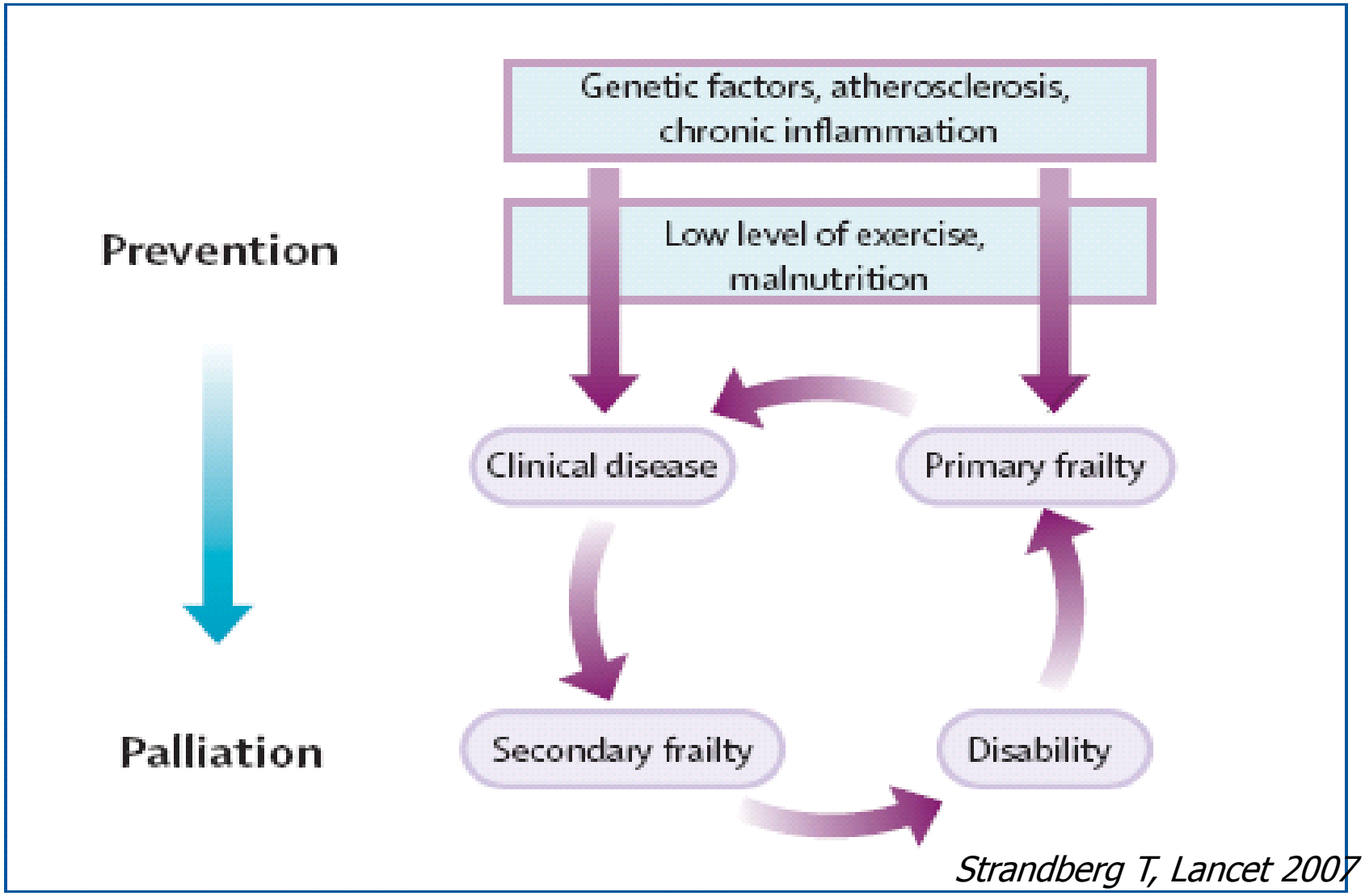


Fried LP, et al. J Gerontol Med Sci 2004

Critiche mosse al modello di frailty di Fried

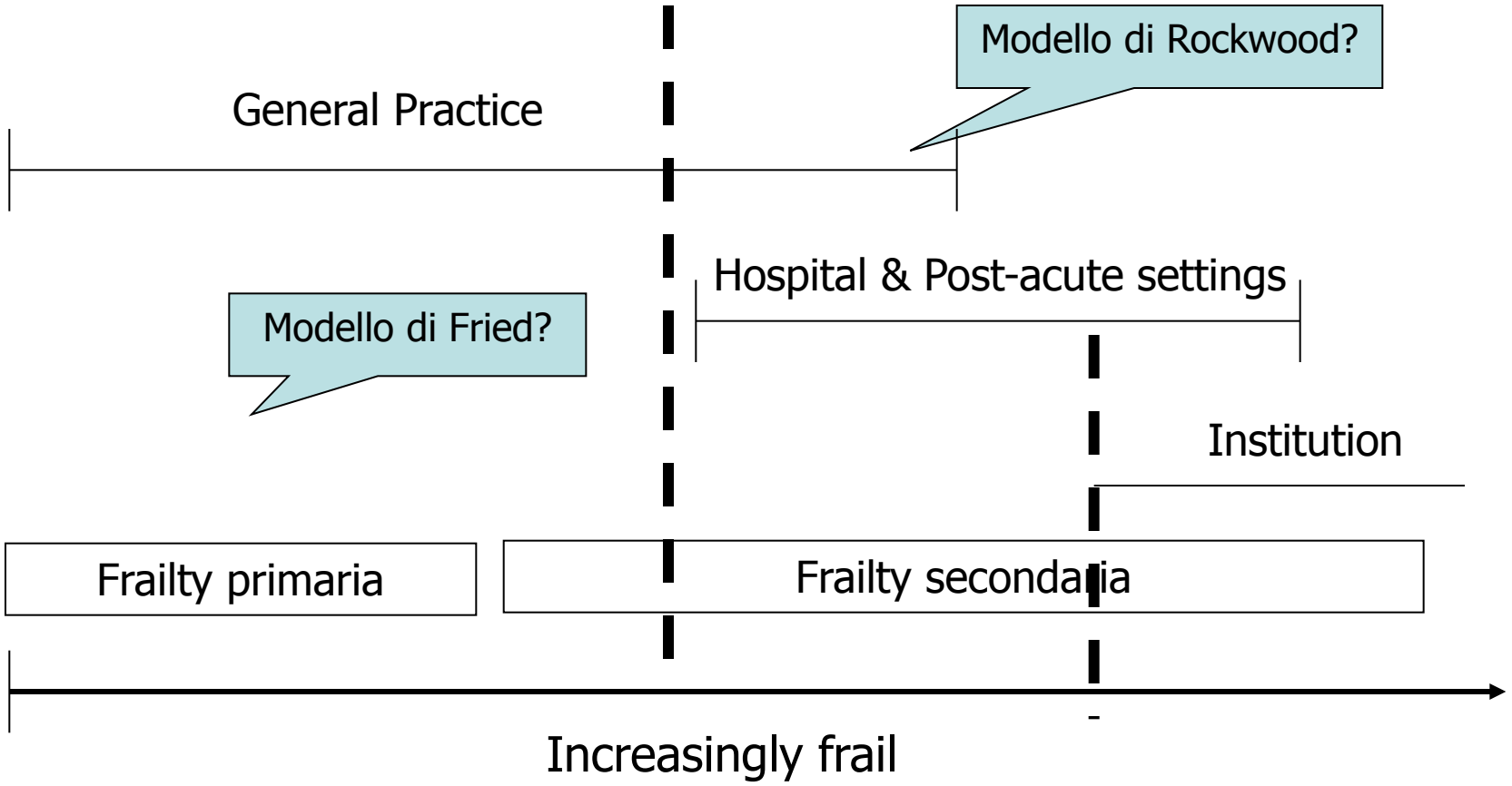
- È adottato un approccio unidimensionale ad un concetto che per natura è complesso e multidimensionale
- Poca applicabilità in un contesto clinico
- L'esclusione di indici di misura della cognitività e della depressione è controversa

La necessità di definire più tipi di frailty



Strandberg T, Lancet 2007

Strumenti differenti per ambiti di interesse differenti



Un confronto tra il concetto di fatigue ed i criteri di frailty di Fried

- There is *a danger of missing the trees for the forest*. Focusing on frailty may lead to denying treatment to older persons affected by only one of the frailty components (i.e., poor muscle strength), which may in itself be an important predictor for adverse outcomes. At the same time, individuals with diseases that mimic the features of frailty may be erroneously considered to be frail.

Bergman et al. J Gerontol 2007

Initial Manifestations of Frailty Criteria and the Development of Frailty Phenotype in the

Table 5. Discrete-Time Proportional Hazards Analysis of Univariate Associations of Individual Frailty Criterion and the Number of Criteria at Baseline With the Development of Frailty After Adjusting for Age, Race, Education, Comorbidity ($N = 380$*; with 55 Incident Frailty Cases over 7.5 Years)

	Model I†				Model II‡			
		Risk of Frailty Onset				Risk of Frailty Onset		
Baseline Status: Individual Frailty Criterion	Number of Women with Each Criterion	Hazard Ratio	95% CI	*p* Value	Number of Women With 1 Criterion Only	Hazard Ratio	95% CI	*p* Value
Weakness	31	2.60	1.16–5.80	.02	18	2.03	0.68–6.06	.21
Slowness	41	1.46	0.59–3.63	.42	28	1.93	0.76–4.91	.17
Low physical activity	35	2.25	0.94–5.35	.07	24	2.48	0.93–6.60	.07
Exhaustion	26	3.71	1.54–8.91	<.01	17	3.30	1.11–9.76	.03
Weight loss	27	4.37	2.01–9.51	<.01	21	4.82	2.03–11.45	<.01
		Model III§						
No. of criteria at baseline								
0	246	1	–					
1	108	2.99	1.68–5.34	<.001				
2	26	3.01	1.22–7.43	.02				

Notes: *Of the 420 women who were nonfrail or prefrail at baseline, 40 were deleted from this analysis because of study dropout after baseline ($n = 20$), missing data on specific frailty criteria at baseline ($n = 19$), or level of education ($n = 1$).

†Model I: estimating the relative hazard of incident frailty for comparing women with each specific criterion to women without any criterion at baseline.

‡Model II: estimating the relative hazard of incident frailty for comparing women with only one specific criterion to women without any criterion at baseline.

§Model III: estimating the relative hazard of incident frailty for comparing the number of criteria at baseline.

CI = confidence interval; – = inapplicable.

progression.

Conclusioni

- La fatigue è un sintomo da tenere in considerazione nelle persone anziane
- Può essere utilizzato come proxy di fragilità ma probabilmente solo in ambiti di ricerca epidemiologica (anziani pre-disabili)
- È necessario individuare modelli di valutazione della fragilità in base ai differenti ambiti di studio

Fatigue as a symptom of disease

Table 1

Proposed ICD-10 Criteria for Cancer-Related Fatigue

A. Six (or more) of the following symptoms have been present every day or nearly every day during the same 2-week period in the past month, and at least one of the symptoms is (1) significant fatigue.
   1. Significant fatigue, diminished energy, or increased need to rest, disproportionate to any recent change in activity level.
   2. Complaints of generalized weakness or limb heaviness.
   3. Diminished concentration or attention.
   4. Decreased motivation or interest to engage in usual activities.
   5. Insomnia or hypersomnia.
   6. Experience of sleep as unrefreshing or nonrestorative.
   7. Perceived need to struggle to overcome inactivity.
   8. Marked emotional reactivity (e.g., sadness, frustration, or irritability) to feeling fatigued.
   9. Difficulty completing daily tasks attributed to feeling fatigued.
   10. Perceived problems with short-term memory.
   11. Post-exertional malaise lasting several hours.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. There is evidence from the history, physical examination, or laboratory findings that the symptoms are a consequence of cancer or cancer therapy.

D. The symptoms are not primarily a consequence of co-morbid psychiatric disorders such as major depression, somatization disorder, somatoform disorder, or delirium.

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Poststroke Fatigue

A 2-Year Follow-Up Study of Stroke Patients in Sweden

Eva-Lotta Glader, MD; Birgitta Stegmayr, PhD; Kjell Asplund, MD, PhD

TABLE 6. Multivariate Analyses of Case Fatality 1 Year After 2-Year Follow-Up (3 Years After Stroke Event)

	P	OR	95% CI
Age	<0.001	1.06	1.04–1.07
Speech impairment			
Marital status			
Living together	Reference category		
Living alone	0.42	1.13	0.84–1.53
Missing patients	<0.001	2.25	1.64–3.06
Fatigue			
Never or sometimes	Reference category		
Often	0.045	1.31	1.01–1.71
Always	<0.001	1.85	1.35–2.54

Conclusions—Fatigue is frequent and often severe, even late after stroke. It is associated with profound deterioration of several aspects of everyday life and with higher case fatality, but it usually receives little attention by healthcare professionals. Intervention studies are needed. (*Stroke*. 2002;33:1327-1333.)