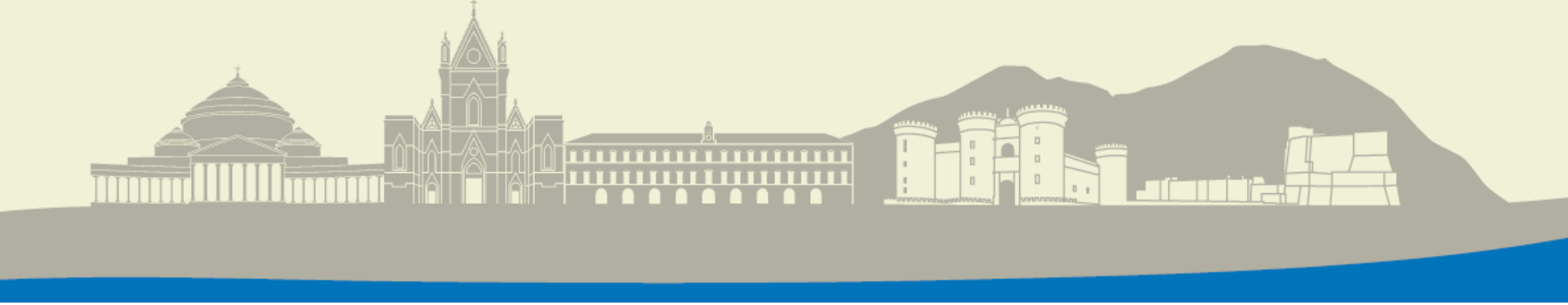

60° CONGRESSO NAZIONALE

NAPOLI

25-28 Novembre 2015

Sarcopenia e Ospedalizzazione

Stefano Volpato

Dipartimento di Scienze Mediche – UNIFE &
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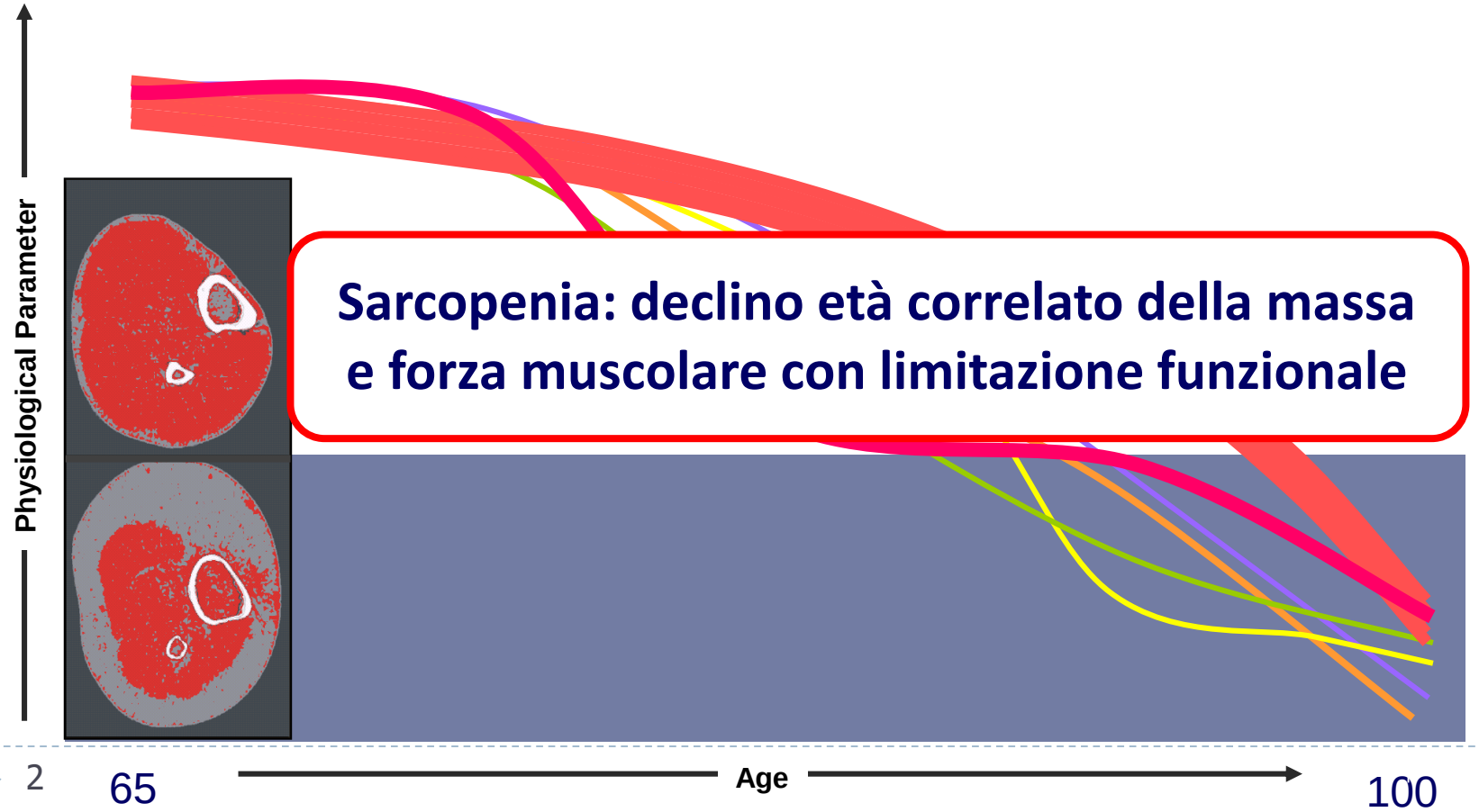
SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Ferrara

Università di Ferrara
- ex labore fructus -

Invecchiamento, meccanismi omeostatici e capacità funzione

Progressivo deterioramento dell'integrità anatomica e funzionale che interessa molteplici sistemi fisiologici



Interazione tra modificazioni età-correlate e malattie croniche

CHD, CHF, CVD, diabete, BPCO, obesità, artrosi, depressione, demenza

Malattie croniche

↓Riserva funzionale

Invecchiamento

Progressivo deterioramento dell'integrità anatomica e funzionale dei sistemi fisiologici

Fragilità

Sarcopenia

Declino funzionale

Cadute

Disabilità

Ospedalizzazione

Instituzionalizzazione

Morte

65 aa — Età — 100 aa

Sarcopenia e Ospedalizzazione

1. Ospedalizzazione come outcome della sarcopenia

2. Ospedalizzazione come fattore di rischio per sarcopenia

3. Sarcopenia come fattore prognostico dell’ospedalizzazione:
   1. Stato funzionale
   2. Comliplicanze
   3. Costi
   4. Mortalità

Sarcopenia nel paziente Ospedalizzato: Quale definizione operativa?

1. **E**uropean **W**orking **G**roup on **S**arcopenia in **O**lder **P**eople (EWGSOP)

2. **I**nternational **W**orking **G**roup

3. **F**oundation of **N**IH **S**arcopenia **P**roject

Sarcopenia nel paziente Ospedalizzato: Quale definizione operativa?

Criteria	Operational Definition: Physical Performance	Operational Definition: Muscle Strength	Operational Definition: ALM
Foundation of NIH Sarcopenia Project			
Weakness and low lean mass	—	Grip strength Men: <26 kg Women: <16 kg	ALM_{BMI} Men: <0.789 Women: <0.512
Slowness with weakness and low lean mass	Gait speed: ≤0.8 m/s	Grip strength Men: <26 kg Women: <16 kg	ALM_{BMI} Men: <0.789 Women: <0.512
International Working Group	Gait speed: <1.0 m/s	—	ALM/ht^2 Men: ≤7.23 kg/m² Women: ≤5.67 kg/m²
European Working Group on Sarcopenia Older Persons			
Sarcopenia	Gait speed: <0.8 m/s or Grip strength Men: <30 kg Women: <20 kg		ALM/ht^2 Men: ≤7.23 kg/m² Women: ≤5.67 kg/m²
Severe sarcopenia	Gait speed: <0.8 m/s	Grip strength Men: <30 kg Women: <20 kg	ALM/ht^2 Men: ≤7.23 kg/m² Women: ≤5.67 kg/m²

Dam TT et al. JGMS 2014;69:584-90

Concordanza diagnostica tra le tre definizioni operative

	IWG			EWGSOP Sarcopenia		
	PPA (%)	NPA (%)	κ	PPA (%)	NPA (%)	κ
Men						
FNIH weakness and low lean mass	9.0	98.5	0.14	19.1	99.1	0.53
FNIH slowness with weakness and low lean mass	7.1	99.7	0.11	4.3	99.7	0.07
Women						
FNIH weakness and low lean mass	9.0	97.8	0.12	11.4	96.8	0.14
FNIH slowness with weakness and low lean mass	4.5	99.6	0.04	4.0	98.5	0.04

PPA: percentuale di concordanda positiva
NPA: percentuale di concordanza negativa

Dam TT et al. JGMS 2014;69:584-90

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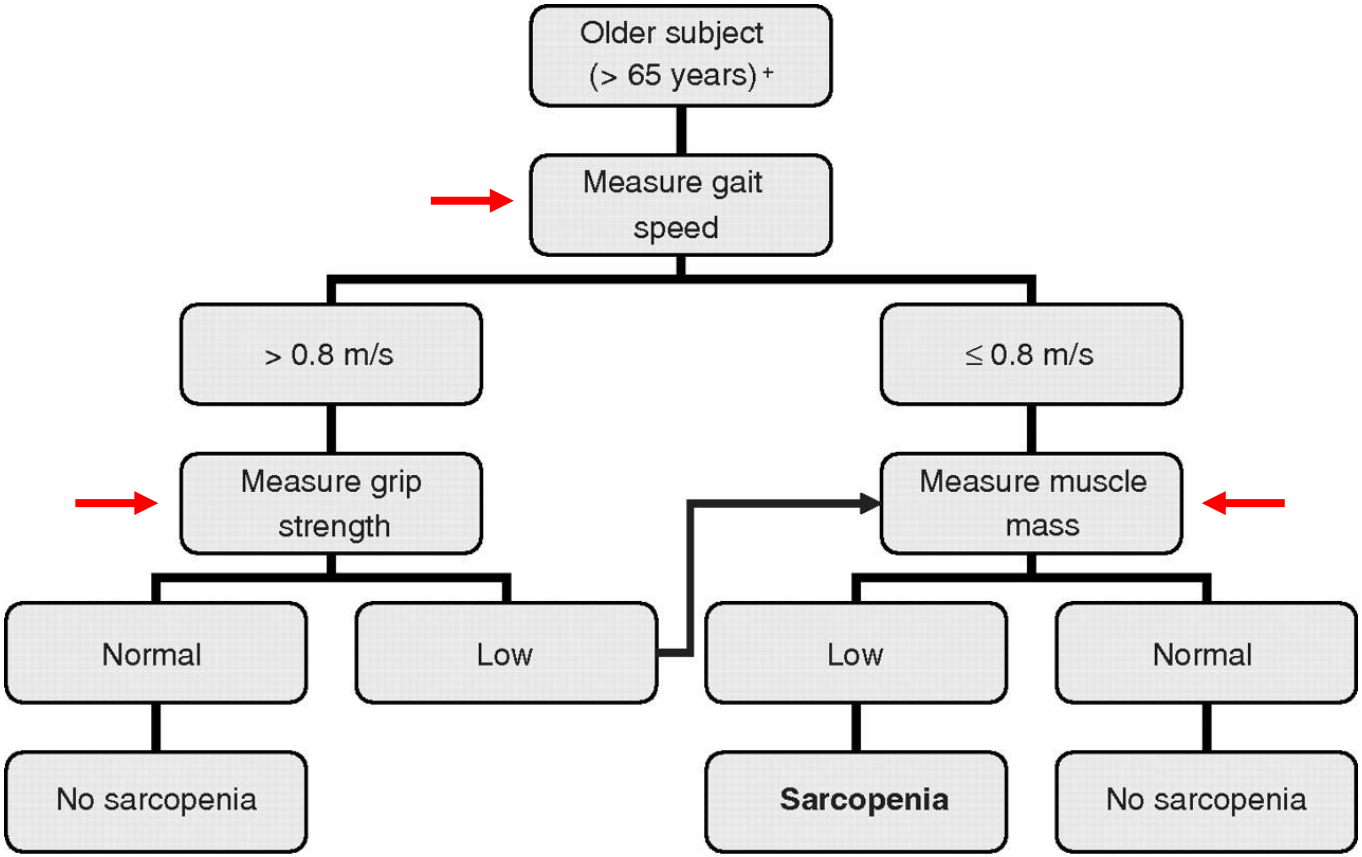
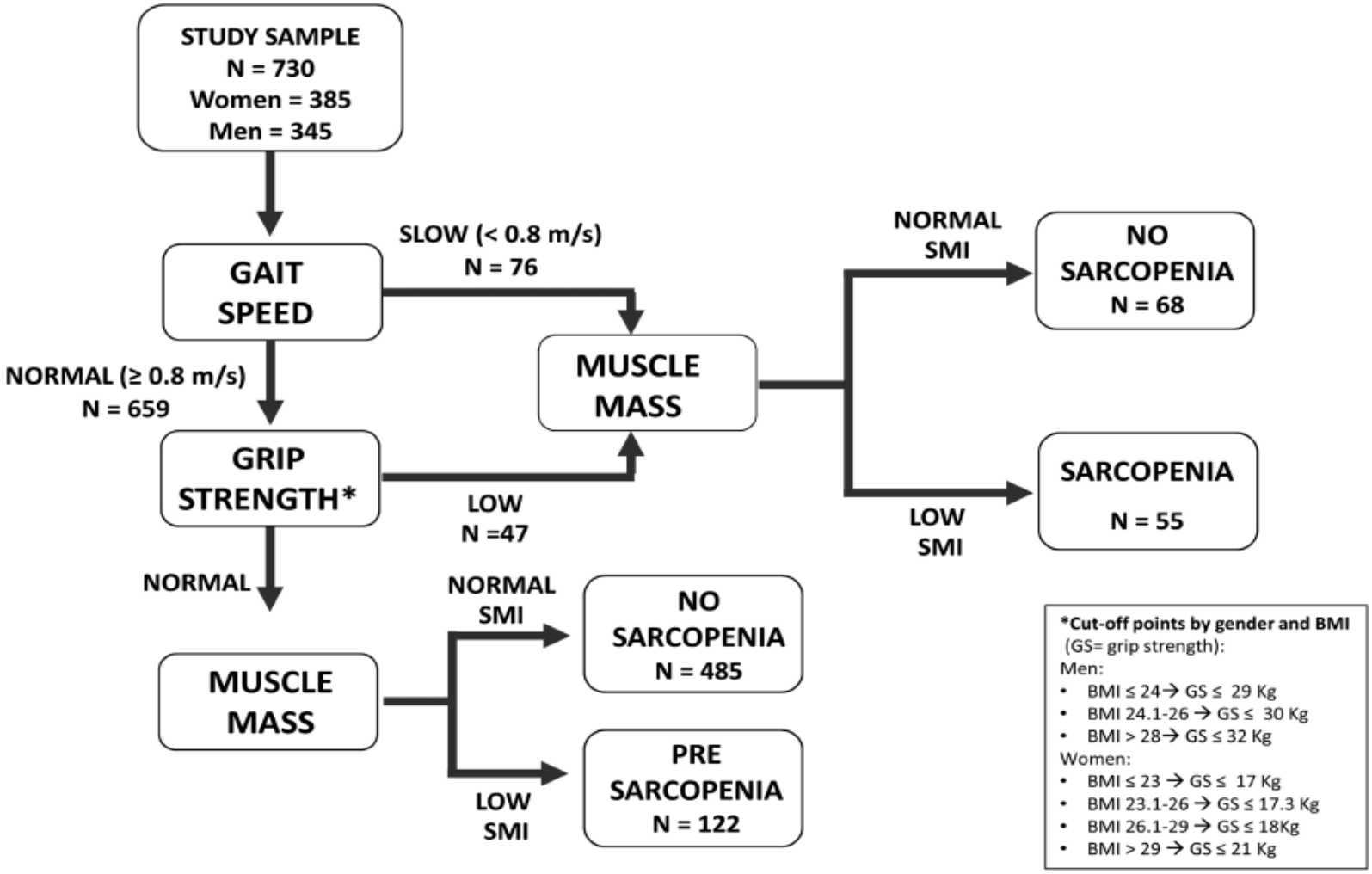
Algoritmo EWGSOP per la diagnosi di sarcopenia nel paziente anziano



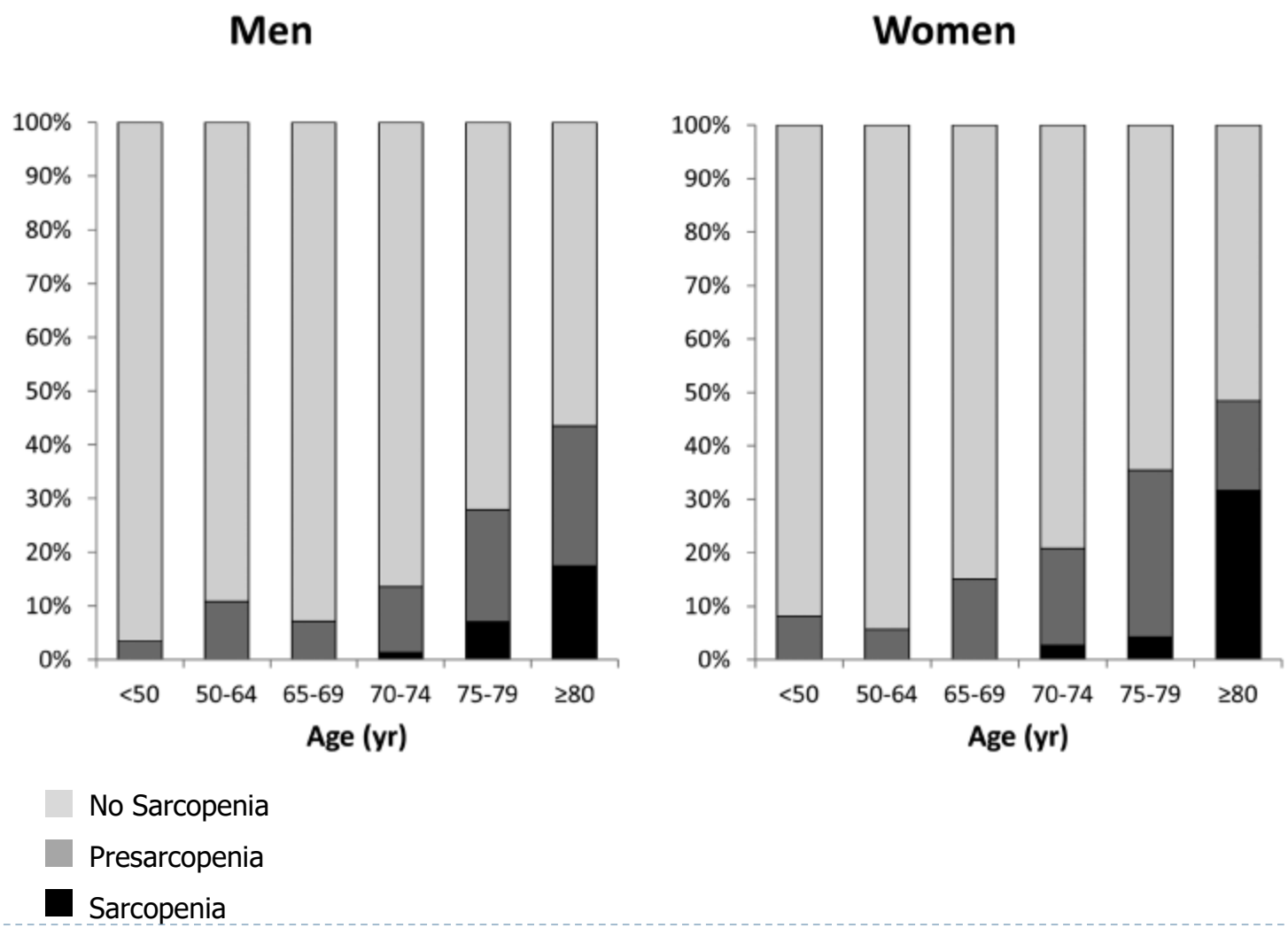
Cruz-Jentoft A J et al. Age Ageing 2010;39:412-423

Prevalenza di sarcopenia (EWGOSP) nella popolazione dello studio InCHIANTI



Volpato S et al. JGMS 2014;69:438-46

Prevalenza di sarcopenia (EWGOSP) in base a età e sesso, nella popolazione dello studio InCHIANTI



Volpato S et al. JGMS 2014;69:438-46

Valore predittivo della sarcopenia secondo l'algoritmo EWGSOP nello studio InCHIANTI

	No sarcopenia	**Pre-sarcopenia**	**Sarcopenia**	**p**
N (%)	373 (69.3)	110 (20.4)	55 (10.2)	
Donne (%)	50.7	58.8	65.4	0.062
Età (aa)	75.9±4.9	77.7±4.9	83.8±5.9	<0.001
Scolarità (aa)	6.1±3.5	6.6±3.7	4.7±2.6	0.001
BMI (kg/m^2)	28.4±3.6	24.7±3.3	25.4±4.0	<0.001
Comorbilità (n)	1.97±1.2	2.20±1.2	2.65±1.2	<0.001
Hb (g/dl)	14.2±1.3	14.0±1.3	13.0±1.5	<0.001

Bianchi L D et al JGMS, 2015; Epub ahead of print

Valore predittivo della sarcopenia (EWGSOP) nello studio InCHIANTI: **OSPEDALIZZAZIONE**

	No Sarcopenia N= 483		**Sarcopenia** N= 55	
Eventi	47.8%		60.0%	
		Modello Crudo	***Aggiustato per sesso-età***	***Modello finale****
Ospedalizzazione				
HR	1	1.57	1.63	1.57
95% CI	-	(1.09-2.26)	(1.08-2.44)	(1.03-2.40)

* Aggiustato per età, sesso, scolarità, BMI, comorbilità, emoglobina

Bianchi L D et al JGMS, 2015; Epub ahead of print

Sarcopenia e Ospedalizzazione

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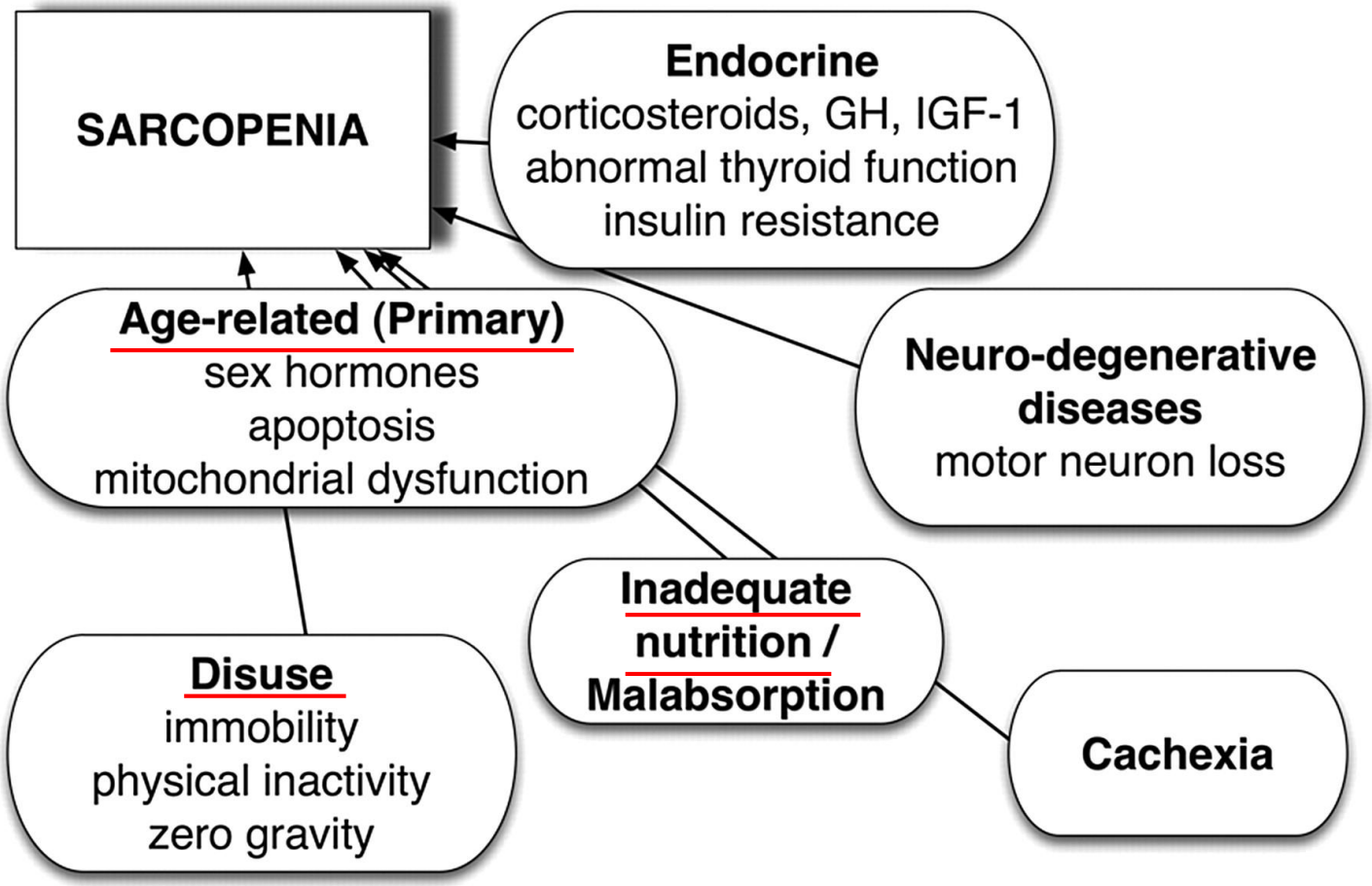
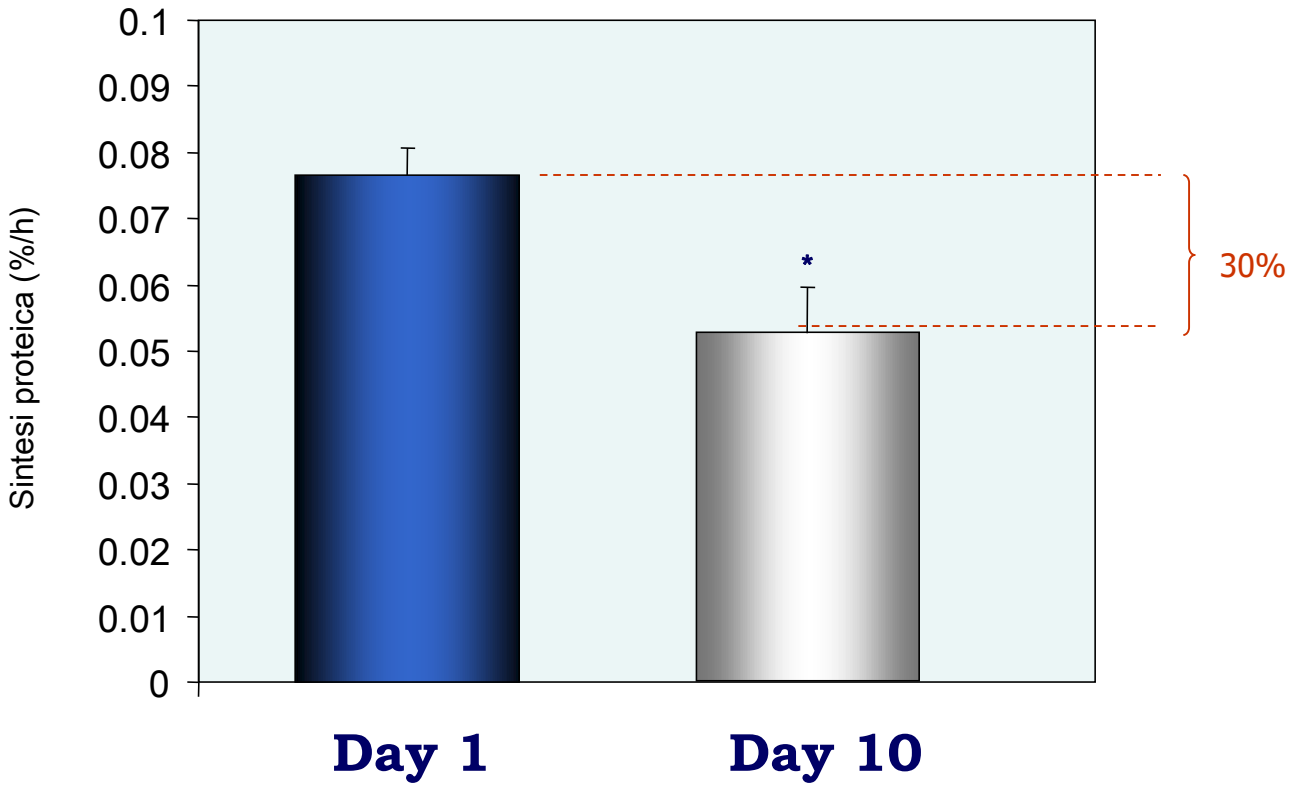
Fattori di Rischio per Sarcopenia nell'anziano



Cruz-Jentoft A J et al. Age Ageing 2010;39:412-423

Inattività fisica e sintesi proteica nell'anziano



Sintesi proteica nelle 24 h duriante10 gg di inattività fisica
(stable isotope methodology)

Kortebein, P. et al. JAMA 2007

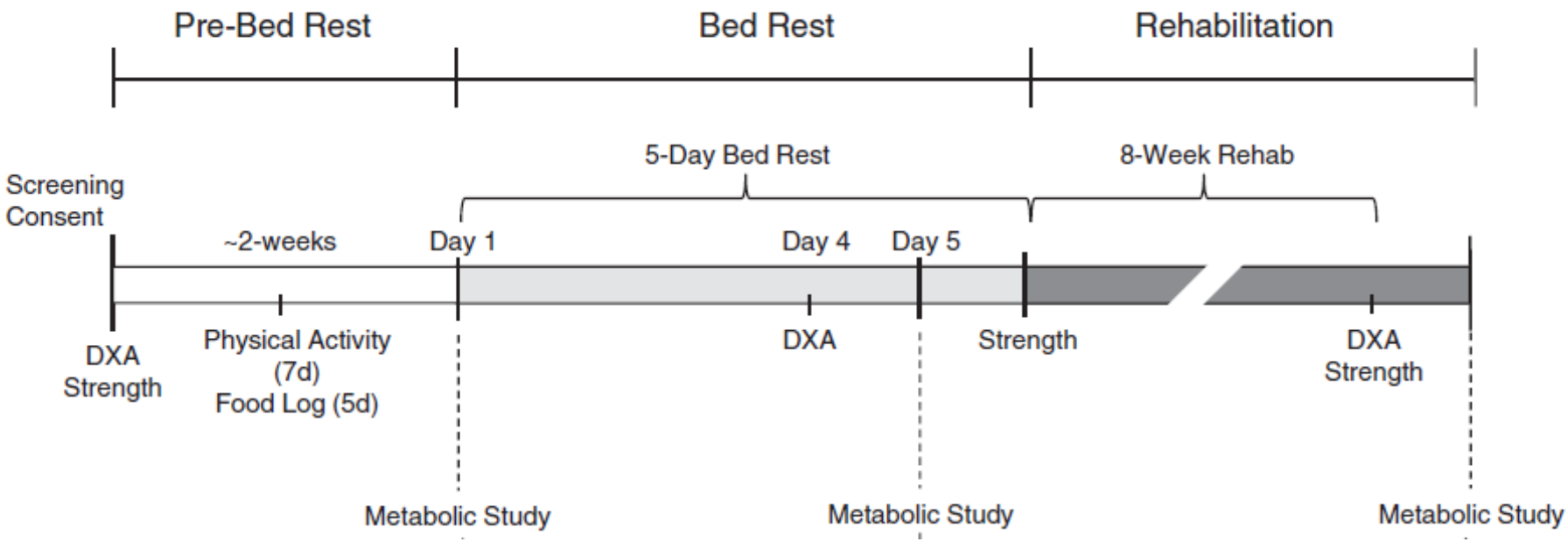
Effetto di 10 giorni di allettamento nell'anziano

Table. Effects of 10 Days of Bed Rest in Older Adults

	No. of Participants (N = 12)*	Mean (95% Confidence Interval)			*P* Value
		Bed Rest			
		Before	After	Change	
Muscle fractional synthetic rate, % per h†	10	0.077 (0.059 to 0.095)	0.051 (0.035 to 0.067)	−0.027 (−0.007 to −0.047)	.02
% Change				−30.0 (−7.0 to −54.0)	
DEXA lean mass, kg‡	10				
Whole body		48.05 (40.61 to 55.49)	46.51 (39.57 to 53.45)	−1.50 (−0.62 to −2.48)	.004
% Change				−3.2 (−1.4 to −5.0)	
Lower Extremity		15.01 (12.41 to 17.61)	14.06 (11.85 to 16.27)	−0.95 (−0.42 to −1.48)	.003
% Change				−6.3 (−3.1 to −9.5)	
Isokinetic muscle strength, Nm per s§	11	120 (96 to 145)	101 (81 to 121)	−19 (−11 to −30)	.001
% Change				−15.6 (−8.0 to −23.1)	

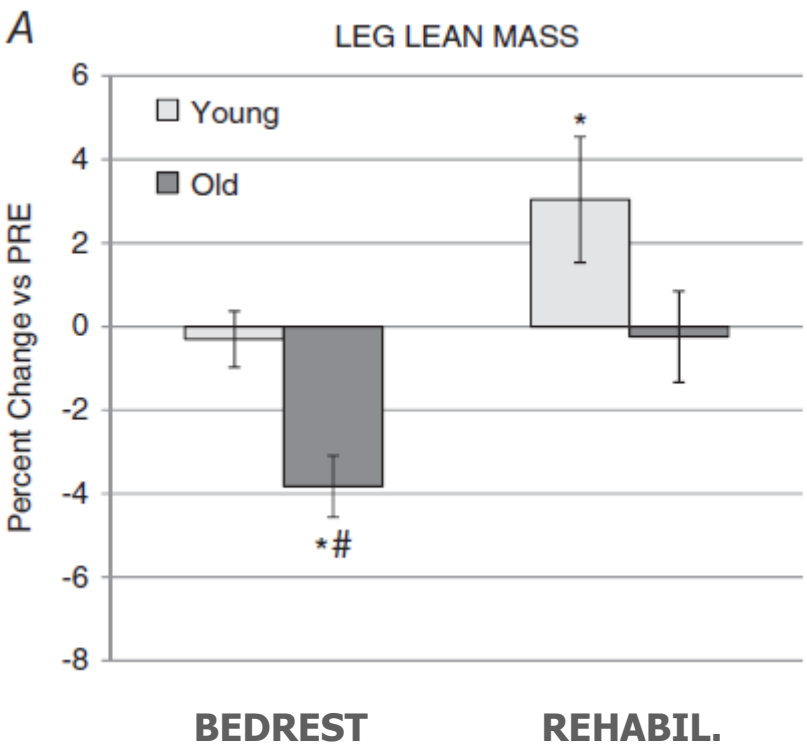
Kortebein, P. et al. JAMA 2007

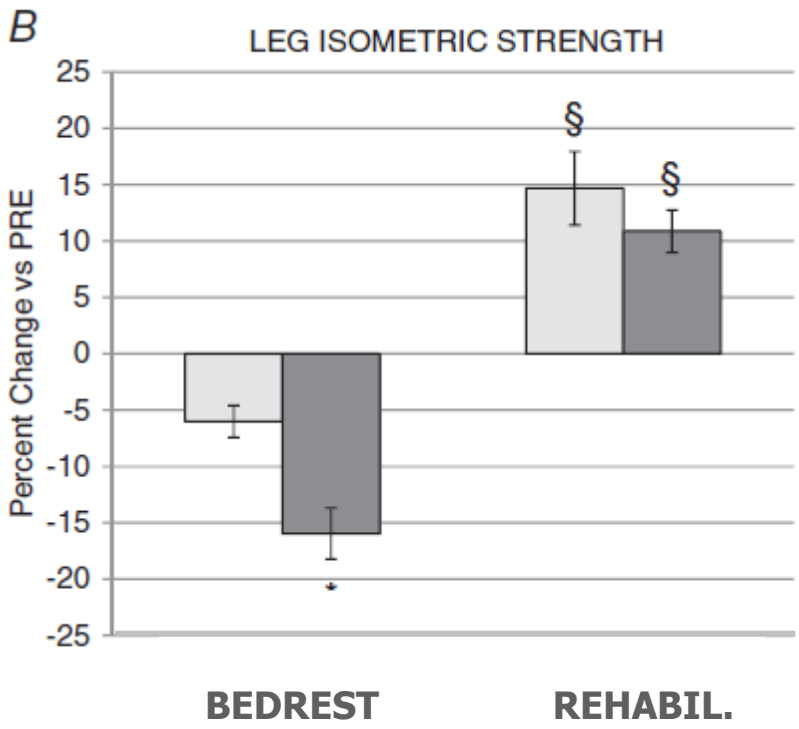
Age-related differences in lean mass, protein synthesis and skeletal muscle markers of proteolysis after bed rest and exercise rehabilitation



Tunner R E. J.Physiol. 2015;593:4259–4273

Age-related differences in lean mass, protein synthesis and skeletal muscle markers of proteolysis after bed rest and exercise rehabilitation





Tunner R E. J.Physiol. 2015;593:4259–4273

Il Gruppo GLISTEN

Gruppo Lavoro Italiano Sarcopenia – Trattamento e Nutrizione

Studio multicentrico osservazionale sulla prevalenza di sarcopenia, e dei suoi correlati clinici, nella popolazione anziana ospedalizzata

Lo Studio GLISTEN

OBIETTIVI PRIMARI

1- Determinare la prevalenza di Sarcopenia (criteri EWGSOP) in soggetti anziani ospedalizzati

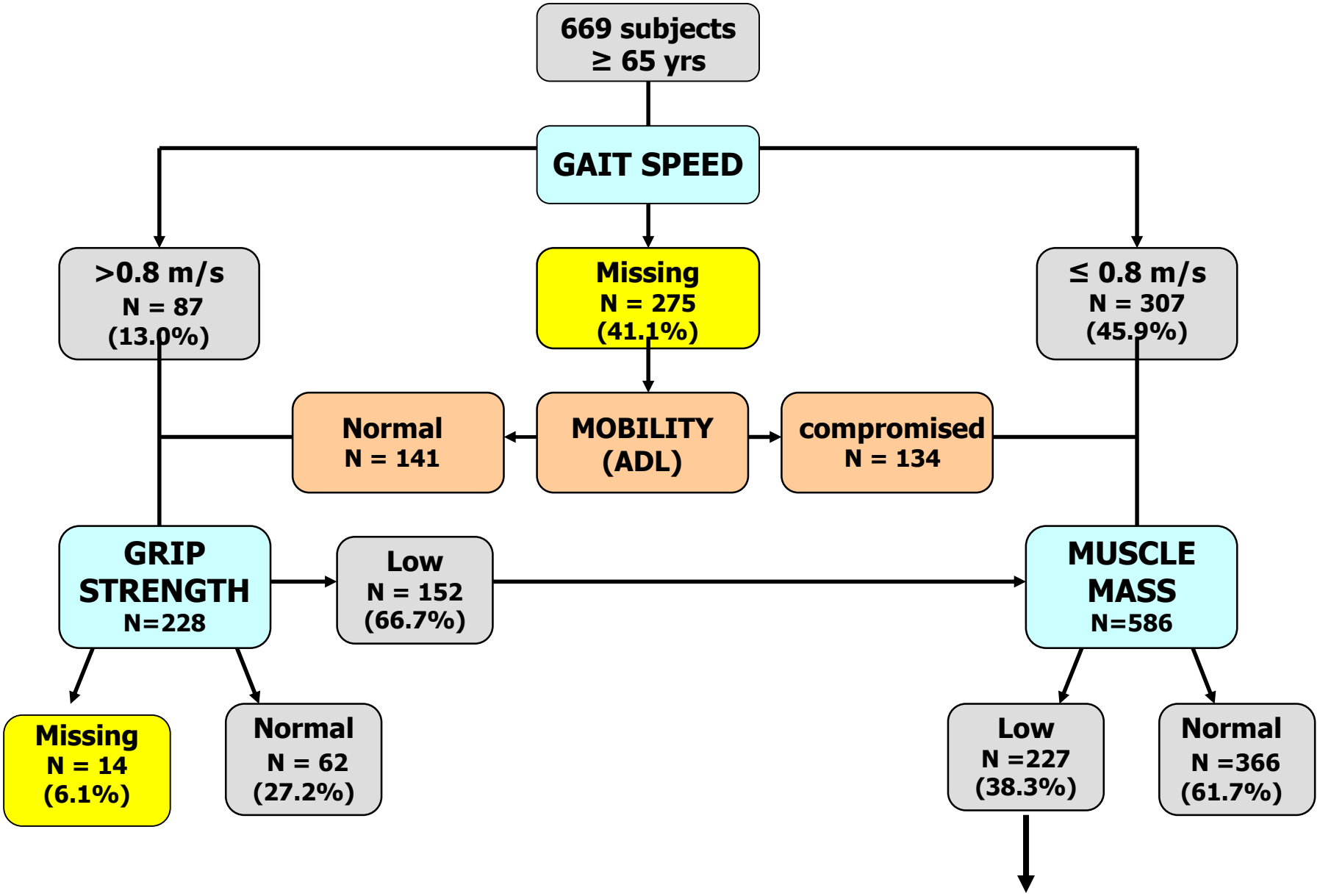
2- Determinazione dell'incidenza di Sarcopenia durante il ricovero ospedaliero

OBIETTIVI SECONDARI

1- Studio dei correlati clinici della sarcopenia nel paziente anziano ricoverato in ospedale

2-Studio dei fattori di rischio per lo sviluppo di sarcopenia nel paziente anziano ricoverato in ospedale

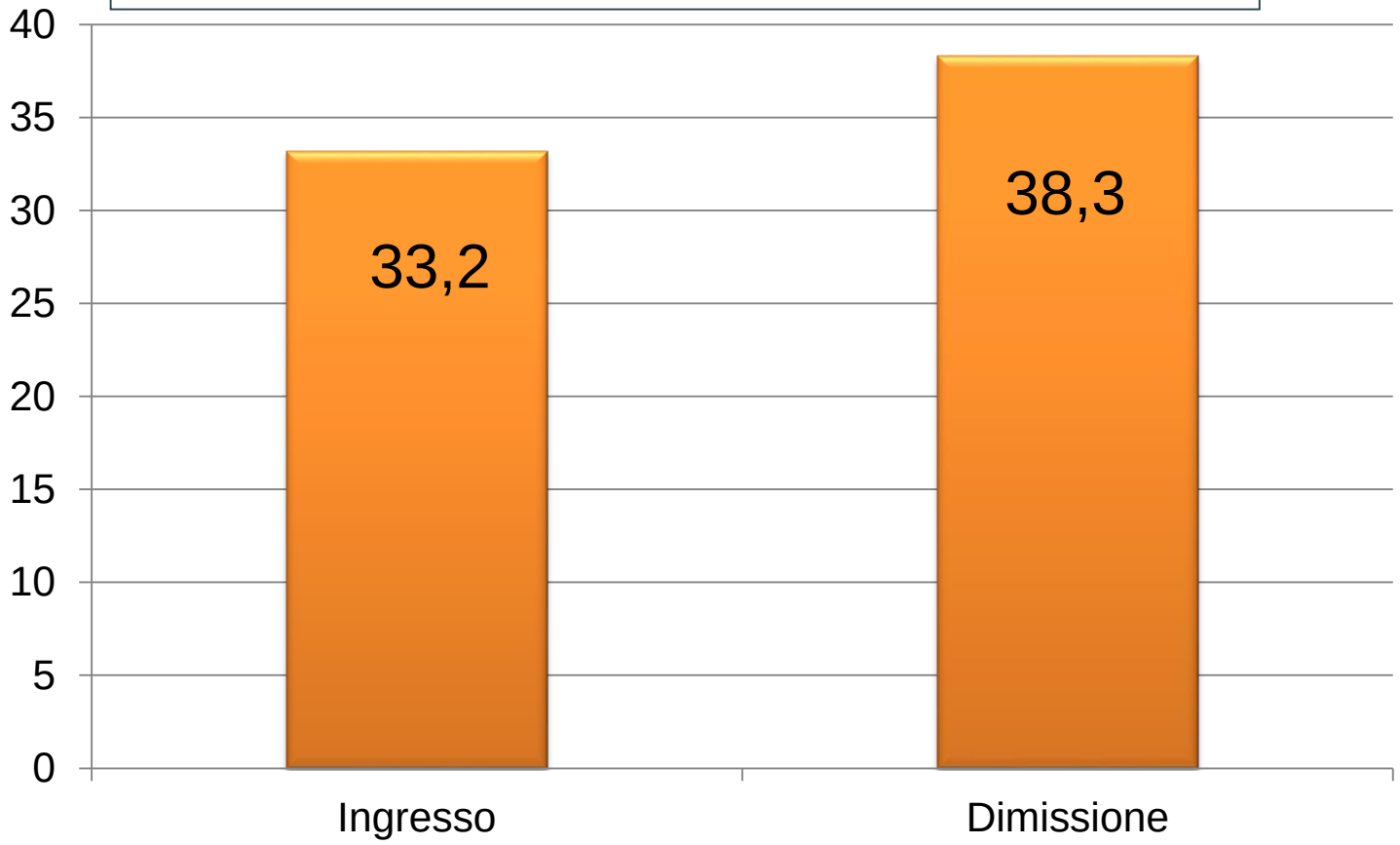
3-Studio della variazione della massa muscolare (SMI) in pazienti anziani ospedalizzati allettati



Sarcopenia: 227/(227+366+62) = 227/655 = 34.66%

Variazione della prevalenza di sarcopenia tra ingresso e dimissione

N=575 pazienti hanno dato in ingresso e dimissione



Test binomiale sulle proporzioni: p-value=0.0062

Sarcopenia e Ospedalizzazione

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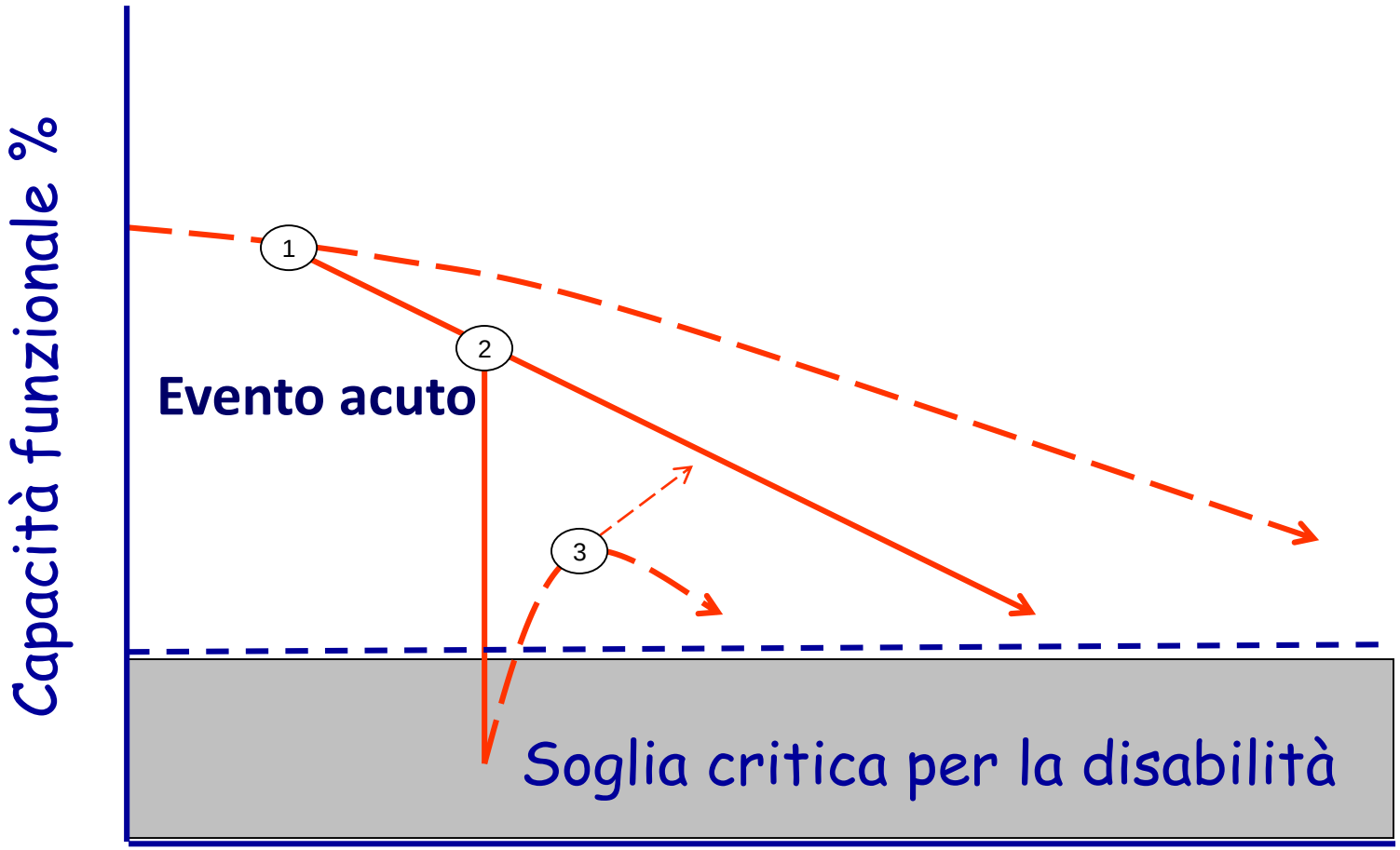
Sarcopenia come modulatore dell'effetto disabilitante delle malattie



GERIATRICS AND GERONTOLOGY SPECIAL SECTION
CLINICAL RESEARCH STUDY
Michael W. Rich, MD, Section Editor

THE AMERICAN JOURNAL of MEDICINE®

Handgrip Strength Predicts Persistent Walking Recovery After Hip Fracture Surgery

Elisabetta Savino, MD,[a] Emilio Martini, MD,[b] Fulvio Lauretani, MD,[c] Giulio Pioli, MD, PhD,[d] Anna Maria Zagatti, MD,[e] Carlo Frondini, MD,[b] Francesca Pellicciotti, MD,[d] Antonio Giordano, MD,[c] Alberto Ferrari, MD,[d] Anna Nardelli, MD,[c] Maria Luisa Davoli, MD,[d] Amedeo Zurlo, MD,[e] Maria Lia Lunardelli, MD,[b] Stefano Volpato, MD, MPH[a]

- Multicenter prospective cohort study;
- 504 patients, aged ≥70 years
- Able to walk independently before the fracture
- Sex-specific HGS tertiles:
  - Men: I:0.5-14, II:15-22, III: 23-40 kg
  - Women: I:0.5-9, II:10-15, III: 16-28 kg

Handgrip Strength Predicts Persistent Walking Recovery After Hip Fracture Surgery

Table 1 Selected General and Clinical Characteristics of the Sample by Gender-specific Handgrip Strength Tertiles

	Handgrip Strength Tertiles (N = 504)			
	Lowest (n = 172)	Intermediate (n = 173)	Highest (n = 159)	*P* Value
Age (mean ± SD)	86.5 (5.7)	85.6 (5.5)	83.8 (4.8)	<.001
Men, n (%)	45 (26.2)	40 (23.1)	39 (24.5)	.81
Married, n (%)	41 (23.8)	28 (16.2)	53 (33.3)	.02
Home residents, n (%)	154 (89.5)	159 (91.9)	153 (96.2)	.20
Caregiver assistance, n (%)	123 (71.5)	114 (65.9)	74 (46.5)	<.001
Cognitive impairment, n (%)	117 (68.0)	87 (50.3)	48 (30.2)	<.001
Depressive symptoms, n (%)	85 (49.4)	69 (39.9)	54 (34.0)	<.001
Charlson Index, median (IQR)	2 (1-4)	2 (1-3)	1 (0-3)	<.001
No. of medications at admission, median (IQR)	5 (3-7)	4 (2-6)	4 (3-5)	.04
BADL difficulty, n (%)	129 (75.0)	95 (54.9)	36 (22.6)	<.001
IADL difficulty, n (%)	170 (98.8)	172 (99.4)	159 (100)	.39
Vitamin D (25-OH) ng/mL, median (IQR)	7.5 (4.3-13.2)	9.0 (6.1-13.2)	9.0 (5.7-14.1)	.03
C-reactive protein mg/L, median (IQR)	4.2 (2.3-9.8)	5.3 (2.6-8.0)	4.1 (1.8-9.1)	.19
Hemoglobin g/dL, median (IQR)	12.0 (10.9-13.3)	12.4 (10.9-13.5)	12.2 (11.0-13.3)	.55
Type of fracture: n (%)				
Intracapsular	77 (44.8)	83 (48.0)	81 (50.9)	
Trochanteric	87 (50.6)	82 (47.4)	60 (37.7)	.03
Subtrochanteric	8 (4.6)	8 (4.6)	18 (11.3)	
Days before surgery, median (IQR)	2 (2-4)	3 (2-4)	3 (2-5)	<.001
Type of surgery, n (%)				
Endoprosthesis	75 (43.6)	71 (41.0)	76 (47.8)	
Arthroplasty	3 (1.7)	6 (3.5)	3 (1.9)	<.001
Other	94 (54.7)	96 (55.5)	80 (50.3)	
Early rehabilitation, n (%)	157 (91.3)	162 (93.6)	136 (85.5)	.04

Savino E et al. Am J Med, 2013;126:1068-75

Handgrip Strength Predicts Persistent Walking Recovery After Hip Fracture Surgery

Table 3 Multivariable Logistic Regression Analyses Predicting Persistent Walking Recovery in Patients with Independent Walking Before Fracture (N = 409)

		Odds Ratio (95% CI)			
	No. of Events (%)	Model 1	Model 2	Model 3 (Fully Adjusted)	Model 3* (Most Parsimonious)
Grip strength, tertiles					
Lowest	66 (49.6)	1	1	1	1
Intermediate	103 (70.1)	2.83 (1.64-4.90)	2.12 (1.16-3.87)	2.40 (1.24-4.62)	2.33 (1.25-4.34)
Highest	99 (76.7)	4.07 (2.11-7.85)	2.09 (1.00-4.37)	2.46 (1.11-5.44)	2.79 (1.35-5.79)
P value of test for trend		<.001	.04	.02	.005
Age, y		0.95 (0.91-0.99)	0.95 (0.91-1.00)	0.98 (0.93-1.03)	
Gender, m		0.78 (0.47-1.30)	0.57 (0.33-0.99)	0.50 (0.27-0.92)	0.51 (0.29-0.92)

Model 3 includes age, gender, medical center, cognitive decline, depressive symptoms, BADL difficulty, caregiver assistance, time before surgery, type of surgery, early rehabilitation, Charlson Index, and vitamin D levels.

Savino E et al. Am J Med, 2013;126:1068-75

Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery

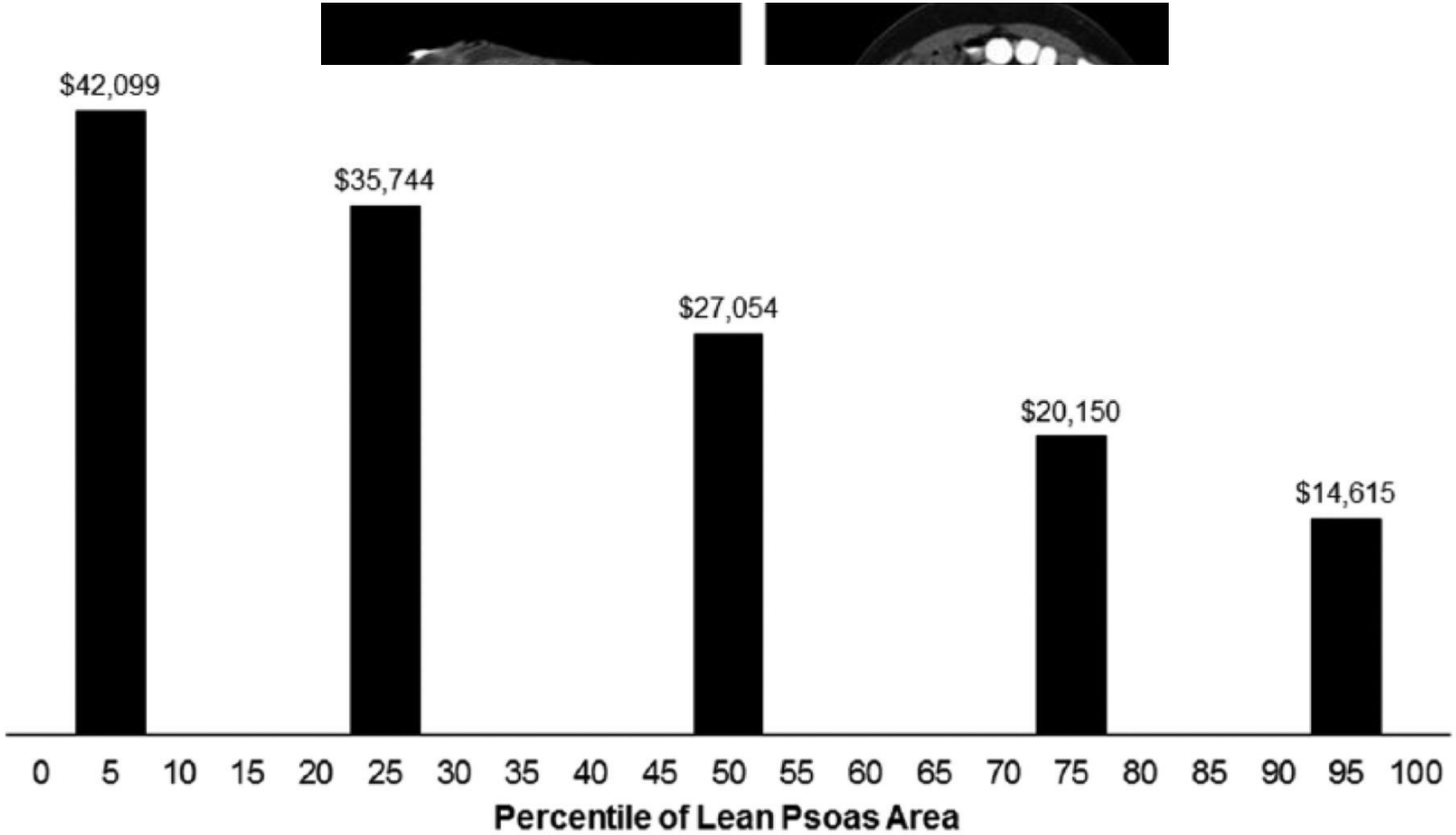
- ✓ Computed tomography scans taken for planning surgery was evaluated
- ✓ Total skeletal muscle tissue surface area (cm2) was evaluated on a single image at the third lumbar vertebrae
- ✓ Sarcopenia was defined using sex-specific skeletal muscle index cutpoints

	Infection				Convalescent/rehabilitation care			
	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Sarcopenia								
No	1.0		1.0		1.0		1.0	
Yes	4.4 (1.5, 13.0)	0.008	4.6 (1.5, 13.9)	0.007	2.6 (0.92, 7.6)	0.070	3.1 (1.04, 9.4)	0.043
Sex								
Female	1.0		1.0		1.0		1.0	
Male	1.1 (0.43, 2.8)	0.84	0.99 (0.36, 2.7)	0.98	0.68 (0.25, 1.8)	0.45	0.65 (0.22, 1.9)	0.43
Cancer stage								
II	1.0		1.0		1.0		1.0	
III	0.63 (0.21, 1.9)		0.63 (0.20, 2.0)		1.5 (0.46, 4.6)		1.6 (0.48, 5.5)	
IV	0.45 (0.14, 1.5)	0.42	0.42 (0.12, 1.5)	0.40	0.60 (0.16, 2.4)	0.40	0.74 (0.18, 3.1)	0.48
Primary tumour site								
Colon/rectosigmoid junction	1.0		1.0		1.0		1.0	
Rectum	1.2 (0.43, 3.6)	0.67	1.1 (0.37, 3.5)	0.82	2.6 (0.92, 7.3)	0.073	2.7 (0.88, 8.1)	0.082

Lieffers JR British Journal of Cancer 2012 107, 931–936

Costi associati alla chirurgia maggiore nel paziente sarcopenico

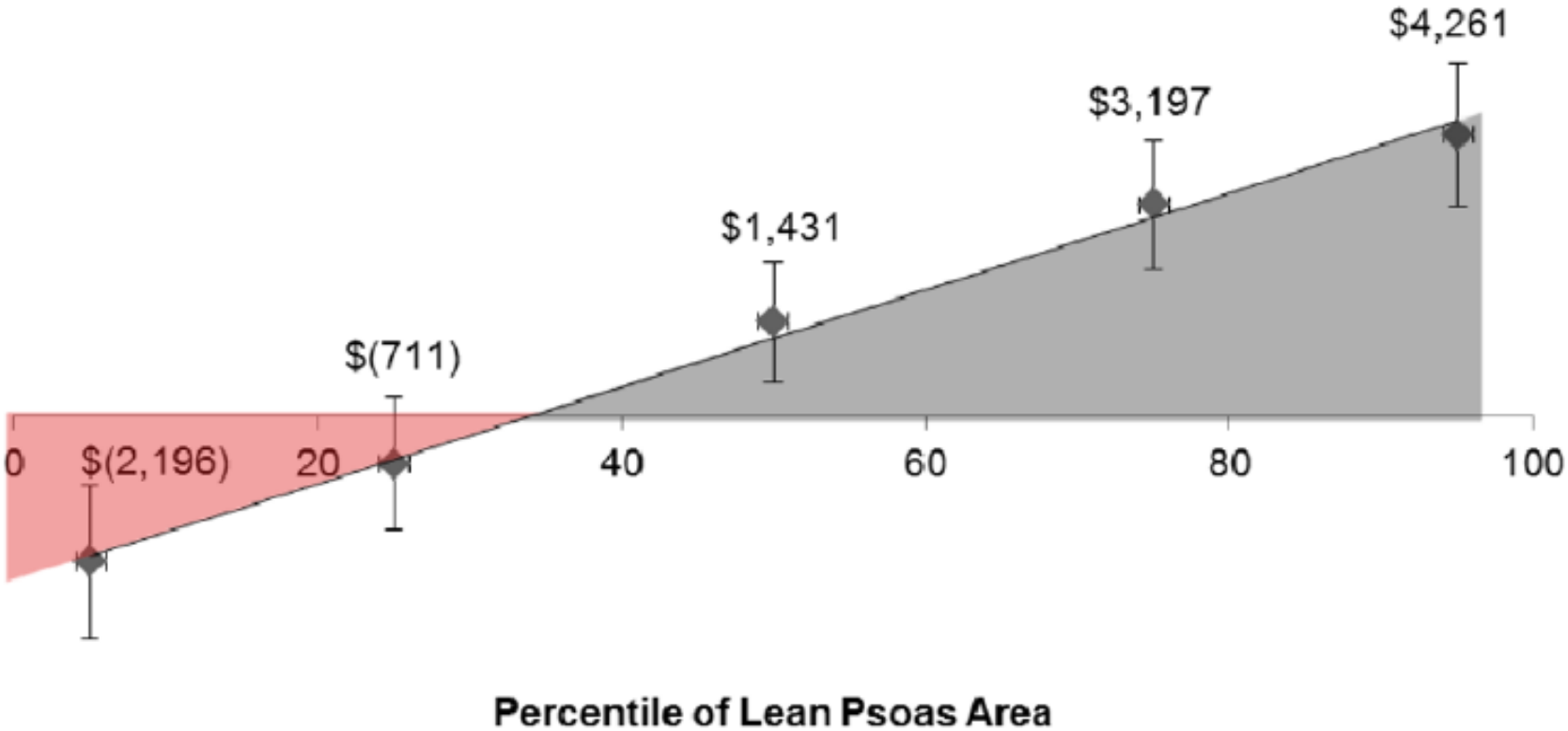
Mean adjusted payer cost for major general elective surgery by lean psoas area



Sheetz KH et al. J Am Coll Surg 2013;217:813-818

Costi associati alla chirurgia maggiore nel paziente sarcopenico

Adjusted Hospital Marginal: payer costs-hospital costs



Sheetz KH et al. J Am Coll Surg 2013;217:813-818

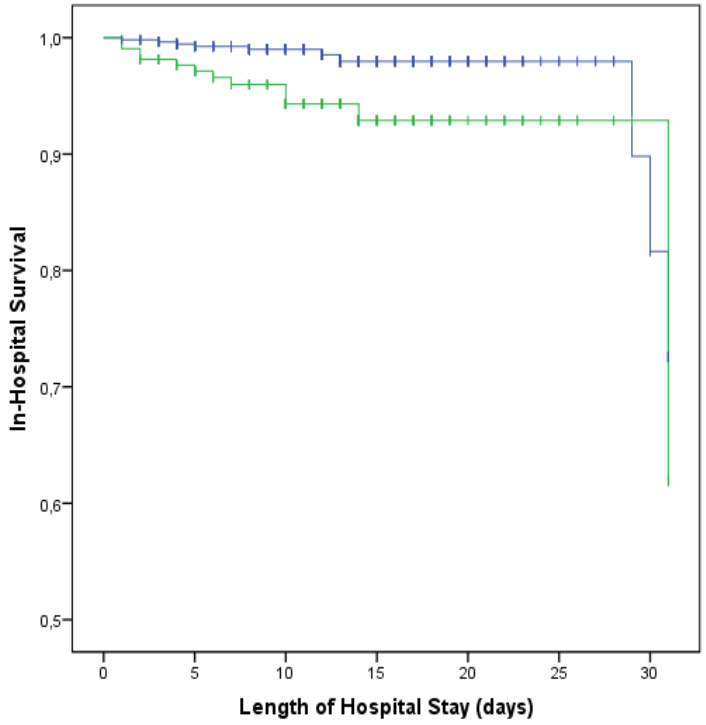
Sarcopenia e mortalità a breve e lungo termine nel paziente ospedalizzato

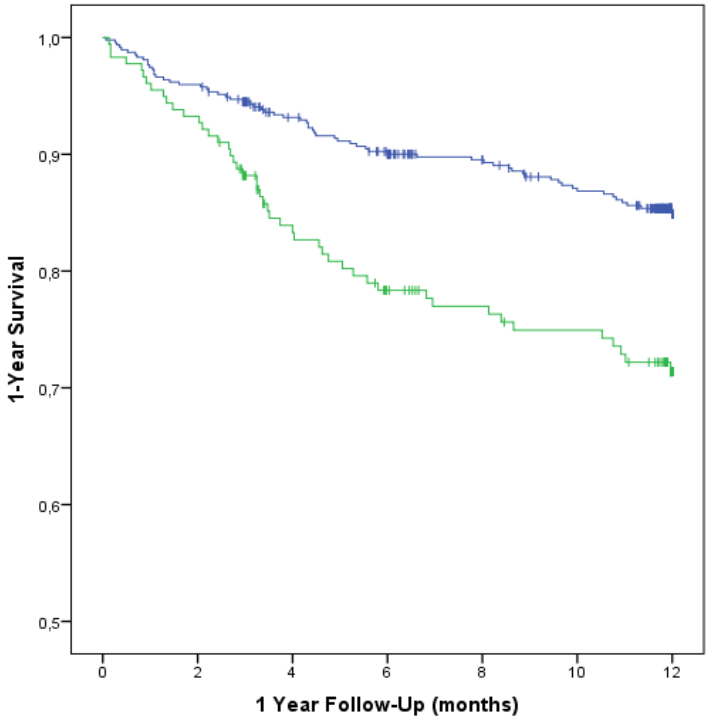
Results From the CRIME Study

	Total ($n = 770$)	No Sarcopenia $n = 556$ (72%)	Sarcopenia $n = 214$ (28%)	p
Demographics				
Age	80.8±7.0	80±7.1	82.8±6.9	<.001
Gender (women)	428 (56)	327 (59)	101 (47)	.005
Smoker (actual/former)	322 (42)	219 (40)	103 (48)	.034
Alcohol consumption (current)	224 (30)	172 (32)	52 (25)	.051
Living alone	184 (24)	120 (22)	64 (30)	.018
Objective parameters				
Activities of daily living at admission (0–6; compromised)	2.3±2.4	2.1±2.4	2.6±2.4	.024
Mini Mental State Examination (0–30)	23 (17–27)	24 (17–28)	22 (17–27)	.226*
Geriatric Depression Scale (0–15)	4.7±3.5	4.7±3.5	4.8±3.5	.974
Body mass index (Kg/m^2)				<.001
<18.5	25 (3)	4 (1)	21 (10)	
18.5–24.9	266 (36)	167 (31)	99 (49)	
25–30	298 (40)	231 (42)	67 (34)	
>30	158 (21)	144 (26)	14 (7)	

Vetrano D et al JGMS, 2014;69:1154-61

Curve di sopravvivenza intraospedaliera e a un anno in base alla presenza di sarcopenia (Studio CRIME)





No Sarcopenia
Sarcopenia

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HR crudo e aggiustato per la mortalità intraospedaliera e a 1 anno

Outcomes	Events		Unadjusted Model		Age and Gender Adjusted Model		Totally Adjusted Model †	
Total sample (N = 770)								
		p	HR	95% C.I.	HR	95% C.I.	HR	95% C.I.
In-Hospital Mortality								
No Sarcopenia	12/556 (2 %)	0.007	1	-	1	-	1	-
Sarcopenia	10/214 (6 %)		3.19	1.38 – 7.38	3.00	1.23 – 7.28	3.51	1.41 – 8.75
1-Year Mortality [Ω]								
No Sarcopenia	47/474 (14 %)	< 0.001	1	-	1	-	1	-
Sarcopenia	66/176 (26 %)		2.12	1.45 – 3.10	1.56	1.10 – 2.30	1.66	1.09 – 2.51
Subgroup 1 (N = 602) [α]								
		p	HR	95% C.I.	HR	95% C.I.	HR	95% C.I.
1-Year Mortality								
Non Sarcopenia	48/449 (12 %)	0.002	1	-	1	-	1	-
Sarcopenia	32/153 (24 %)		2.09	2.34 – 3.27	1.57	1.10 – 2.50	1.69	1.02 – 2.78
Subgroup 2 (N = 550) [β]								
		p	HR	95% C.I.	HR	95% C.I.	HR	95% C.I.
1-Year Mortality								
Non Sarcopenia	29/408 (8 %)	0.001	1	-	1	-	1	-
Sarcopenia	25/142 (20 %)		2.62	1.53 – 4.45	1.97	1.14 – 3.41	2.04	1.12 – 3.70

† Adjusted for: age, gender, smoking habit, living alone, compromised activities of daily living, body mass index, infectious diseases and Charlson Comorbidity Index.

[Ω] 22 patients died during hospital stay and 98 with incomplete follow up data were excluded from this analysis.

[α] Analysis performed excluding 168 patients with diagnosis of dementia. Results on in-hospital mortality were omitted due to insufficient events.

[β] Analysis performed excluding 220 patients with > 4 impaired activities of daily living. Results on in-hospital mortality were omitted due to insufficient events.

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Alterazioni età-correlate della massa e funzione muscolare

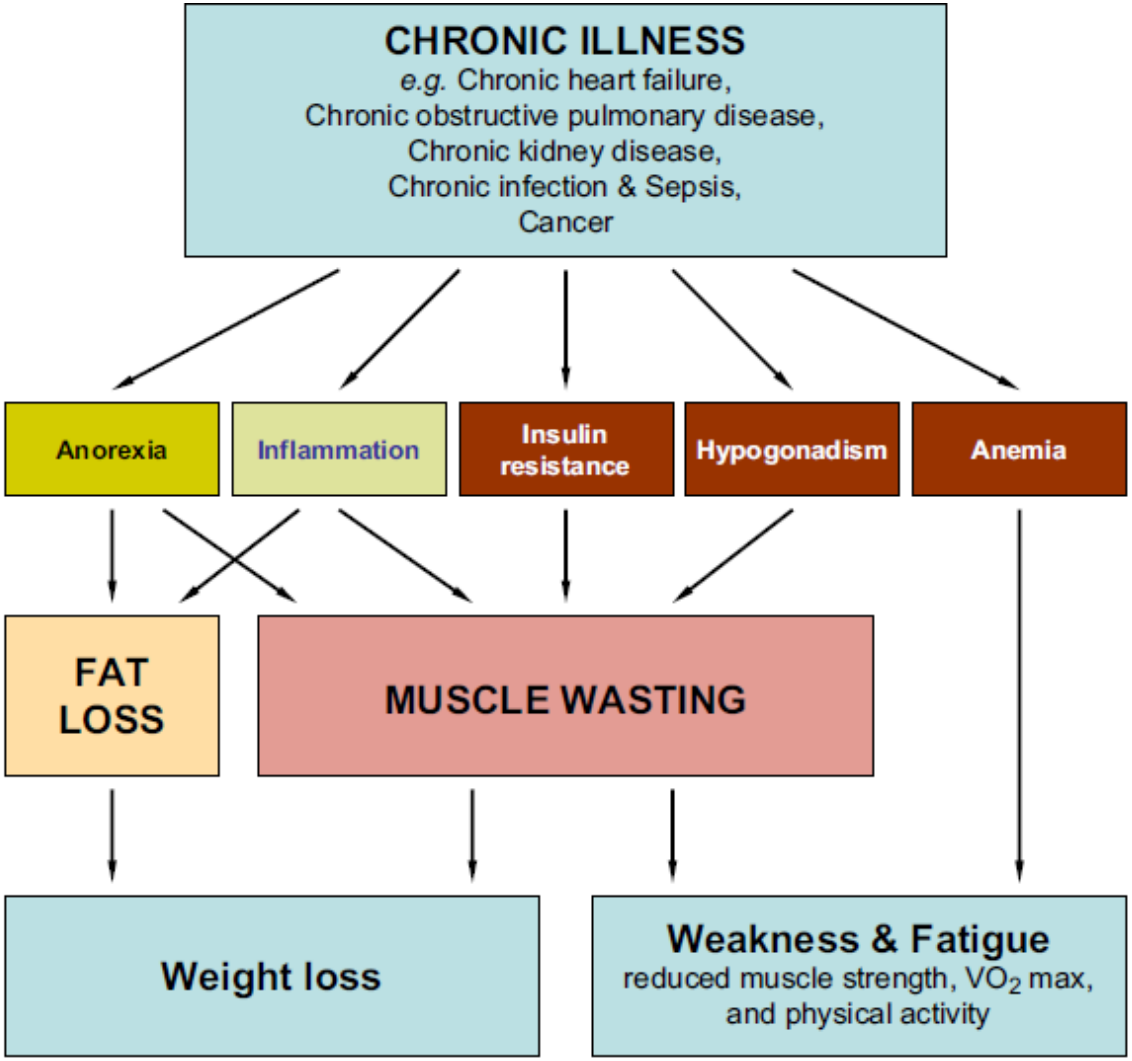
1) *Sarcopenia* (*sarx penia*)
   - Perdita di massa e forza muscolare

2) *Cachexia* (*kakòs héxis*)
   - Perdita di peso
   - Perdita di massa muscolare e/o massa grassa
   - Aumentato catabolismo proteico
   - Associazione con le patologie croniche

3) *Dynapenia*: (*δύναμις penia*)
   - Perdita isolata di forza e potenza muscolare

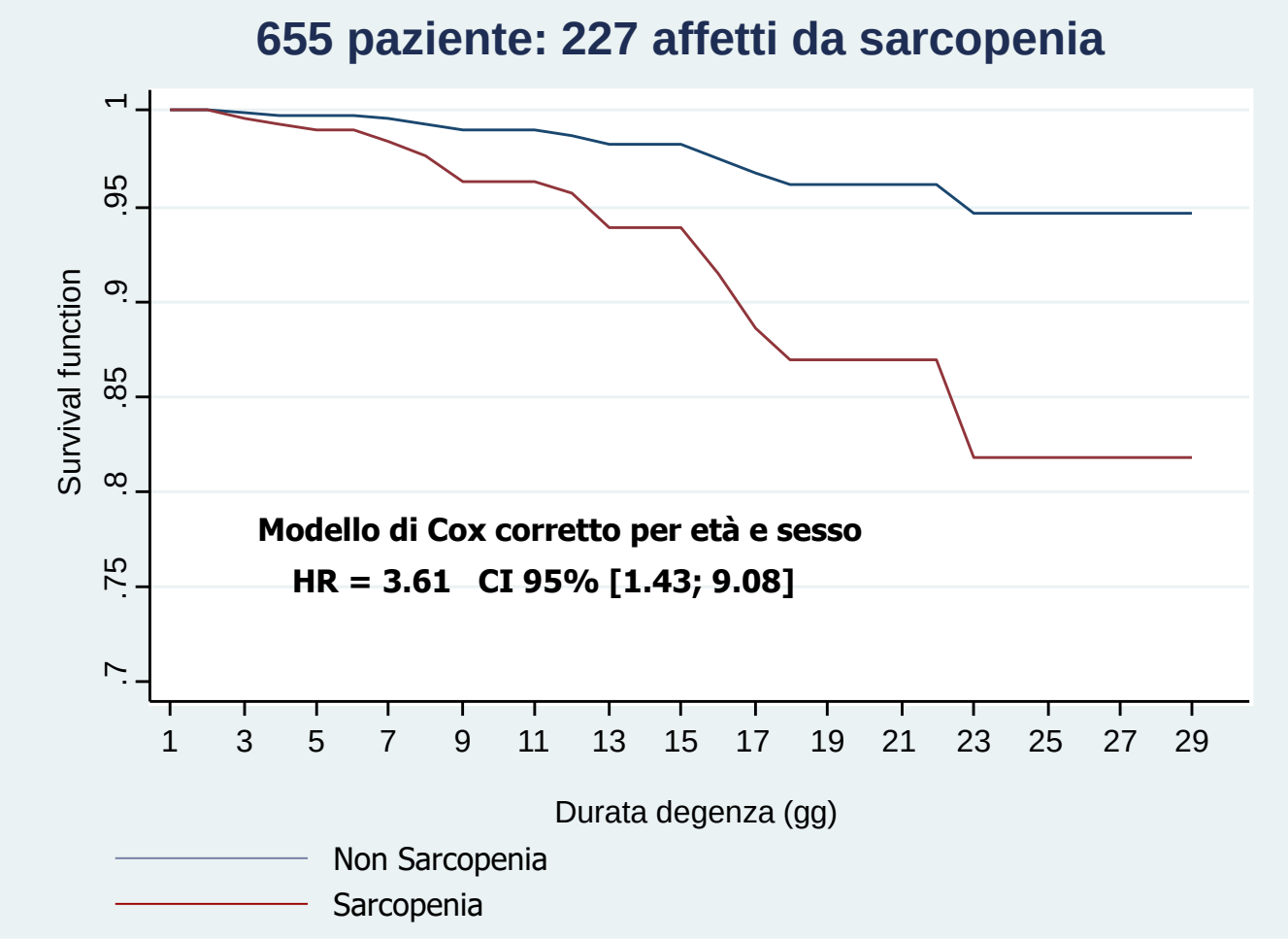
1. **Cruz-Jentoft AJ et al. for the European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis. *Age Ageing* 2010;39:412-23.**
2. **Manini TM, e tal. Dynapenia and aging: an update. *J Gerontol Med Sci.* 2012;67:28-40.**
3. **Evans WJ, et al. Cachexia: a new definition. *Clin Nutr* 2008; 27:793–9.**

Rappresentazione schematica della definizione di cachessia: Cachessia come conseguenza dell'adattamento ad una patologia cronica sottostante



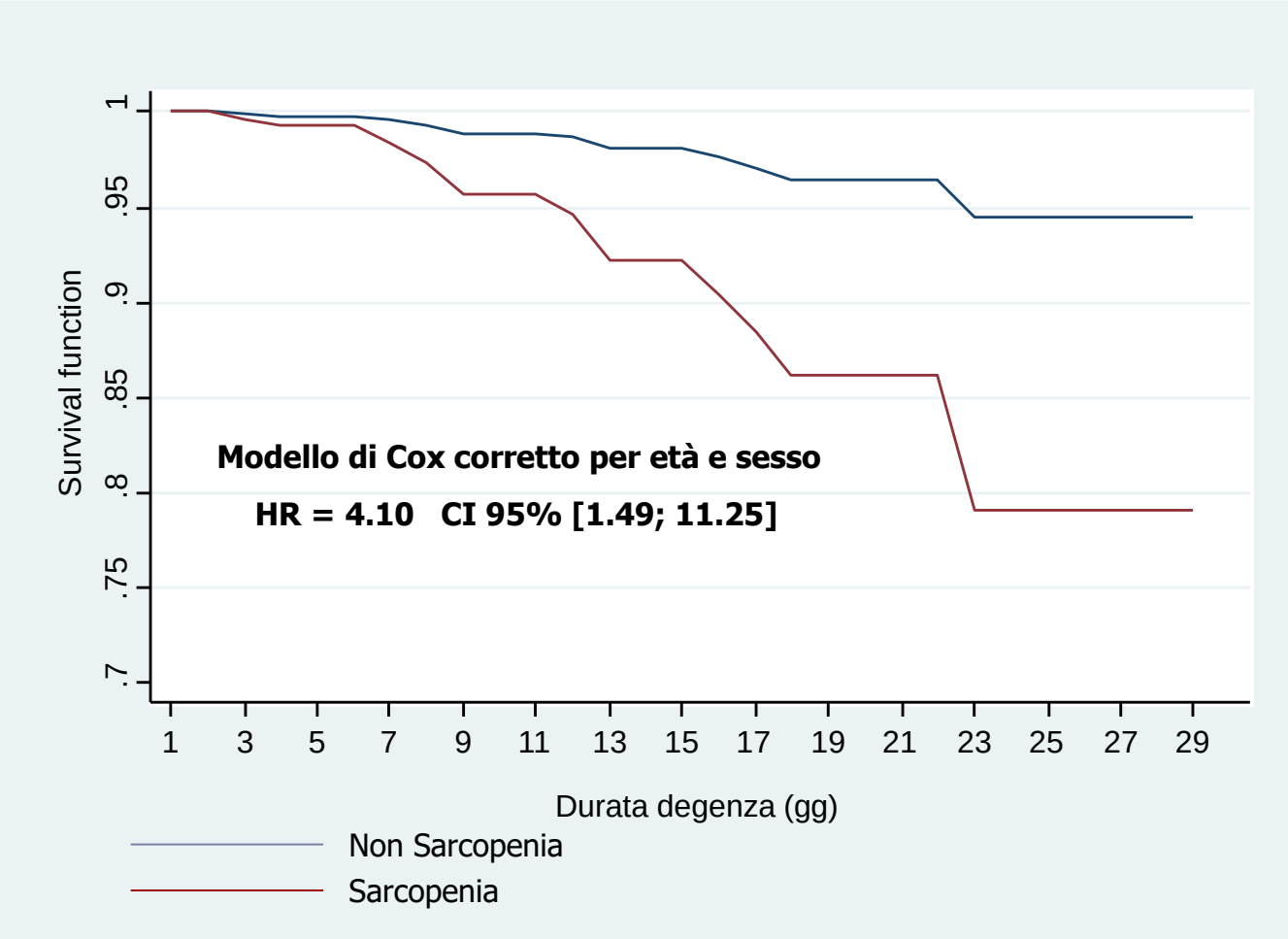
Evans WJ, et al. Clin Nutr 2008; 27:793–9.

Mortalità intraospedaliera in rapporto alla presenza di sarcopenia: studio GLISTEN



Mortalità intraospedaliera in rapporto alla presenza di sarcopenia: studio GLISTEN

Esclusione dei soggetti con BMI <20



Conclusioni

- La sarcopenia è una condizione molto frequente nell’anziano ospedalizzato e aumenta la probabilità di ricovero in emergenza
- Il ricovero in ospedale si associa ad aumento del rischio di sarcopenia
- Nel paziente ospedalizzato la sarcopenia peggiora l’esito clinico e funzionale e si associa ad un aumento dei costi sanitari
- La sarcopenia aumenta il rischio di morte a breve e medio termine

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