FACOLTÀ DI
MEDICINA E CHIRURGIA
Università degli Studi di Verona

La Sarcopenia

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healthy aging center
verona

Azienda Ospedaliera Universitaria Integrata di Verona

Verona, 03 Novembre 2017

1. Definizione
2. Patogenesi
3. Rilevanza clinica

"Sarcopenia is a term that denotes the decline in muscle mass and strength that occurs with healthy aging."

Rosenberg, Am J Clin Nutr 1989

"Sarcopenia is part of normal aging and does not require a disease to occur, although it is accellerated by chronic diseases."

Roubenoff et al, J Gerontol 2000

Definizione di Sarcopenia

- *Modificazione quantitativa del tessuto muscolare scheletrico?*
- *Modificazione qualitativa del tessuto muscolare scheletrico?*
- ***Modificazione funzionale del tessuto muscolare scheletrico?***

Equipment

BK94 (OU site) will use the GE Lunar Prodigy Advance™, system # PA+300532 (see below).
Other makes/models include:

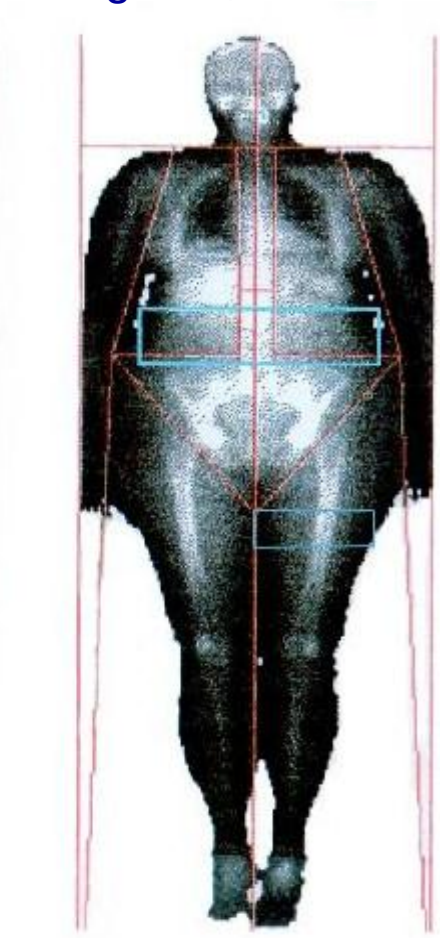
- GE Lunar iDXA™
- GE Lunar Prodigy Pro™ or Primo™
- GE Lunar DPX Pro™, Bravo™, or Duo™
- Hologic Discovery A (serial# xxxxxxx)

NOTE: Densitometrist should be trained and certified to use the specific scanner model.

TOTAL BODY Dual-energy X-ray Absorpiometry (DXA)

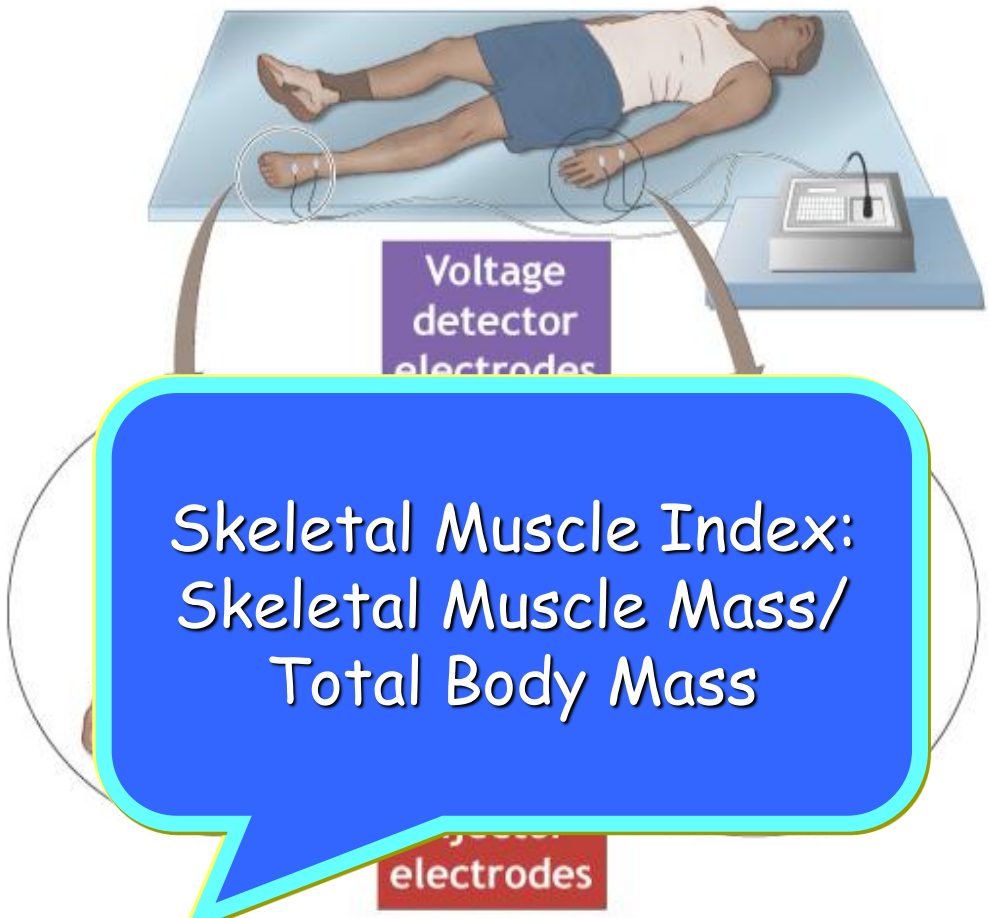
Total body. Women
59 kg, BMI 22.6

Total body. Women
kg 104, BMI 34

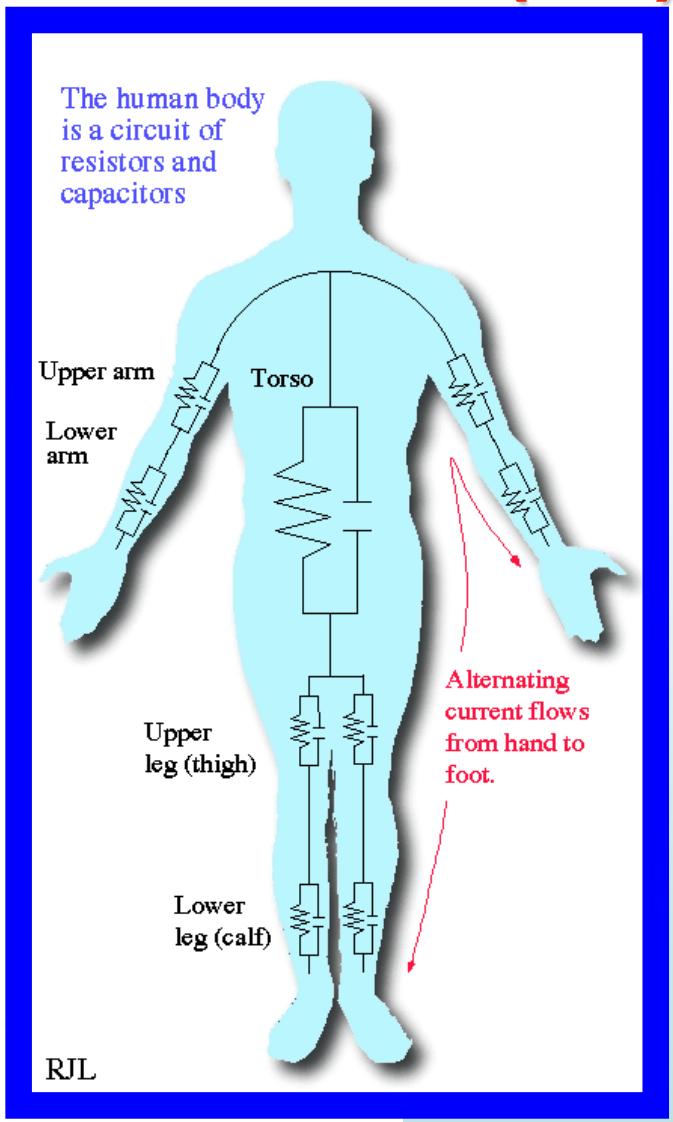


Brownbill RA and Ilich JZ, 2004

Bioelectrical impedance assessment (BIA)



Skeletal Muscle Index:
Skeletal Muscle Mass/
Total Body Mass



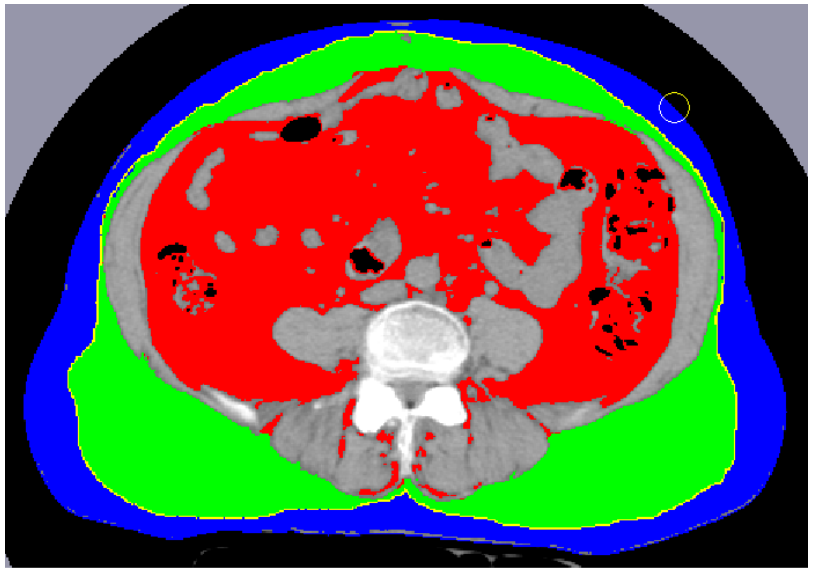
Normal: SMI >37.0% in men, SMI >28% in women.

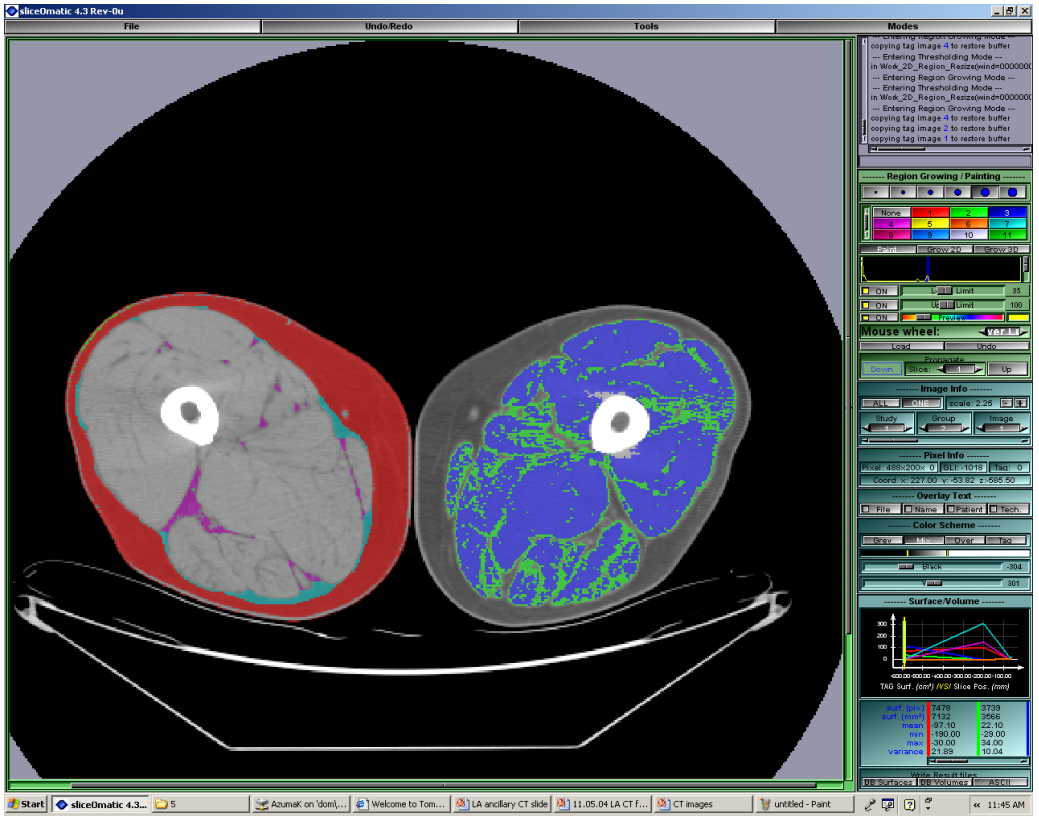
Class I sarcopenia: SMI between 31.0 and 37% in men, SMI between 22.0 and 28.0% in women.

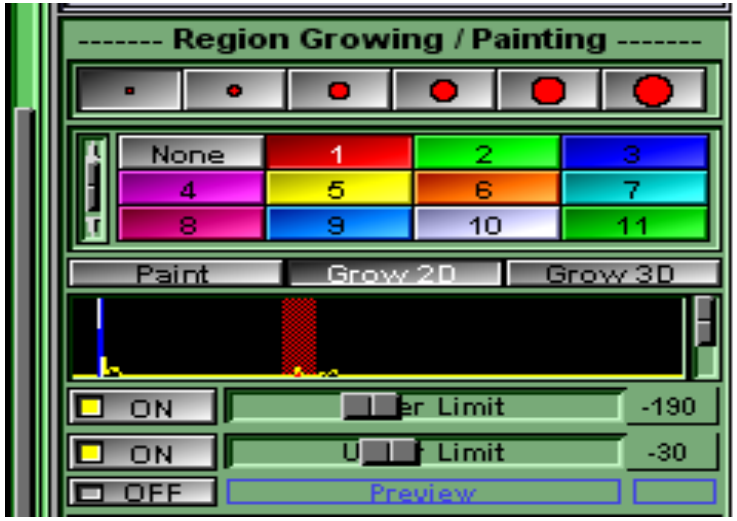
Class II sarcopenia: SMI <31.0% in men, SMI <22.0% in women.

Janssen I,
J Appl Physiol 2001

CT analysis with Sliceomatic Region Growing Mode Abdomen and Thigh







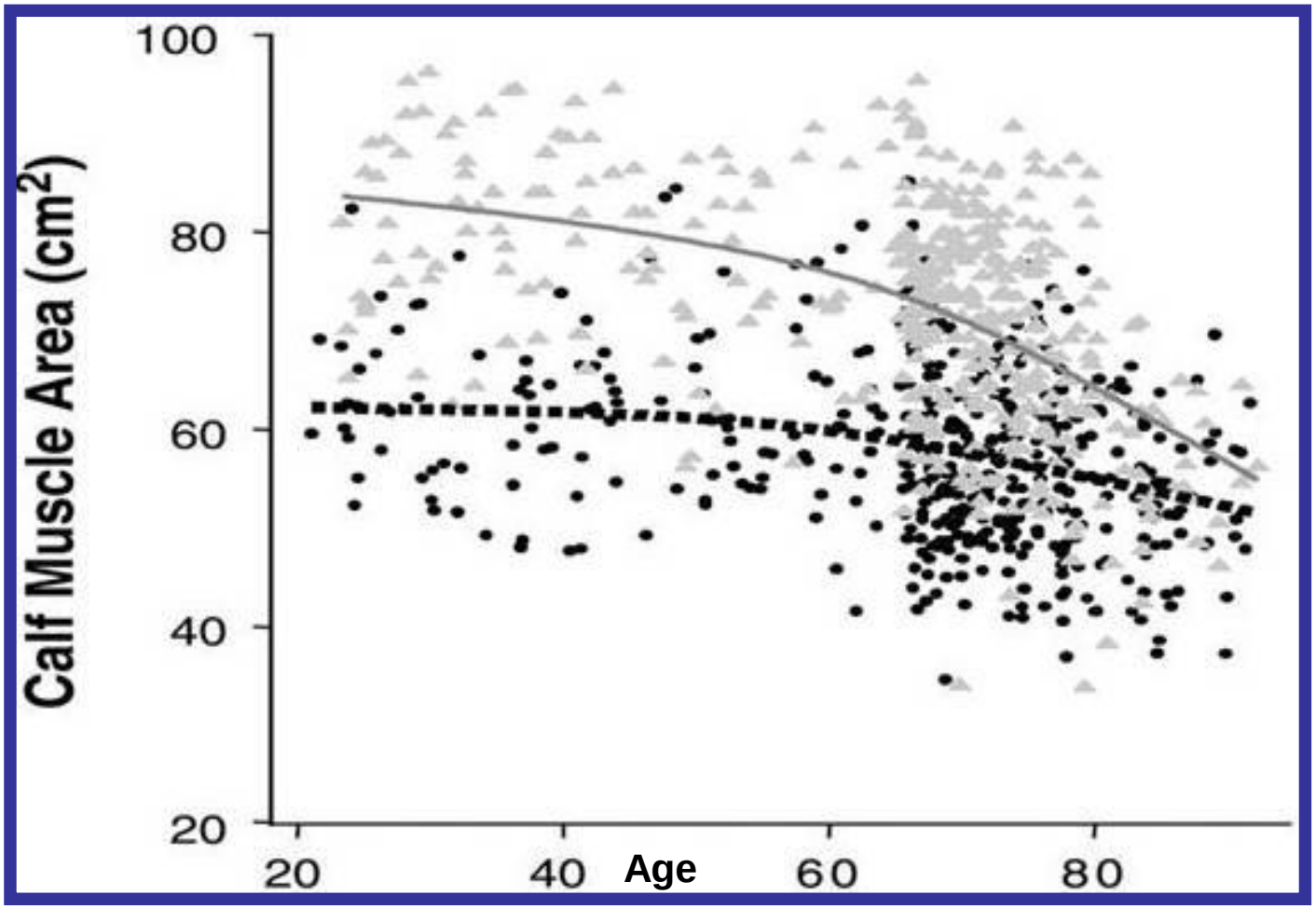
Hounsfield units:

>200 HU for bone

-30 to -190 HU for AT

0 to 100 HU for muscle

La relazione tra età e area della sezione trasversale dei muscoli della gamba in uomini (grigio) e donne (nero) dello Studio InCHIANTI



Lauretani, F. et al. J Appl Physiol 95: 1851-1860 2003

Journal of Applied Physiology

Modificazioni qualitative del tessuto muscolare con l'invecchiamento

Modificazioni istologiche e cellulari del tessuto muscolare scheletrico

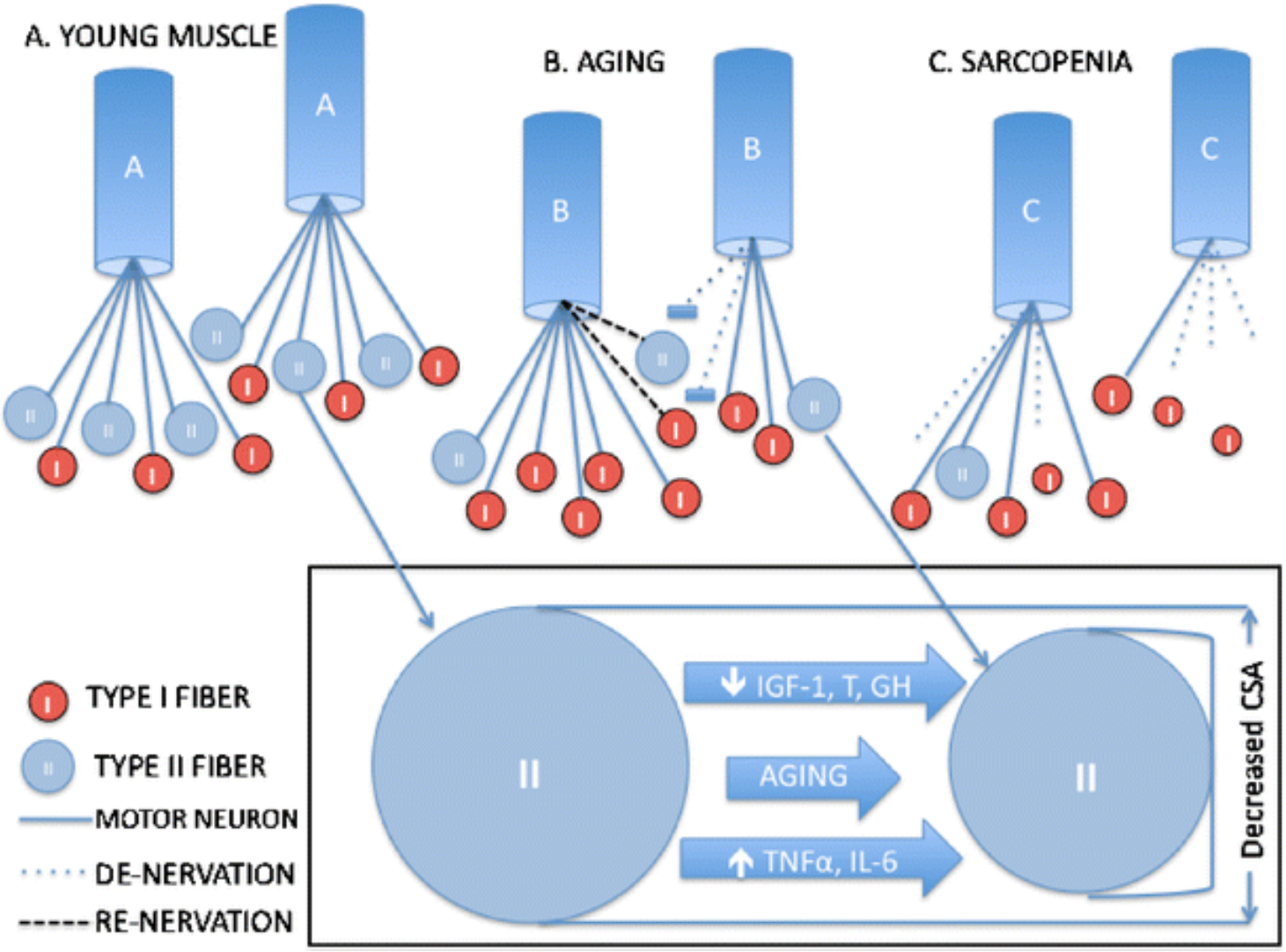
Infiltrazione di tessuto adiposo
Inter e intra-muscolare

hystological changes-1

- Decrease in myofiber cross sectional area
- Decrease in cross-bridging between Fibers
- Decrease in Number and Size of Mithocondria
- Decrease in protein synthesis, particularly of myosin
- Decrease in type II fibers
- Decrease in motor unit

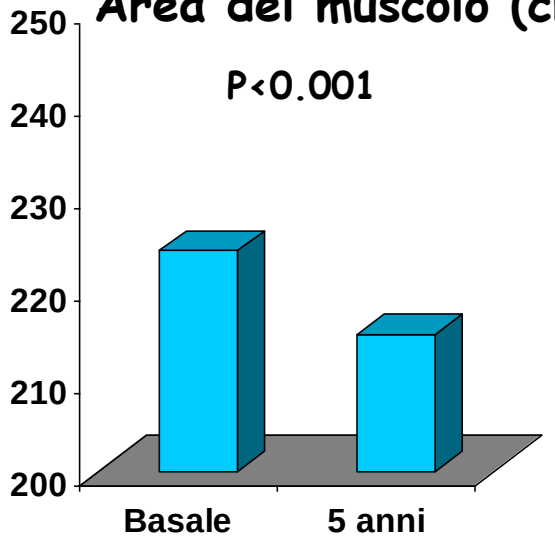
Thomas DR, Clinical Nutrition 26: 389-399, 2007
Ryall et al, Biogerontology 9: 213-228, 2008
Lang et al, Osteoporosis Int 21: 543-559, 2010

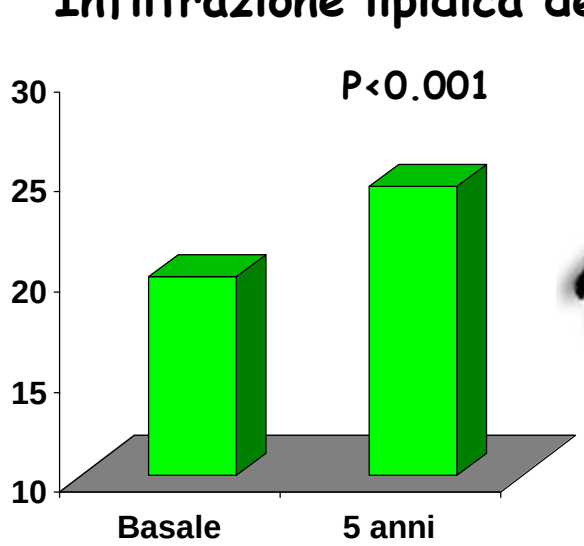
hystological changes-2



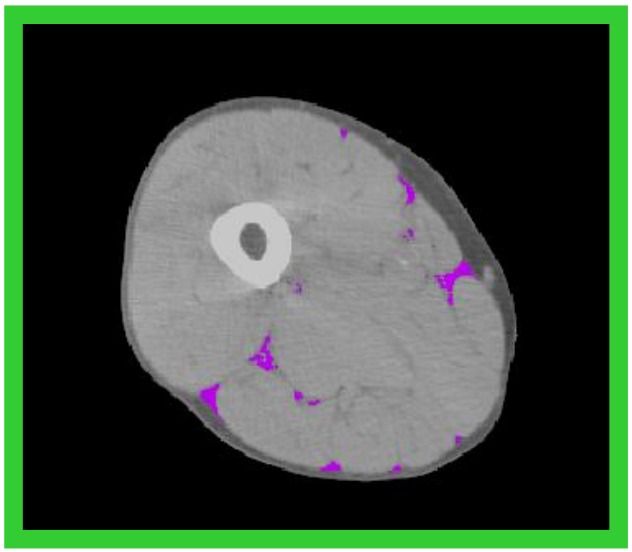
Lang T et al, Osteoporos Int 2010, 21, 543-559

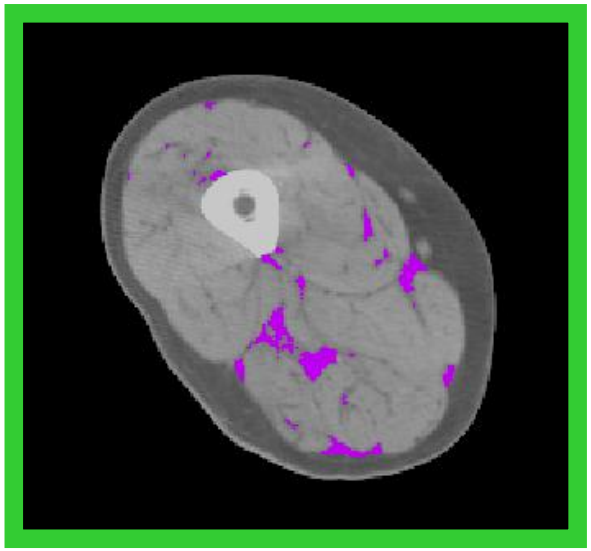
Modificazione della composizione corporea della coscia valutate mediante TAC nella popolazione in studio (n=1981) nel periodo di 5 anni di follow-up

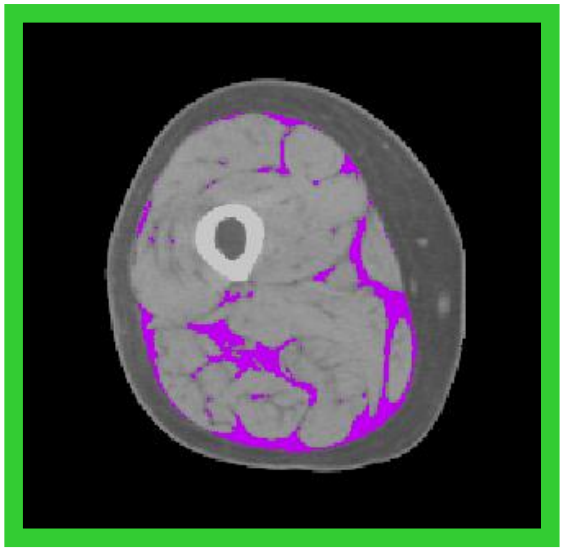




Health ABC







Rossi AP et al. J Geront 2011

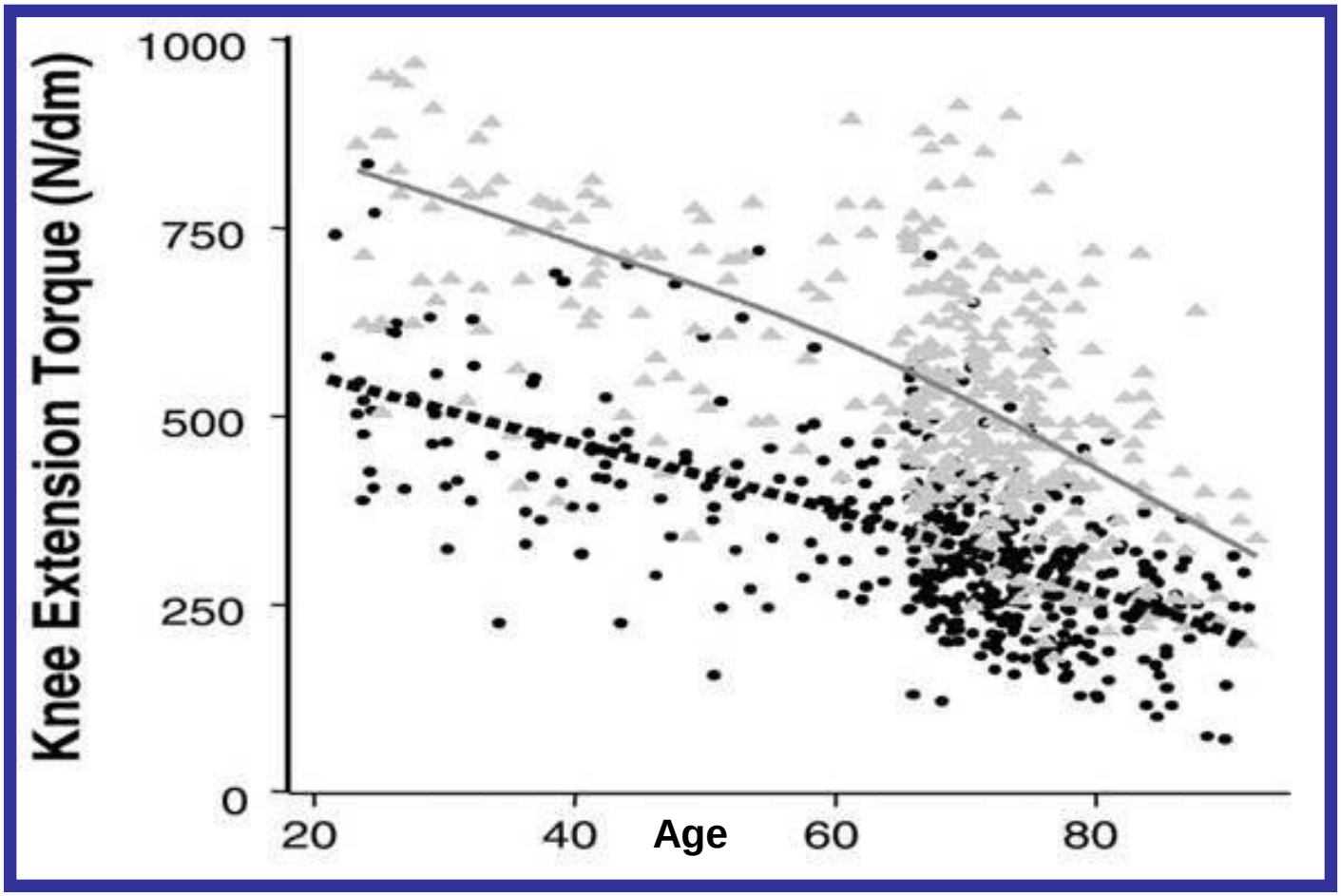
Equipment

- Dinamometria isocinetica

HANDGRIP

Criterio per screening della sarcopenia basato sull'handgrip:
per gli uomini < 30 kg
per le donne < 20 kg

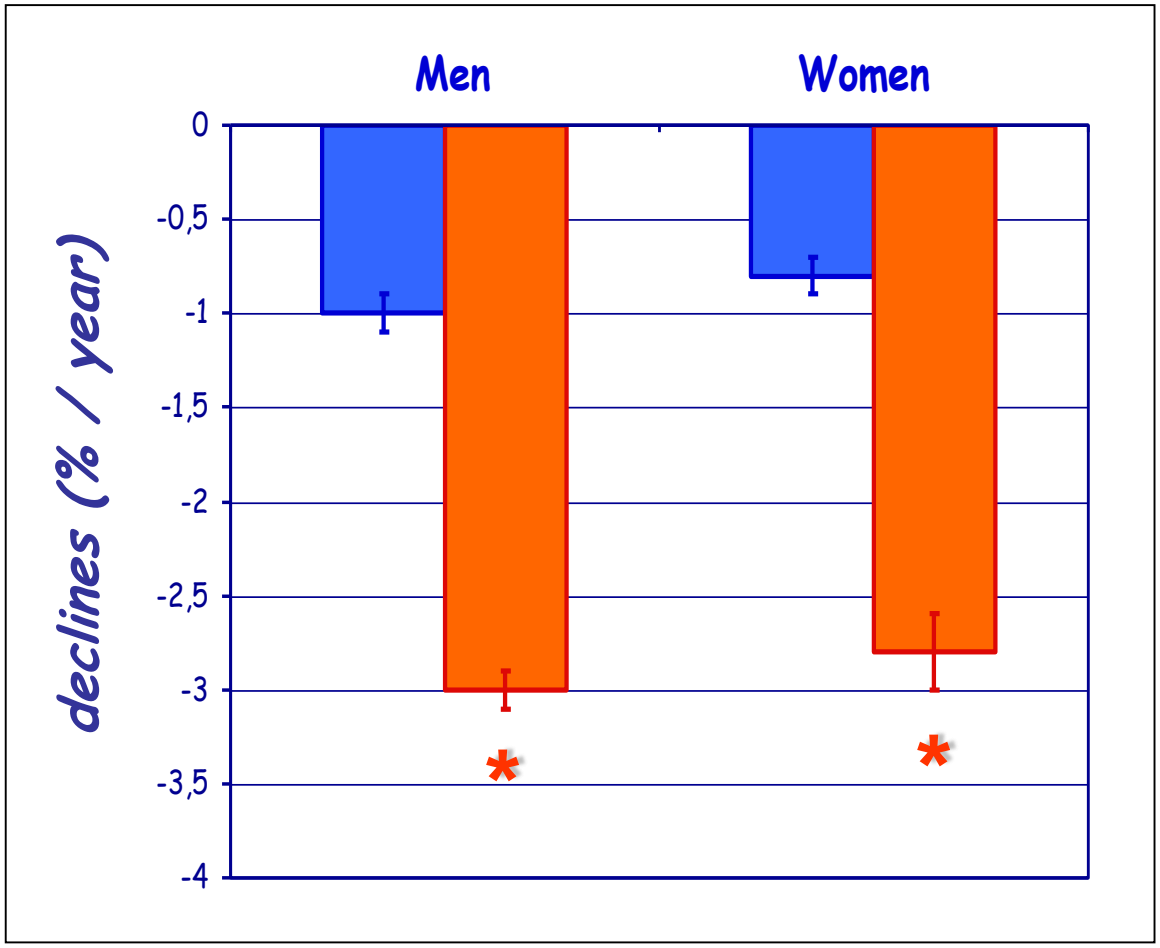
La relazione tra età e "Picco di Forza" degli estensori degli arti inferiori in uomini (grigio) e donne (nero) dello Studio InCHIANTI



Lauretani, F. et al. J Appl Physiol 95: 1851-1860 2003

Journal of Applied Physiology

Qualitative changes in muscle: longitudinal data

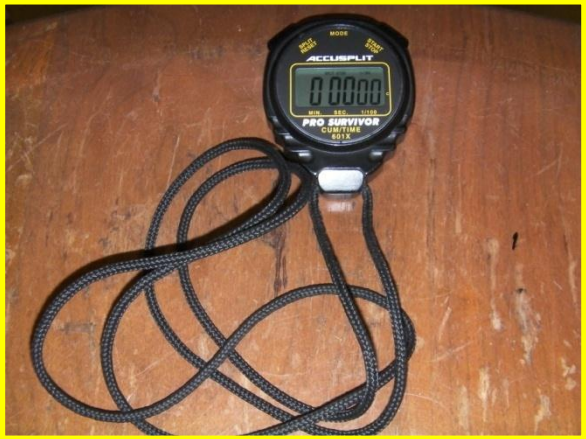


Loss of leg lean mass (Blue bar) and muscle strength (orange bar) in older adults Results from the Health, Aging and Body Composition Study

** Gender difference: p < .01, † Racial difference: p < .05*

Goodpaster et al. J Gerontol Med Sci, 2006, 61 (10), 1059- 1064

SHORT PHYSICAL PERFORMANCE BATTERY



Criterio per screening della sarcopenia basato su Gait speed: velocità inferiore a 0.8 m/sec

1. **Balance Tests**

< 10 sec (0 pt)

pt
pt
pt
pt
0 pt

3. **Chair Stand Test**

Pre-test
Participants fold their arms across their chest and try to stand up once from a chair

unable → Stop (0 pt)

able

5 repeats
Measures the time required to perform five rises from a chair to an upright position as fast as possible without the use of the arms

≤11.19 sec	4 pt
11.20-13.69 sec	3 pt
13.70-16.69 sec	2 pt
>16.7 sec	1 pt
>60 sec or unable	0 pt

NEJM 1995, Guralnik J

REPORT

Sarcopenia: European consensus on definition and diagnosis

Report of the European Working Group on Sarcopenia in Older People

ALFONSO J. CRUZ-JENTOFT[1], JEAN PIERRE BAEYENS[2], JÜRGEN M. BAUER[3], YVES BOIRIE[4], TOMMY CEDERHOLM[5], FRANCESCO LANDI[6], FINBARR C. MARTIN[7], JEAN-PIERRE MICHEL[8], YVES ROLLAND[9], STÉPHANE M. SCHNEIDER[10], EVA TOPINKOVÁ[11], MAURITS VANDEWOUDE[12], MAURO ZAMBONI[13]

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Age and Ageing 2010; 39: 412–423

EWGSOP Definition of Sarcopenia

Ridotta **massa muscolare**

+

Ridotta **forza muscolare**

e/o

Ridotta **performance fisica**

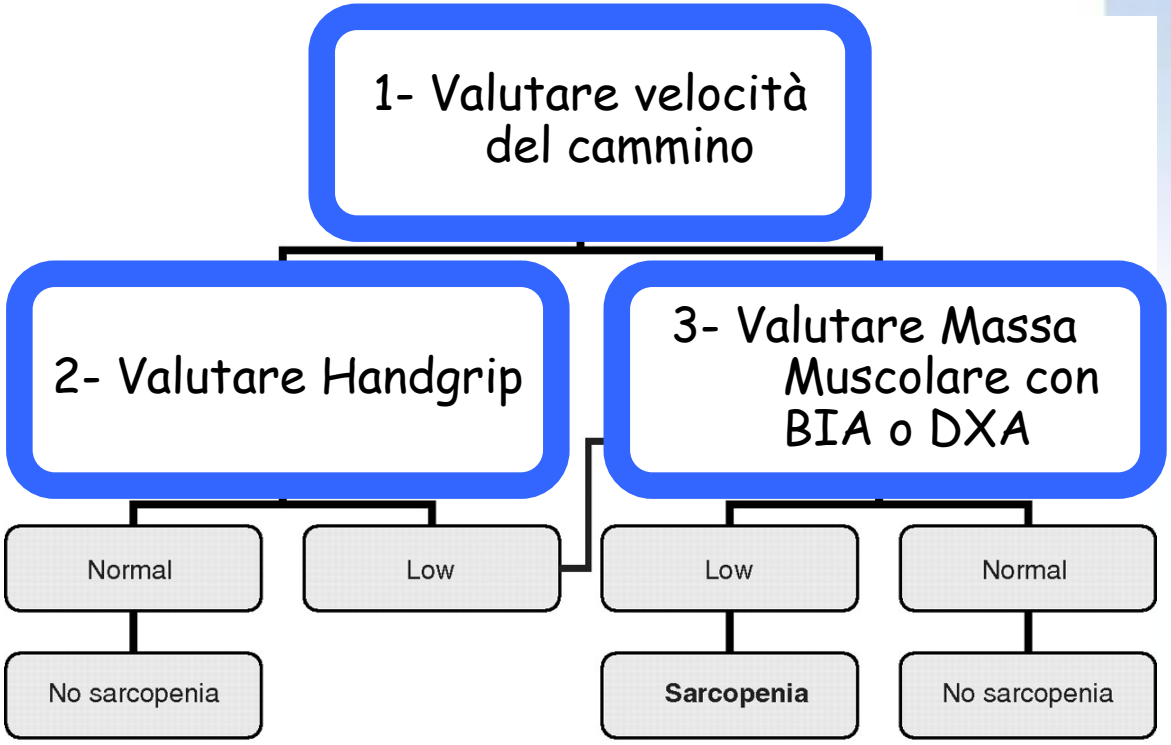
=

SARCOPENIA

Cruz-Jentoft Alfonso J et al Sarcopenia: European Consensus on Definition and Diagnosis. Report of the European Working Group on Sarcopenia in Older People- Age and Ageing,2010 ; 1-12

Sarcopenia case finding

EWGSOP-suggested algorithm in older individuals



* Comorbidity and individual circumstances that may explain each finding must be considered

+ This algorithm can also be applied to younger individuals at risk

Cruz-Jentoft, A. J. et al. Age Ageing 2010 ; 1-12

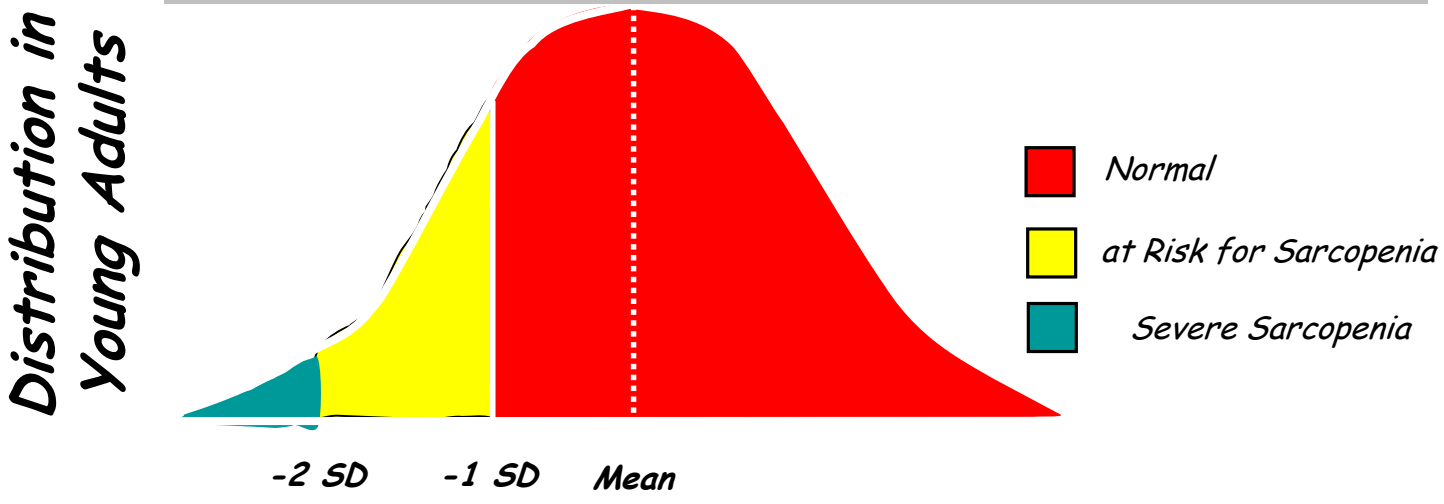
Operative definitions based on muscle mass

appendicular Fat Free Mass (Kg)/h (mt)²

Baumgartner et al, Am J Epidemiol 1998, 147 (8), 755-763

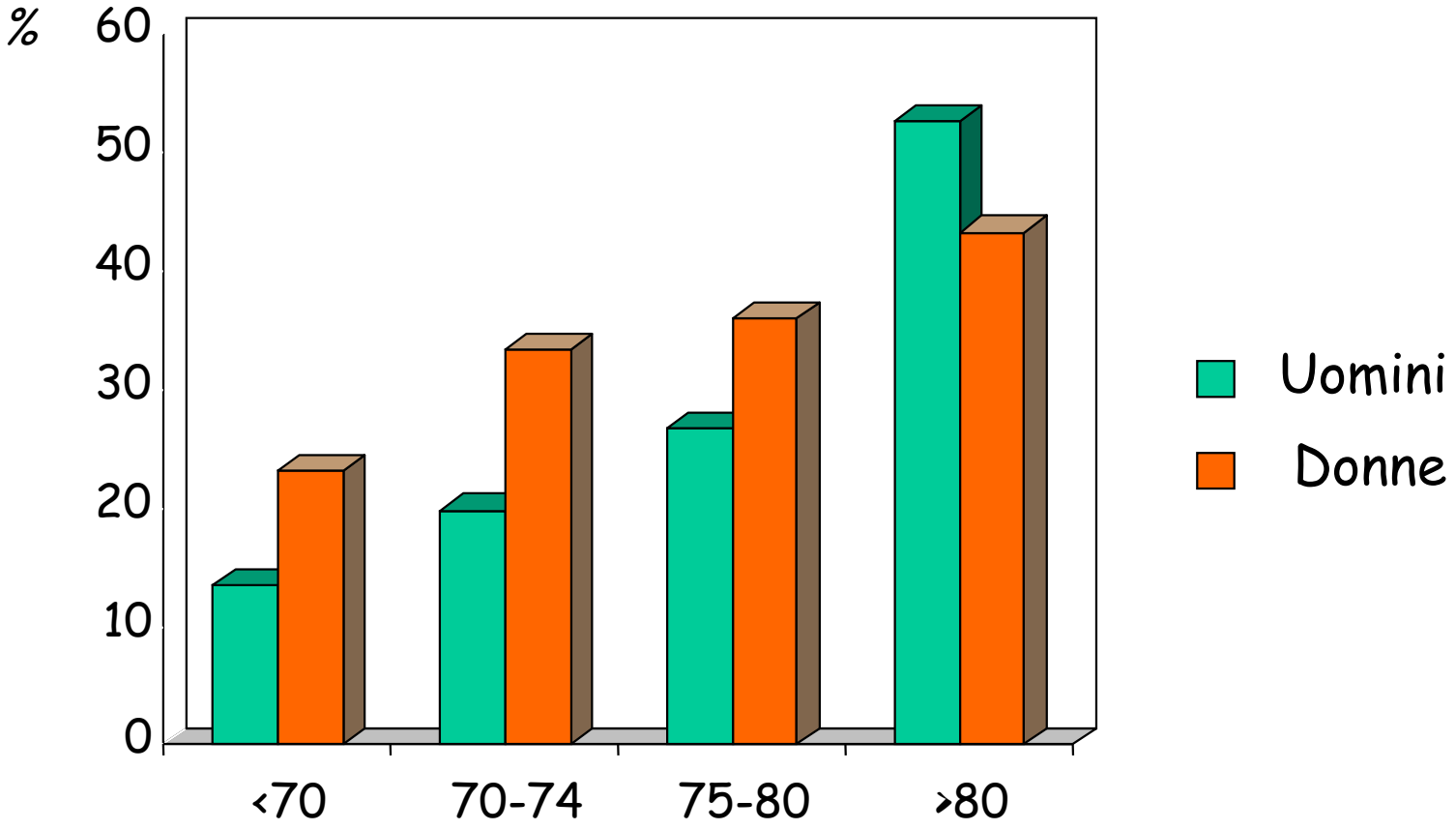
total Fat Free Mass (Kg)/ body weight (kg)

Janssen et al, J Am Geriatr Soc 2002, 50 (5), 889-896



Prevalenza di Sarcopenia - The New Mexico Elder Health Survey (n =883)

Baumgartner et al, 1998



massa muscolare appendicolare (Kg)

altezza $(mt)^2$

Questionario SARC-F

Component	Question	Scoring
Strength	How much difficulty do you have in lifting and carrying 10 pounds?	None = 0 Some = 1 A lot or unable = 2
Assistance in walking	How much difficulty do you have walking across a room?	None = 0 Some = 1 A lot, use aids, or unable = 2
Rise from a chair	How much difficulty do you have transferring from a chair or bed?	None = 0 Some = 1 A lot or unable without help = 2
Climb stairs	How much difficulty do you have climbing a flight of 10 stairs?	None = 0 Some = 1 A lot or unable = 2
Falls	How many times have you fallen in the last year?	None = 0 1-3 falls = 1 4 or more falls = 2

JAMDA
The Journal of Post-Acute and Long-Term Care Medicine

Malmstrom TK, Morley JE J Am Med Dir Assoc 2013; 14 (8): 531-2

3 Studi di validazione del questionario SARC-F

Studio di Woo
su una coorte di 4000 soggetti cinesi con età > 65 anni

JAMDA
The Journal of Post-Acute and Long-Term Care Medicine

il SARC-F presenta elevata specificità (94-99%) e ridotta sensibilità (4.2% uomini, 9.9% donne) rispetto ai criteri diagnostici Europei (EWGSOP)

Studio di Malmstrom sulle popolazioni dei BLSA, NHANES, AAH

Journal of Cachexia, Sarcopenia and Muscle

Il SARC-F è risultato associato ad un maggior rischio di disabilità e mortalità

Studio di Cao in un gruppo di 230 anziani cinesi

JNHA
The Journal of Nutrition, Health & Aging

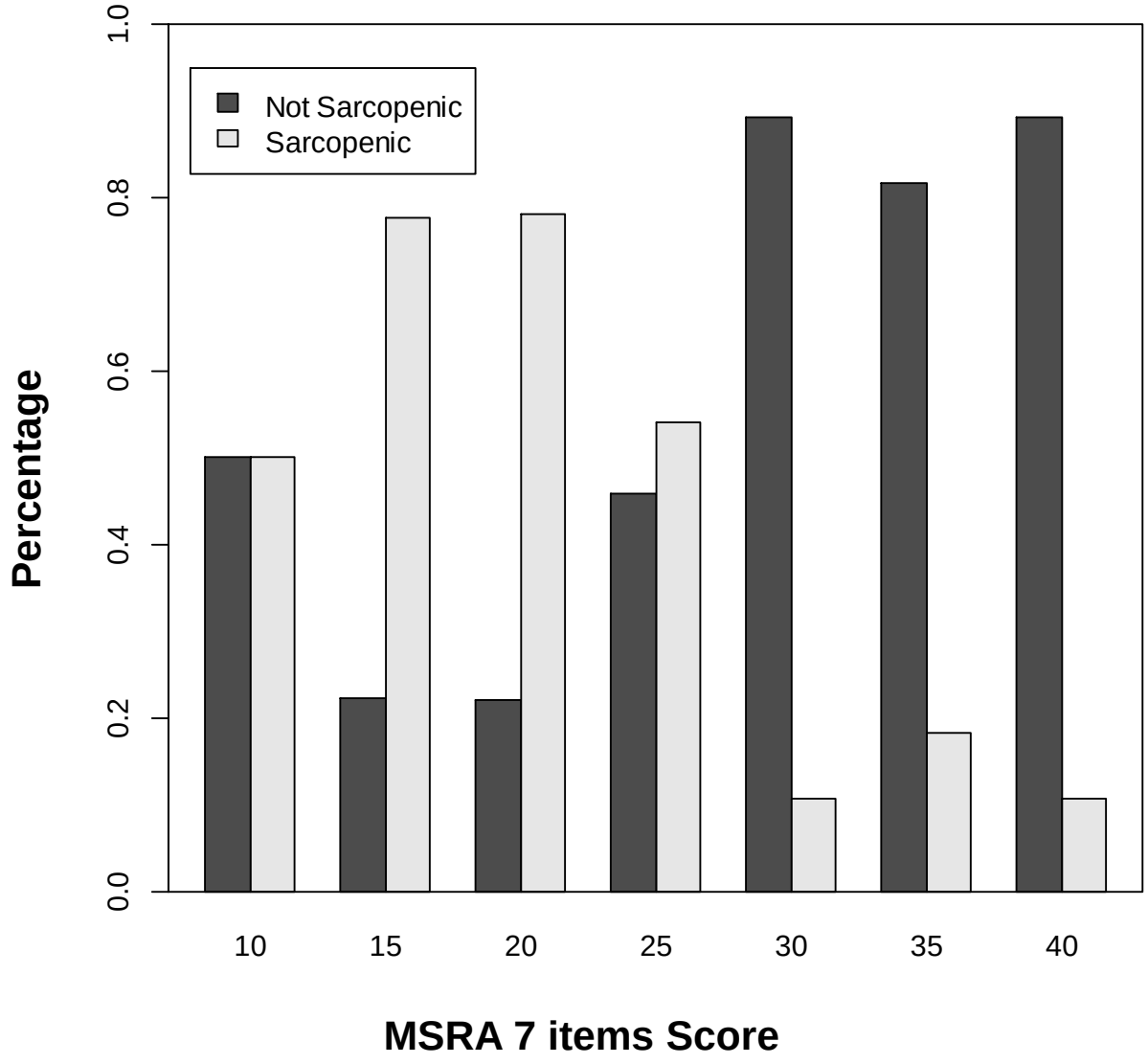
Il questionario SARC-F è stato correlato al numero di ricoveri negli ultimi due anni precedenti

Mini Sarcopenia Risk Assessment (MSRA)

1- How old are you?		
	≥70 years	0
	<70 years	5
2- Did you had hospitalization in the last year?		
	Yes, and more than an hospitalization	0
	Yes, one hospitalization	5
	No	10
3- What is your performance level?		
	I'm able to walk less than 1000 meters	0
	I'm able to walk more than 1000 meters	5
4- Do you eat regularly 3 meals per day		
	No, until twice per week I skip a meal (for example I skip breakfast or I have only milky coffee or soup for dinner)	0
	Yes	5
5- Do you consume any of the following?		
	Milk or dairy products (yogurt, cheese), but not every day	0
	Milk or dairy products (yogurt, cheese) at least once per day	5
6- Do you consume any of the following?		
	Poultry, meat, fish, eggs, legumes, ragout or ham, but not every day	0
	Poultry, meat, fish, eggs, legumes, ragout or ham at least once per day	5
7- Did you have weight loss in the last year?		
	Yes	0
	No	5

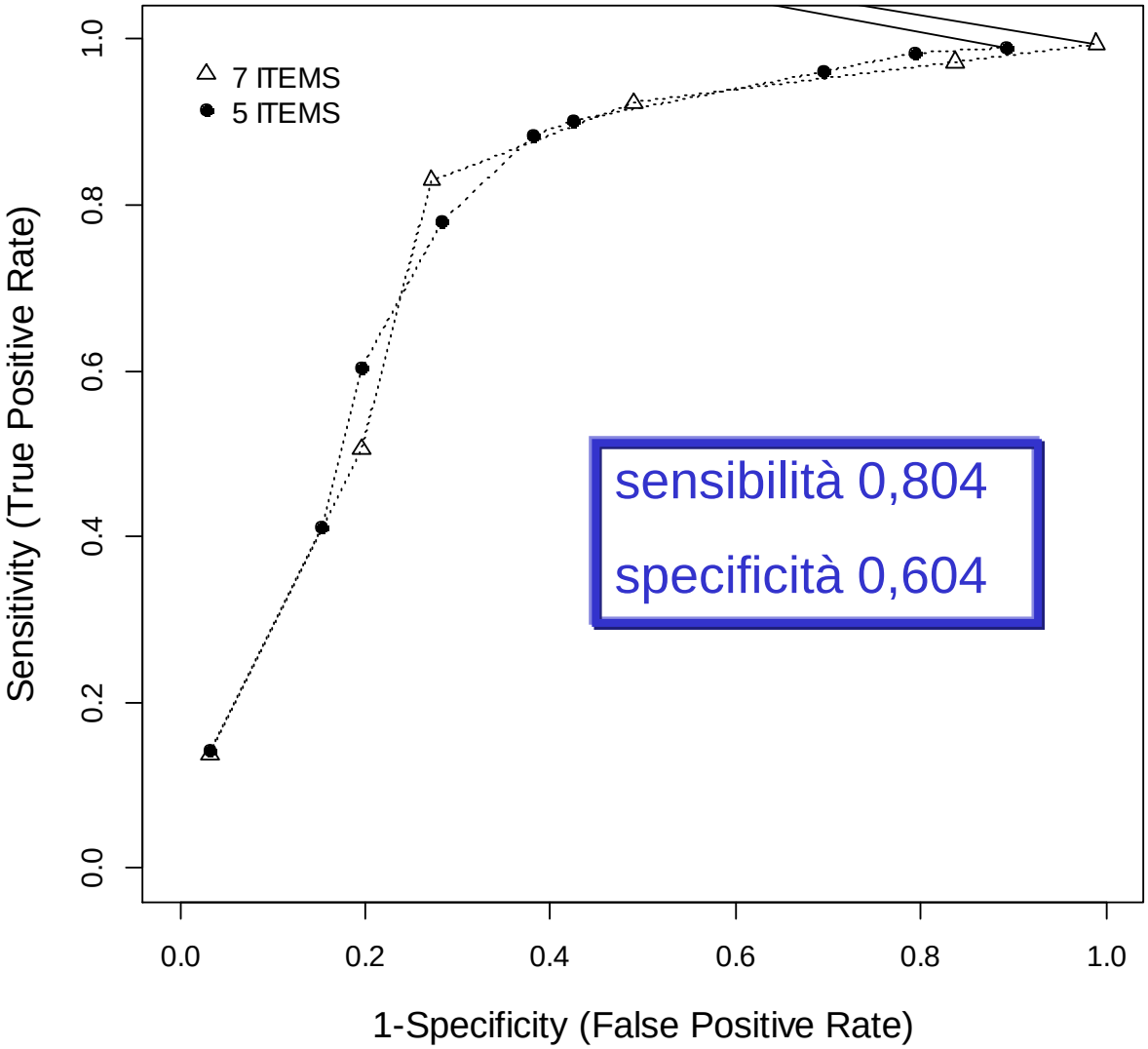
Rossi AP, Zamboni M J Nutr Heal Aging 2017; in press

Percentuali di soggetti sarcopenici e non per ogni gruppo di MSRA score



Rossi AP, Zamboni M J Nutr Heal Aging 2017; in press

Curve di ROC relative a MSRA a 7 e 5 items



Rossi AP, Zamboni M J Nutr Heal Aging 2017; in press

1. Definizione
2. Patogenesi
3. Rilevanza clinica

Meccanismi eziopatogenici coinvolti nella Sarcopenia

↓ stimolazione neuronale dovuta alla ***diminuzione di motoneuroni-alpha***

↓ livello di attività fisica *stile di vita sedentario* ***allettamento***

diminuzione ormonale:
↓GH/IGF1
↓ Testosterone, DHEAS
↓ Estrogeni
↓ Vitamina D

perdita di peso

↑ miostatina

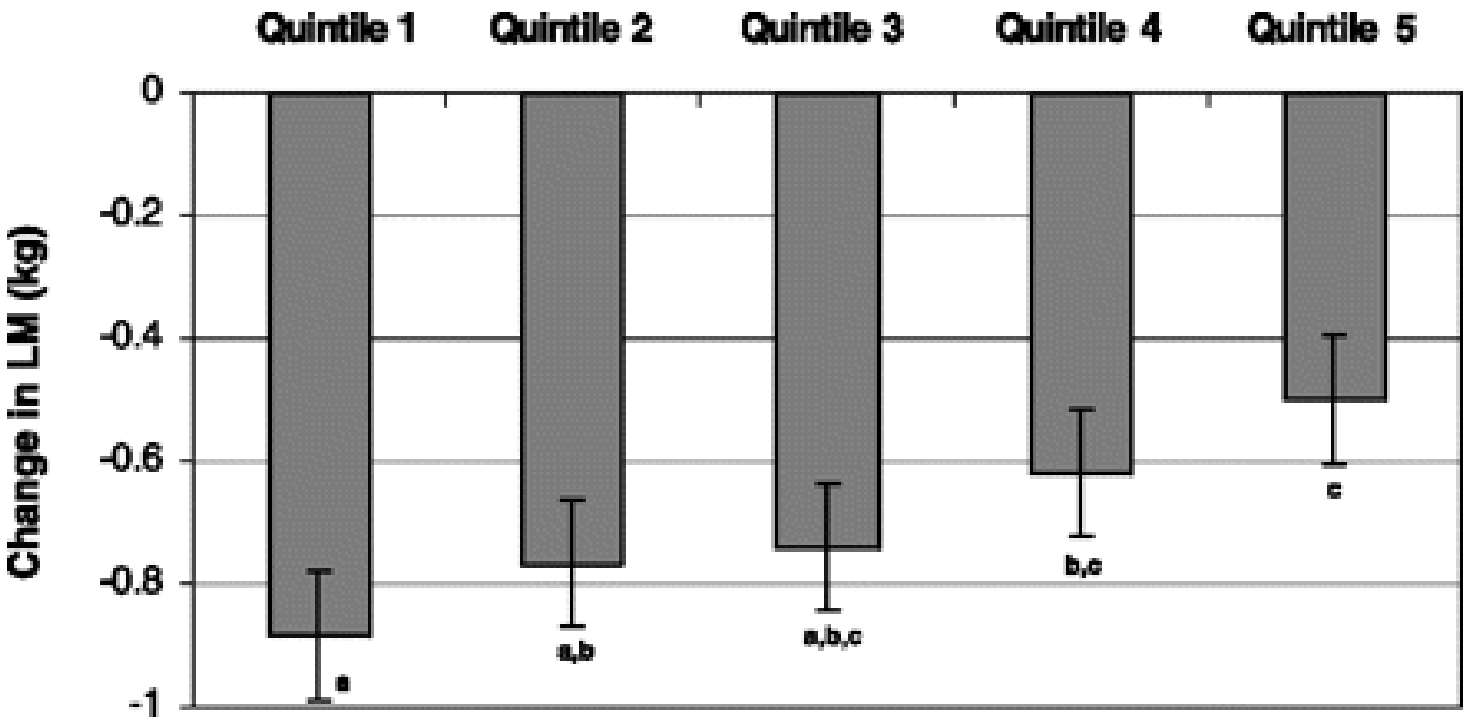
disregolazione delle ***citochine cataboliche***

ROS

↓ introito calorico e proteico *con la dieta, anoressia*

sarcopenia

Budui S, Rossi AP, Zamboni M. Clinical Cases in Mineral and Bone Metabolism 2015; 12(1):22-6



Introito di proteine: da 0.7 g/kg a 1.2 g/kg

Perdita di massa muscolare in 3 anni aggiustata per quintile di introito proteico totale.
N= 2066 - Health ABC study

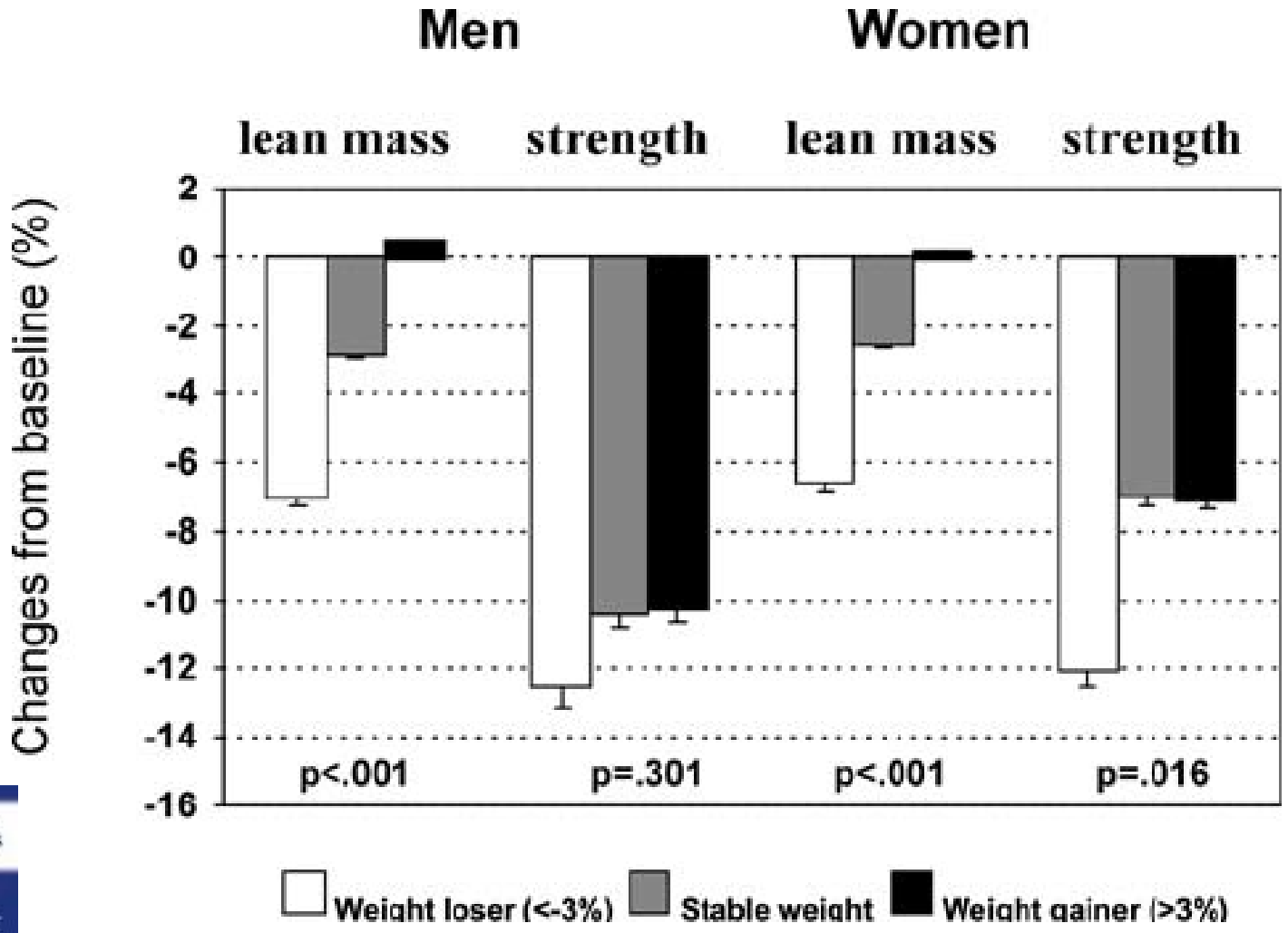
Evidenza epidemiologica che associa un relativamente basso introito proteico ad alto rischio di Sarcopenia

The American Journal of CLINICAL NUTRITION

Denise K Houston, 2008

Health, Aging, and Body Composition Study:

- **Campione: 1044 donne e 931 uomini**
- **Esclusi soggetti con patologie neoplastiche o cardiache gravi**



Goodpaster et al J Am Geriatric Soc. 2014; 62: 1476-1483

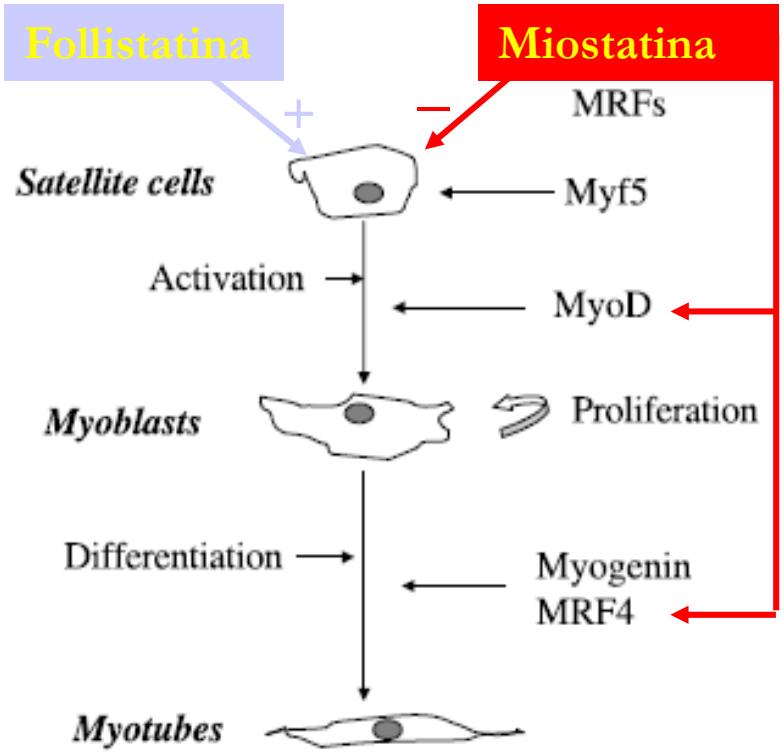
Vitamina D

- *Livelli Vitamina D associati a forza muscolare*
- *Bassi livelli di vitamina D associati ad aumentato rischio di miopatia da statina*
- *Supplementazione Vitamina D aumenta forza muscolare e riduce il rischio di caduta*

Budui S, Rossi AP. Clinical Cases in Mineral and Bone Metabolism 2015; 12(1):22-6

Miostatina

La Miostatina appartiene alla famiglia dei Transforming Growth Factor-β ed è un inibitore della crescita muscolare (McPherron et al., 1997)



-Agonista dei recettori per l'attivina di tipo I (ActR2A e ActR2B)

-Inibitore della sintesi ed attivazione dei fattori regolazione miogena- MRF (myoD)

-Inibitore della attivazione, proliferazione differenziazione delle cellule satelliti

-Modulatore della differenziazione delle cellule mesenchimali verso la linea adipogenica

Welle, 2002; Siriett, 2006; McCroskery, 2003

FIG. 2. A fullblood Belgian Blue bull showing the double muscling phenotype.

Effect of 10 Days of Bed Rest on Skeletal Muscle in Healthy Older Adults

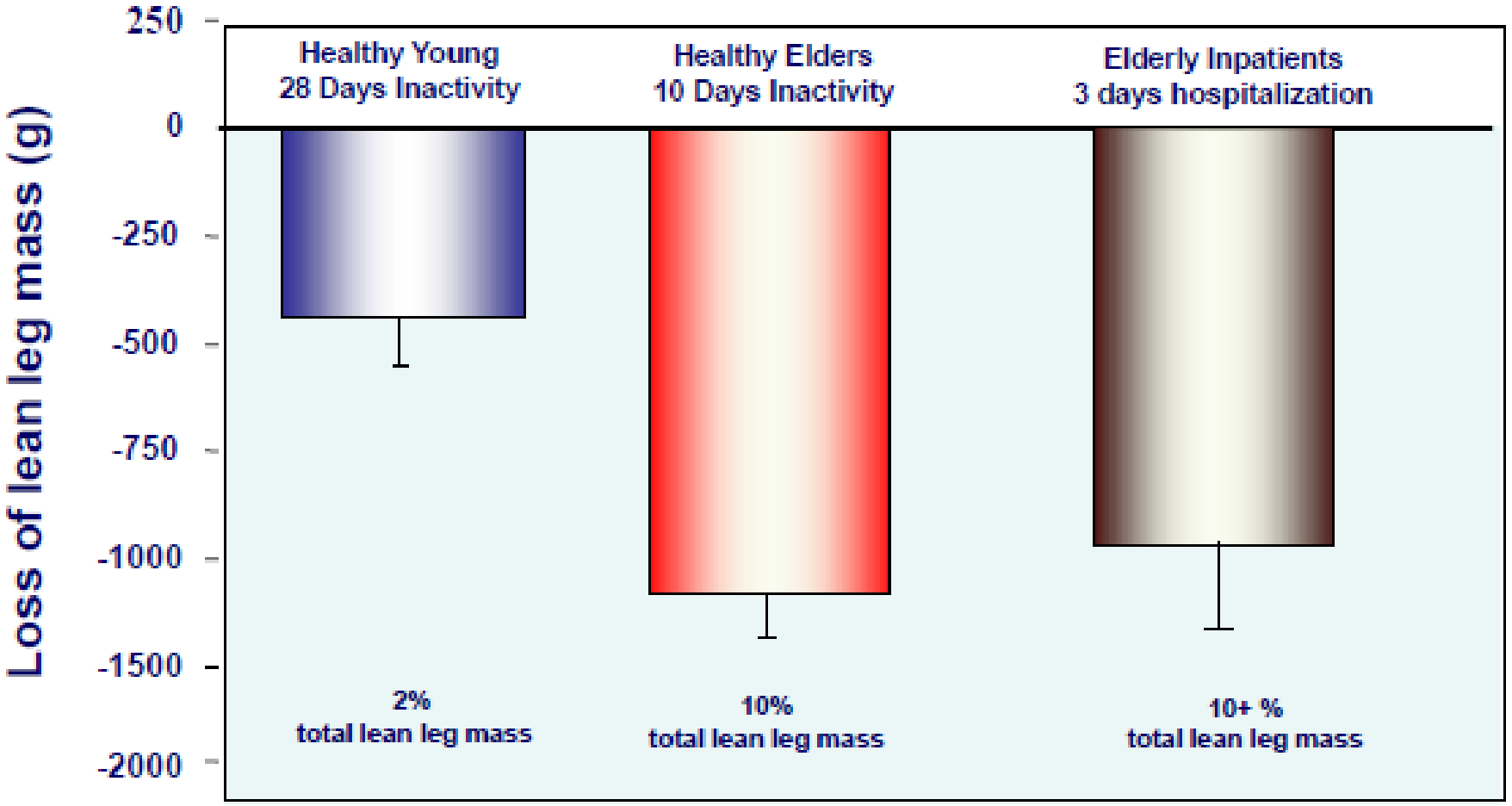
Table. Effects of 10 Days of Bed Rest in Older Adults

	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)	

Abbreviation: DEXA, dual-energy x-ray absorptiometry; Nm, Newton meter.
*One participant was excluded from all analyses because of insufficient protein intake.
†Because of a technical error, the muscle fractional synthesis rate measurement was excluded for 1 participant.
‡One participant was excluded from the DEXA analysis because the scan before bed rest was not administered.
§Isokinetic knee extension at 60° per second.

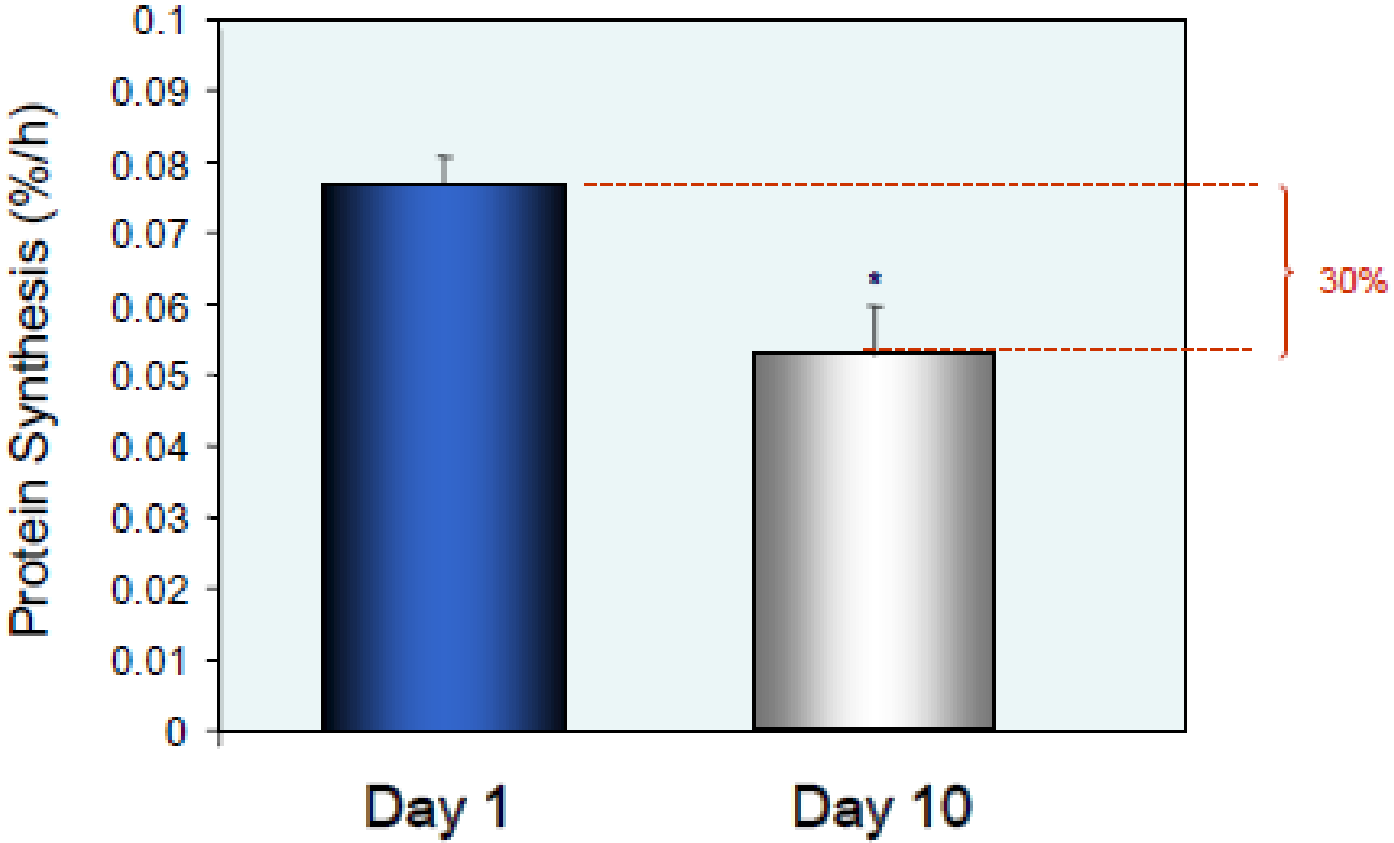
Kortbein JAMA. 2007;297(16):1769-1774

Perdita di massa muscolare arti inferiori in soggetti anziani ospedalizzati



Paddon-Jones ,

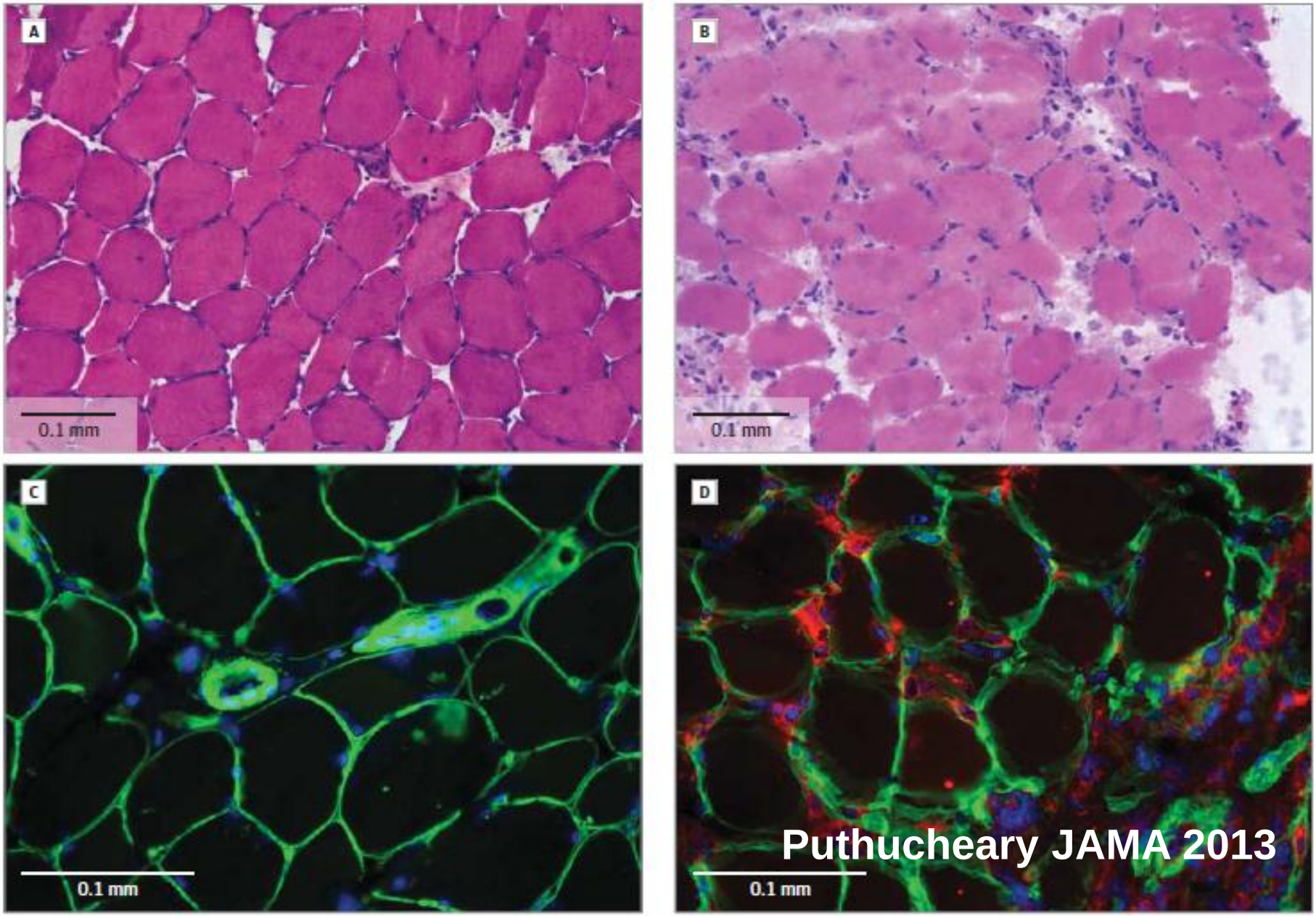
L’inattività riduce l’abilità di costruire e riparare le proteine e il muscolo



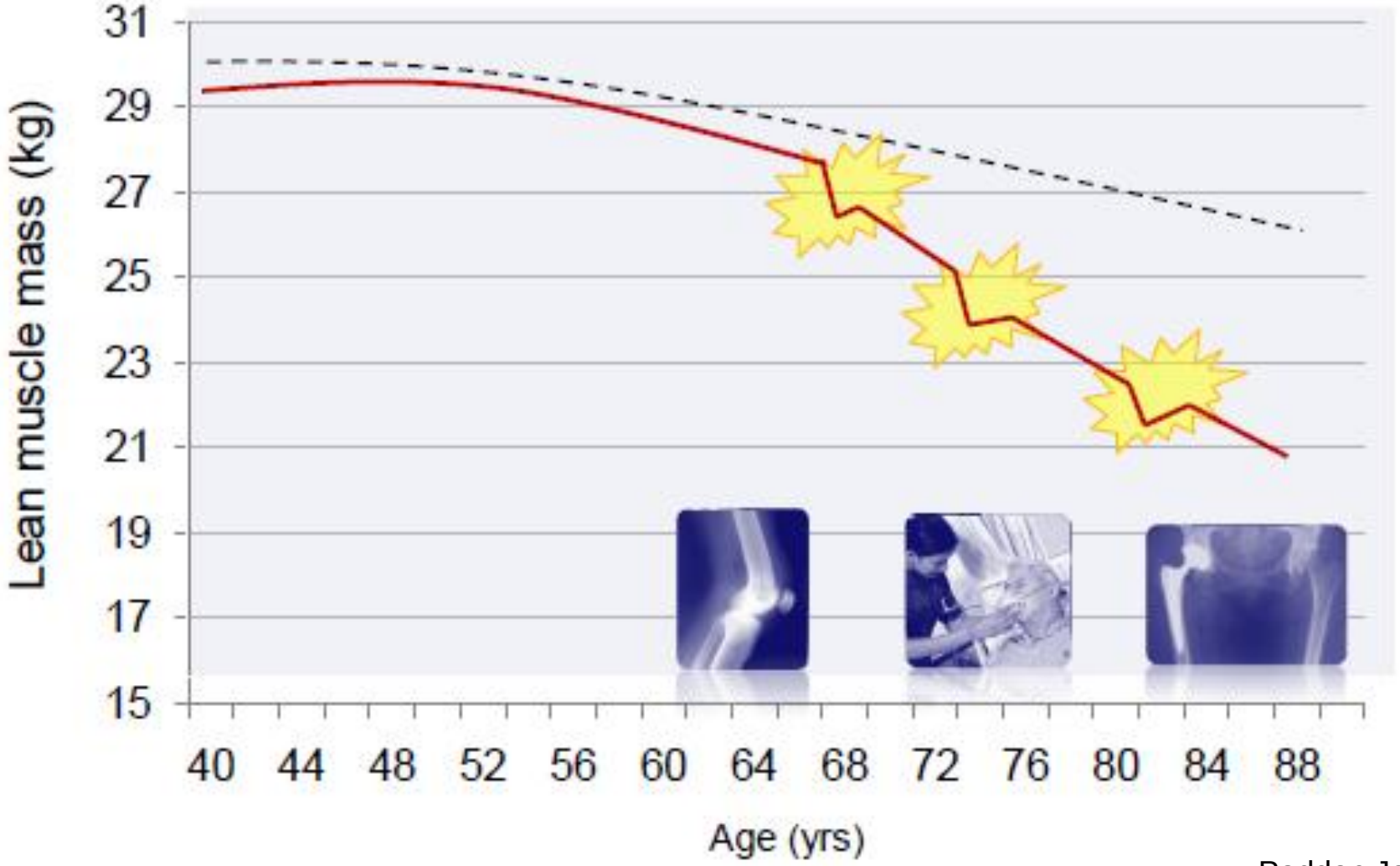
24 h muscle protein synthesis during 10 day of inactivity in elders
(stable isotope methodology)

Kortebein et al. 2007

Biopsie muscolari di soggetti ricoverati in terapia intensiva giorno 1 e 7

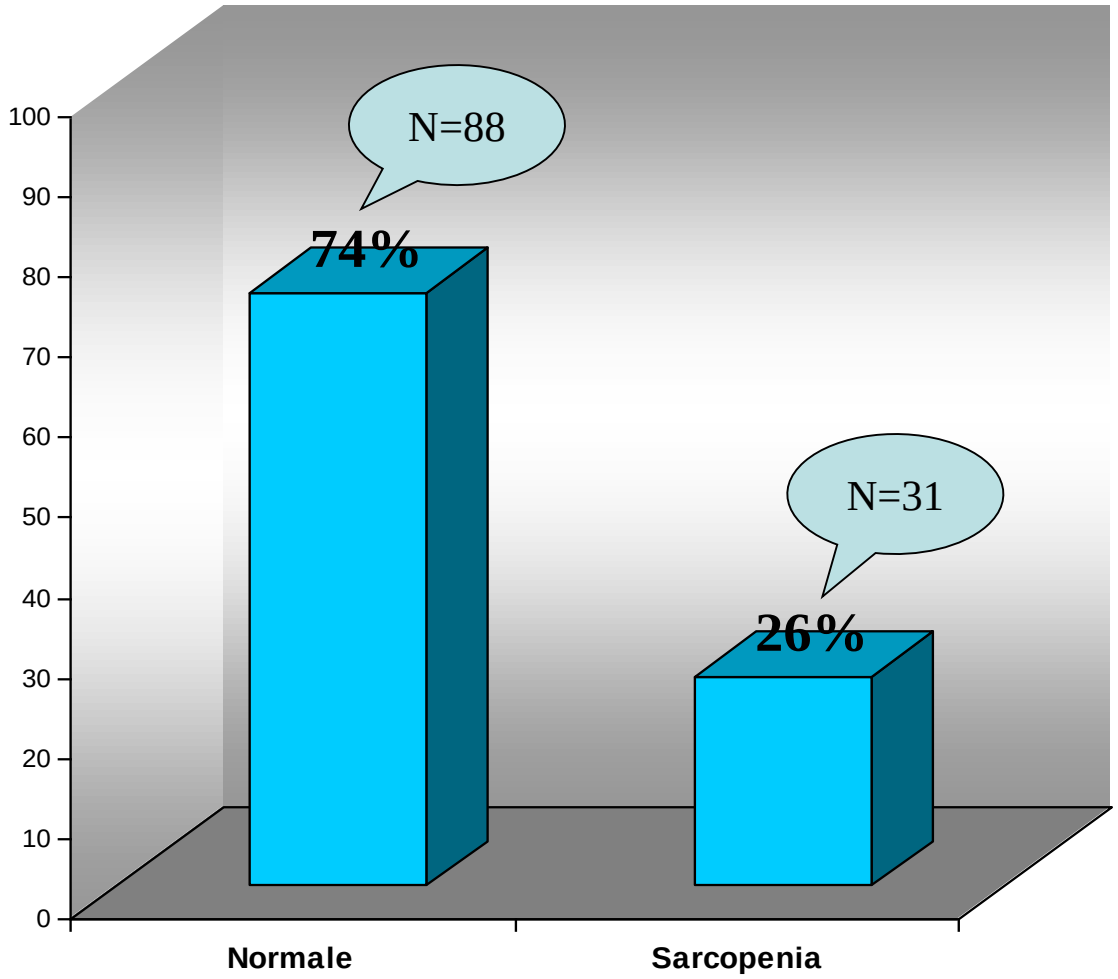


Modello alternativo di perdita di massa muscolare nel soggetto anziano



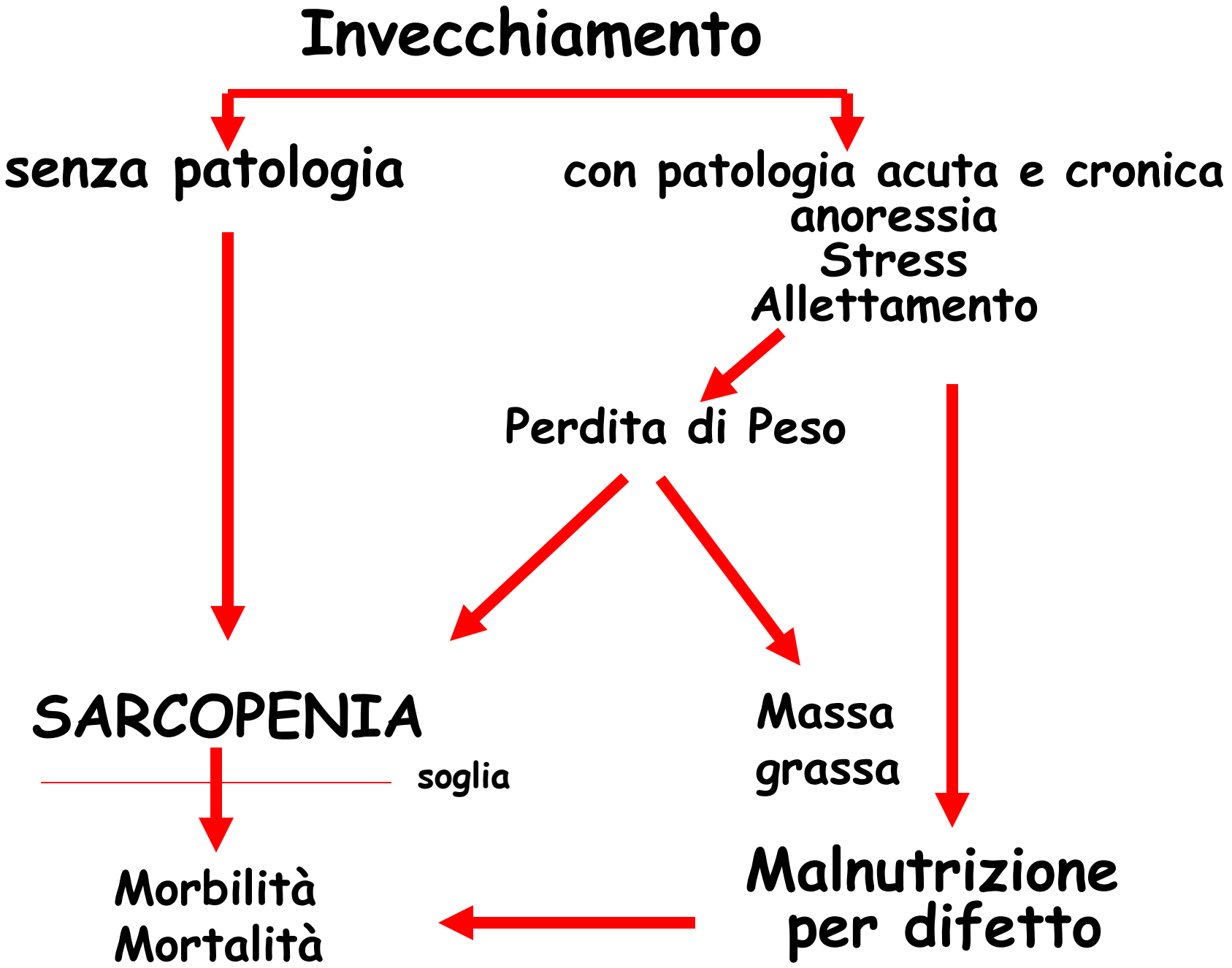
Paddon Jones 2008

Prevalenza di bassi valori di massa magra applicando l'indice di Baumgartner in una popolazione di soggetti ospedalizzati n=119



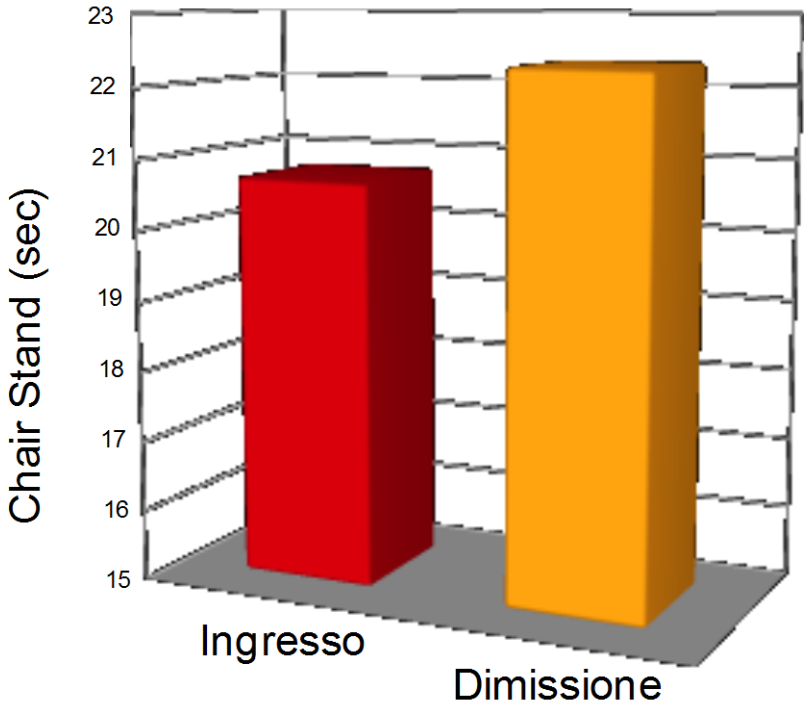
JAMDA
Long Term Care: Management, Applied Research and Clinical Issues

Rossi AP, Fantin F, Zamboni M. JAMDA 2014


Invecchiamento
senza patologia
con patologia acuta e cronica
anoressia
Stress
Allettamento
Perdita di Peso
SARCOPENIA
soglia
Massa grassa
Morbilità
Mortalità
Malnutrizione per difetto

Modificazioni dei test tra l'ingresso e la dimissione

P<0.001



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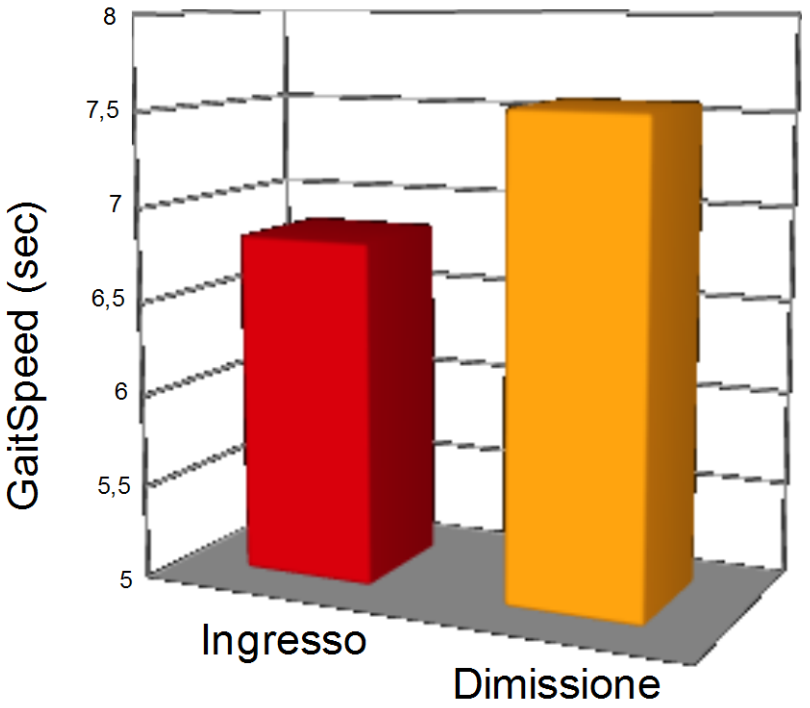
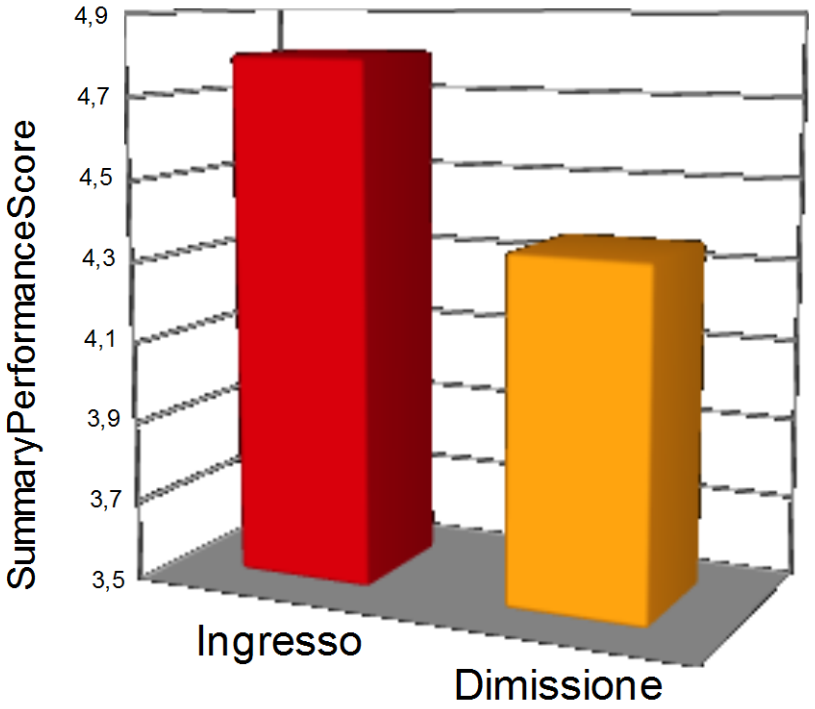


Rossi AP et al. J Geront Geriatrics Research 2017 in press

Modificazioni dei test tra l'ingresso e la dimissione

P=0.001



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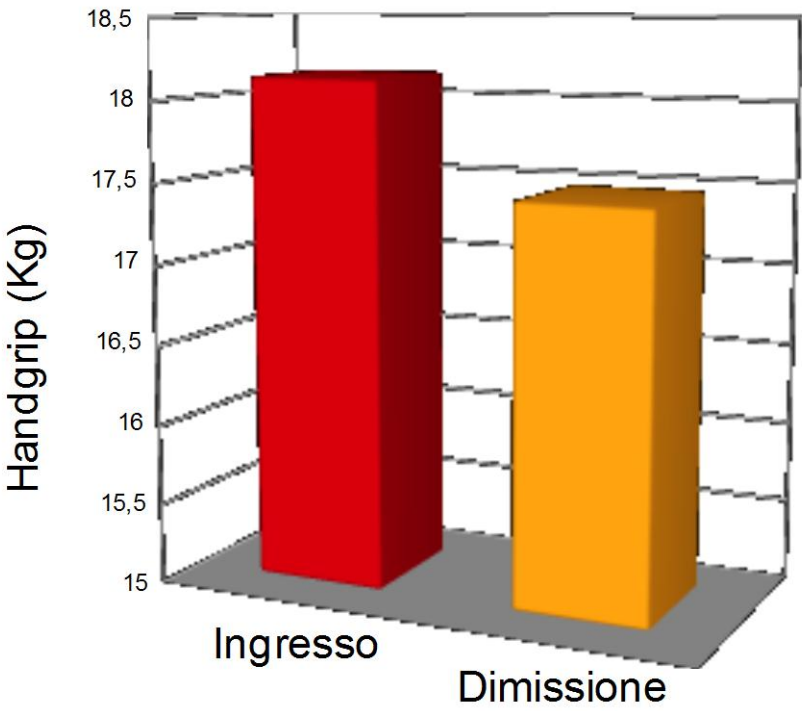
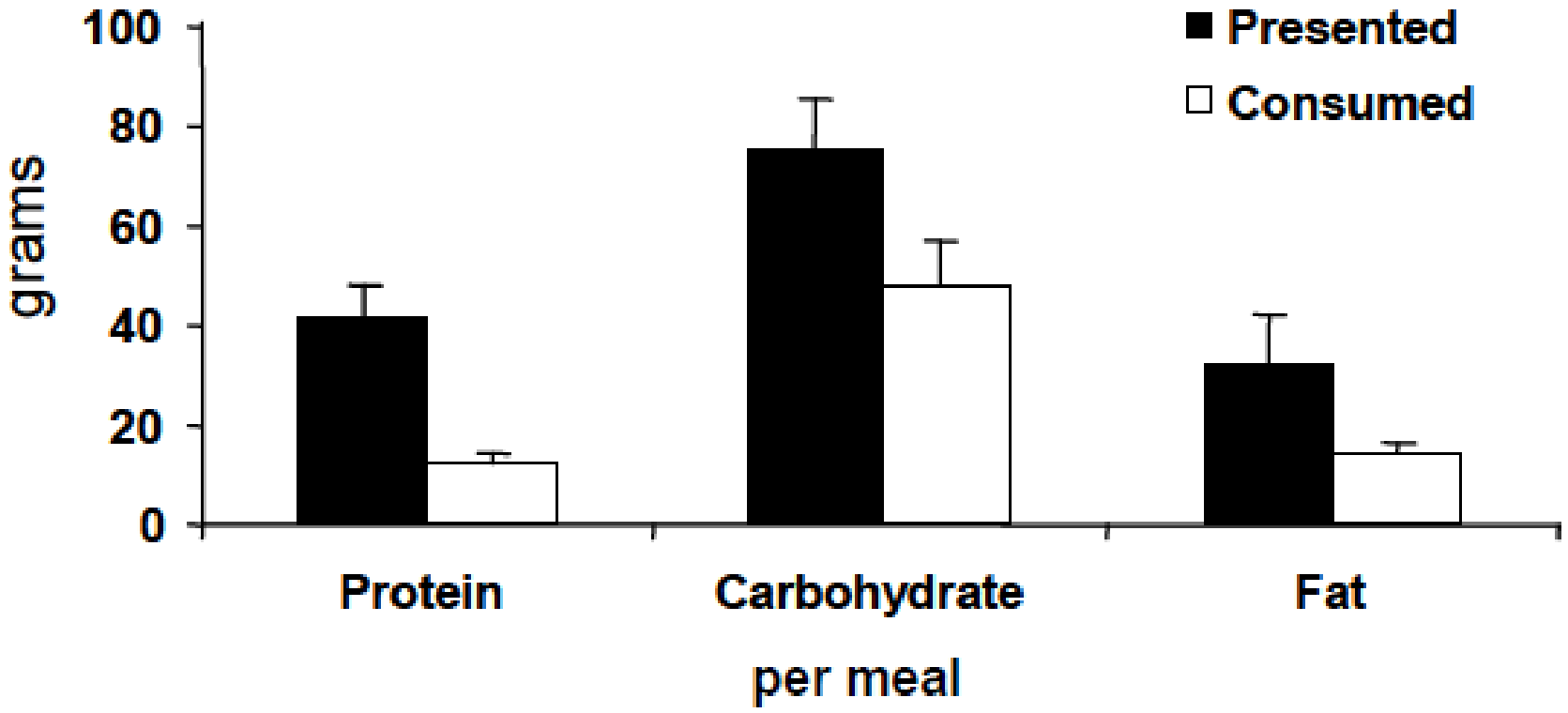


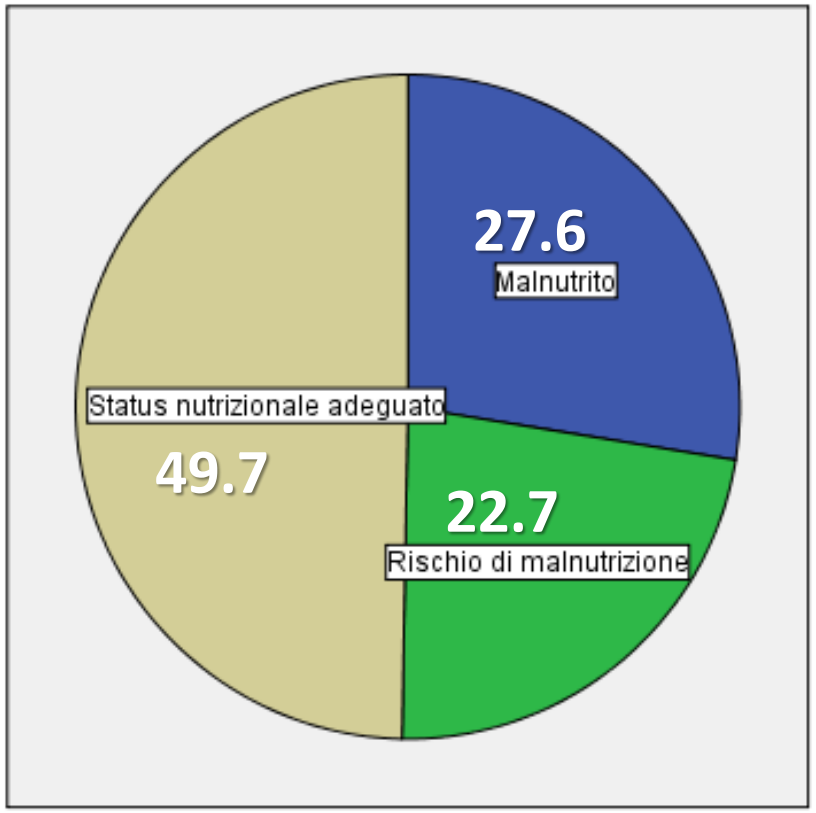
Rossi AP et al. J Geront Geriatrics Research 2017 in press

Cosa mangiano gli anziani ricoverati?

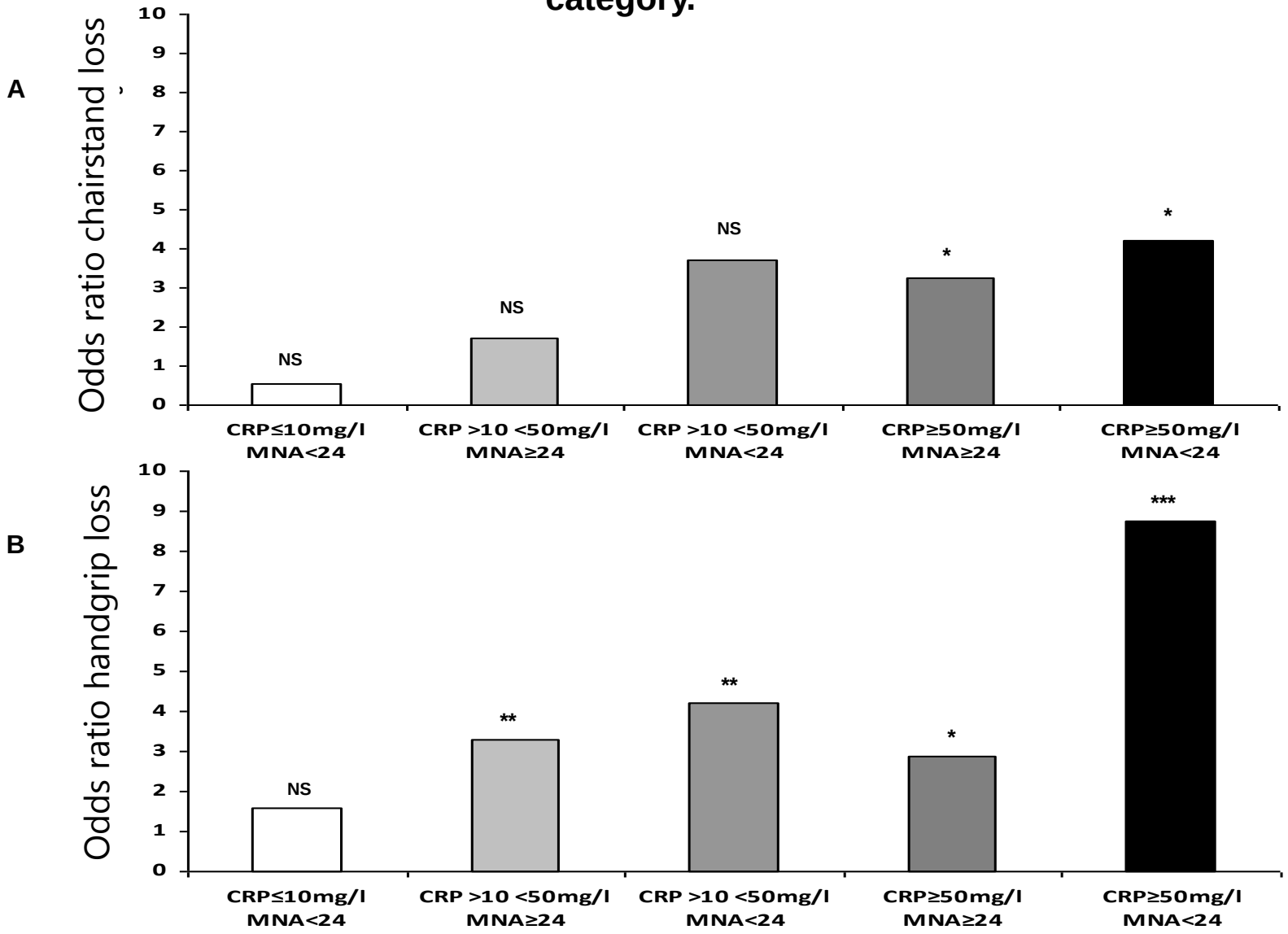


Paddon Jones 2008

MNA n=586, età= 81.6 + 8.03 anni



Odd ratios of chair stand loss (A) and handgrip strength loss (B) in different inflammation and malnutrition categories, considering subjects with MNA≥24 and CRP<10mg/l as reference category.



Adjusted for age, sex, time to perform chair-stand at baseline, days of bed rest, weight, Charlson index, cause of hospitalization, ADL and presence of anemia and hypoalbuminemia MNA= mini nutritional assessment, CRP= C-reactive protein. ***=p<.001, **=p<.001, *=p<.05

Rossi AP et al, Eur J Clin Nutr 2016

1. Definizione
2. Patogenesi
3. Rilevanza clinica

"Sarcopenia, the loss of muscle mass and strength with age, is becoming recognized as a major cause of disability and morbidity in the elderly population."

Roubenoff and Hughes, 2000

Relazione tra Sarcopenia e Disabilità.

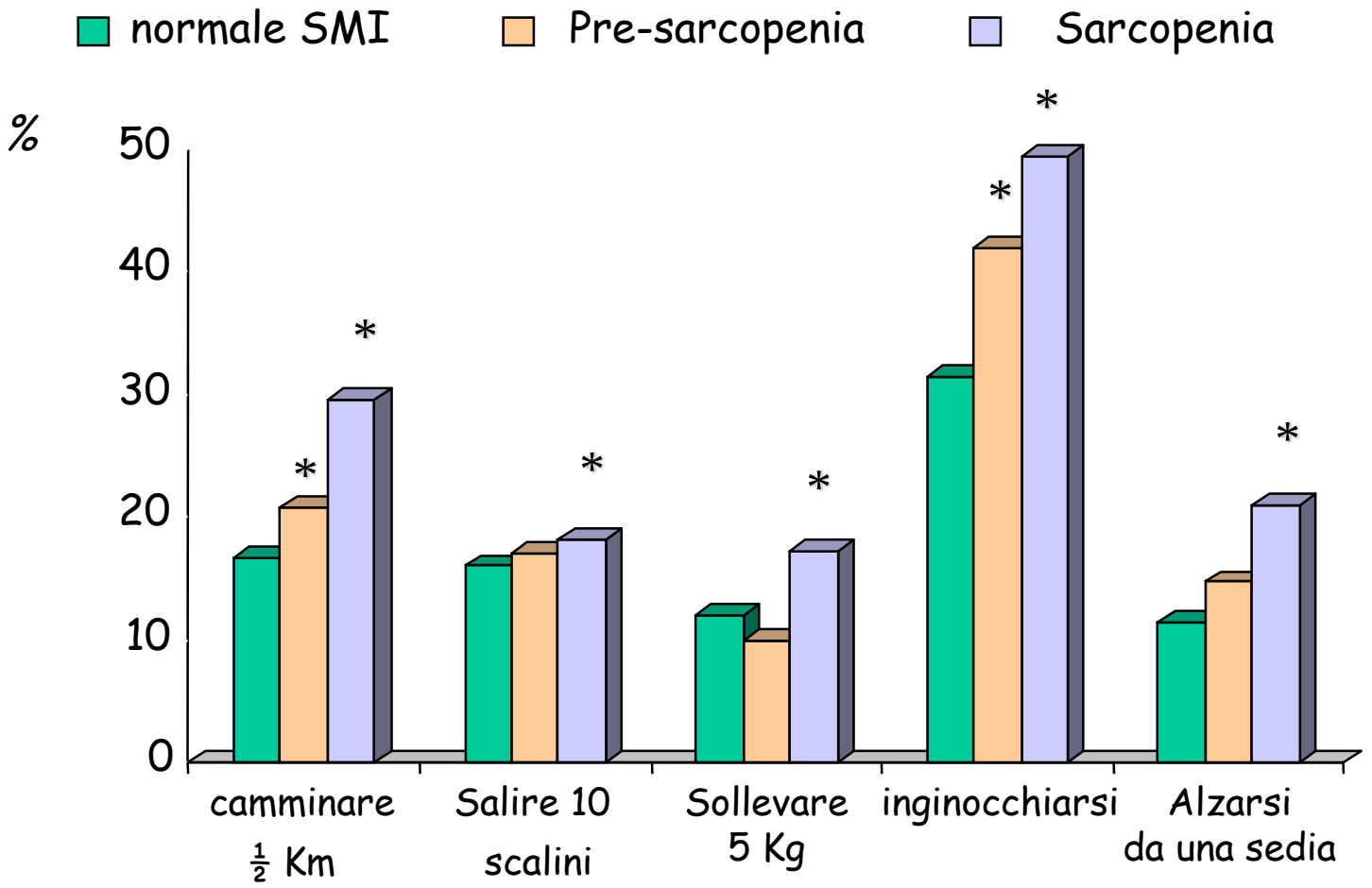
The New Mexico Elder Health Survey (n =883)

	Uomini	Donne
>3 disabilita' all'IADL	3.66 (1.42-10.02)	4.08 (1.52-11.31)
>1 alterazione dell'equilibrio	3.23 (1.13-9.74)	1.77 (0.48-5.75)
>1 anomalia nel cammino	1.87 (0.94-3.74)	1.12 (0.43-2.73)
Uso del bastone	2.29 (1.09-4.88)	1.79 (0.67-4.60)
Caduta nell'anno precedente	2.58 (1.42-4.73)	1.28 (0.60-2.67)

* dopo aggiustamento per eta', obesita', reddito, assunzione di alcolici, fumo, attivita' fisica e comorbilita'

Baumgartner et al, 1998

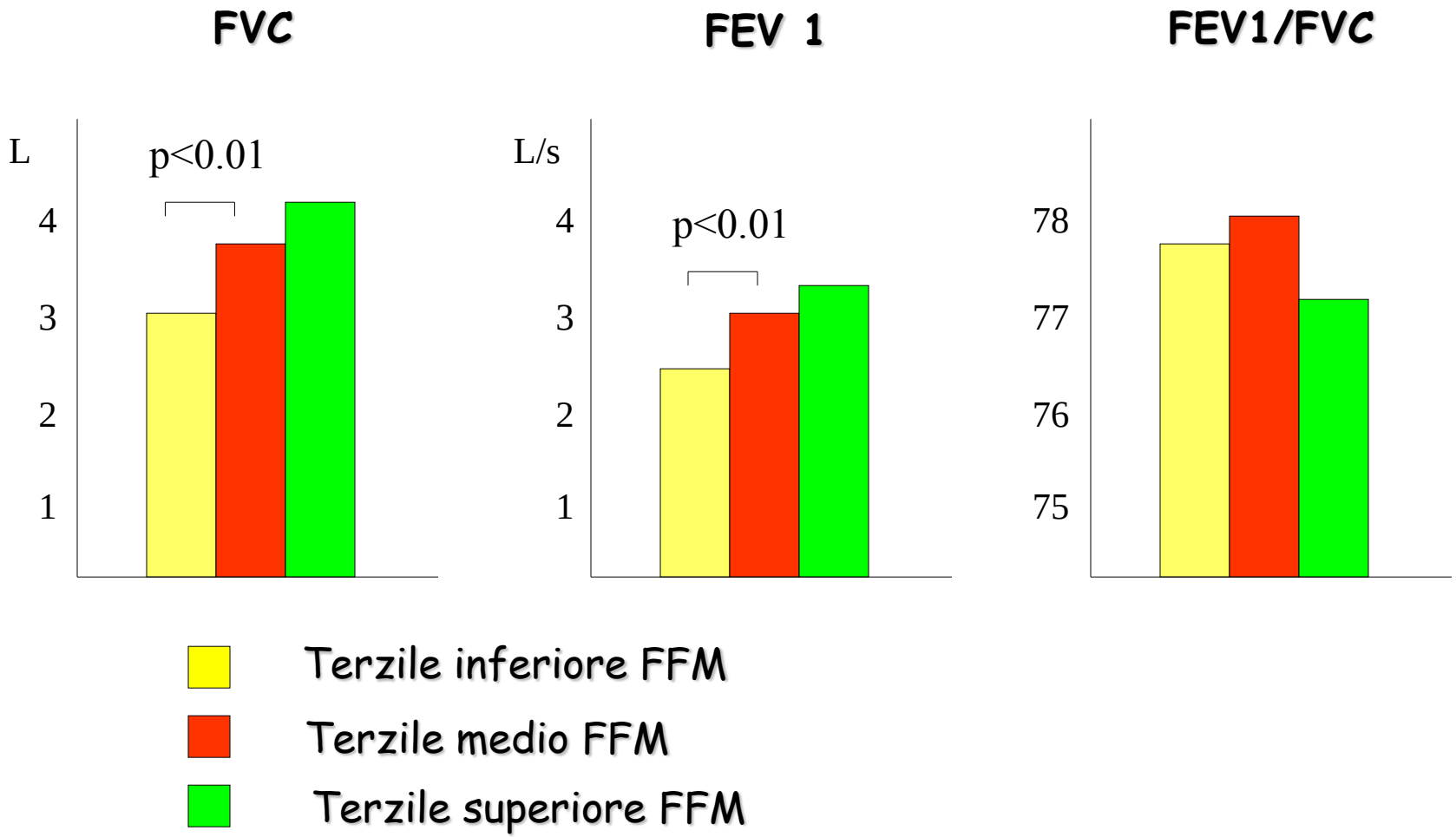
Prevalenza di limitazione funzionale e Sarcopenia
The NHANES III (n =2224 uomini > 60 anni)



* Significativamente maggiore rispetto a SMI normale (p<0.05)

Janssen et al, 1998

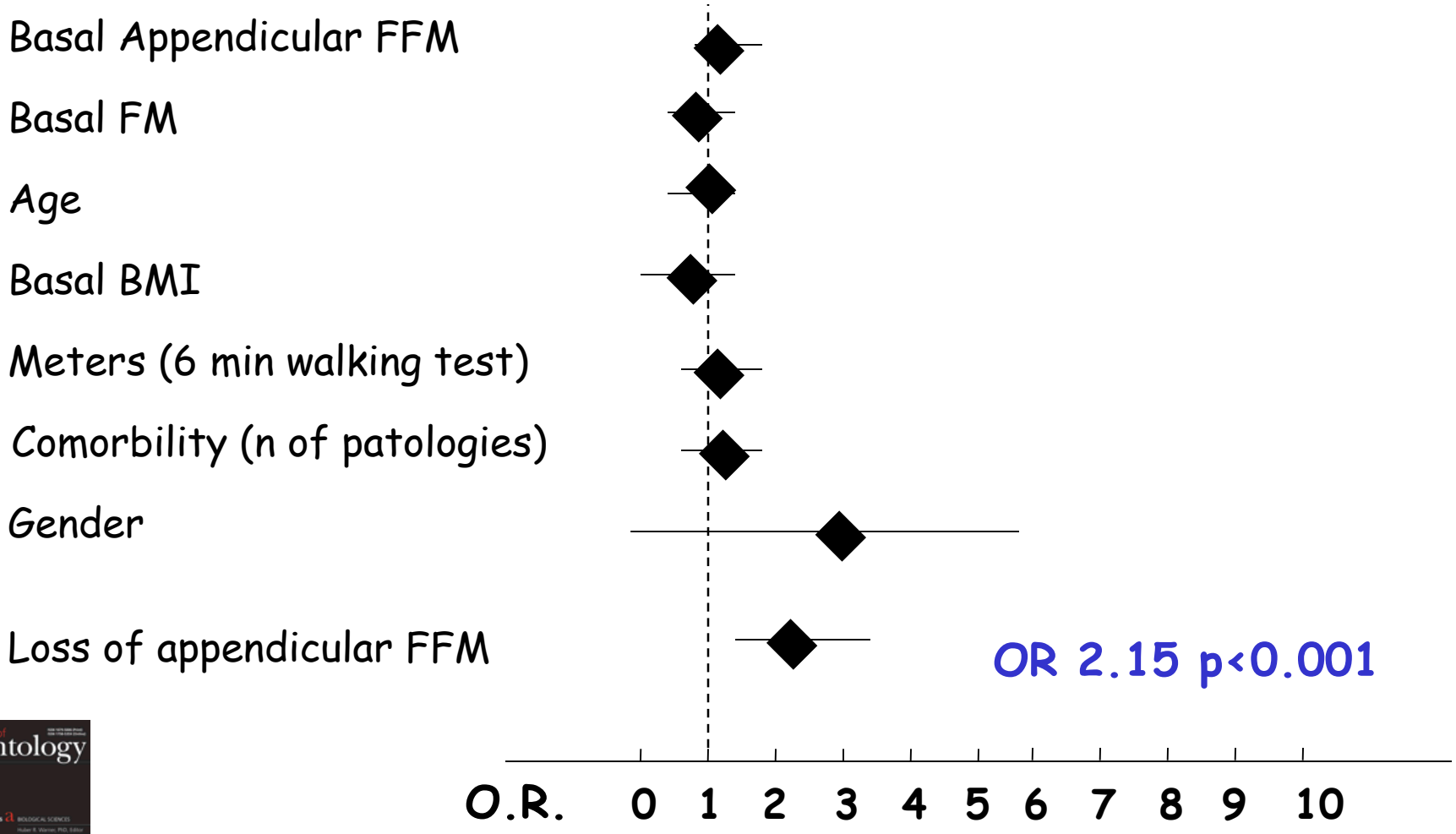
Funzione respiratoria in relazione a terzili di FFM nei soggetti di sesso maschile dopo aggiustamento per eta' e BMI



The American Journal of CLINICAL NUTRITION

Santana et al, 2001

Predictors of worsening disability during the follow-up period 5.5 years (160 subjects older 70)



Fantin et al, 2007

Sarcopenia predicts readmission and mortality in elderly patients in acute care wards: a prospective study

Ming Yang[1*], Xiaoyi Hu[1], Haozhong Wang[2], Lei Zhang[1], Qiukui Hao[1] & Birong Dong[1]

n=288, age=80

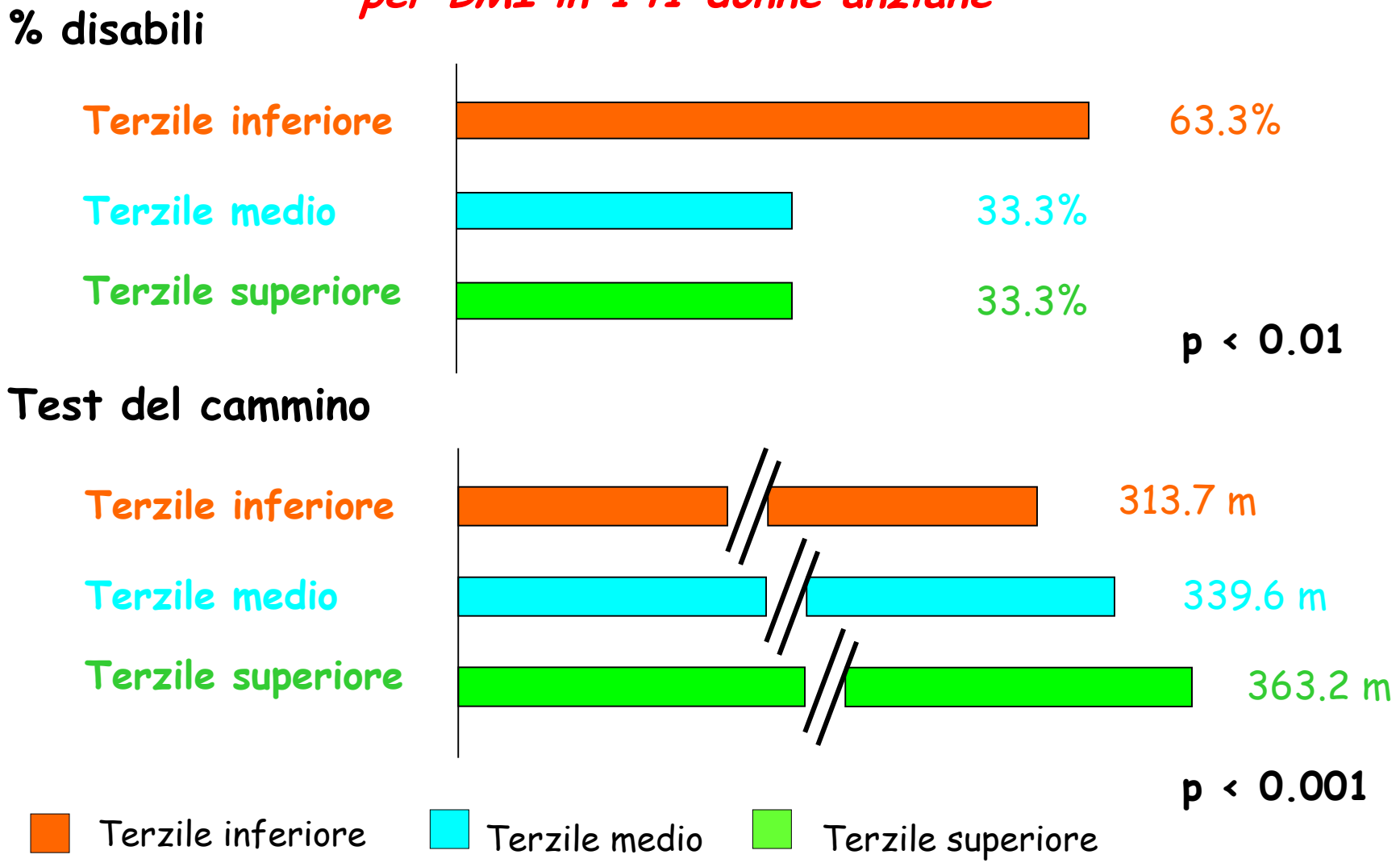
Association between sarcopenia and readmission (3 year follow-up) according to Cox regression models adjusted for potential confounders

	Unadjusted	Model 1	Model 2	Model 3
Sarcopenia	1.82 (1.28–2.59)	1.67 (1.16–2.39)	1.67 (1.16–2.41)	1.81 (1.17–2.80)
Age		1.37 (0.94–2.00)	1.37 (0.94–2.01)	1.45 (0.97–2.17)
Sex (men)		1.03 (1.01–1.06)	1.03 (1.01–1.06)	1.03 (1.01–1.05)
Hypertension			1.01 (0.74–1.36)	1.01 (0.73–1.38)
Malnutrition				1.02 (0.72–1.44)
At risk of malnutrition				1.00 (0.59–1.70)
BMI				1.03 (0.98-1.08)
CC				0.98 (0.94-1.02)

Data are presented as hazard ratios (95% confidential intervals). Model 1: adjusted for age and sex. Model 2: adjusted for age, sex and hypertension. Model 3: adjusted for age, sex, hypertension, nutrition status, BMI, and CC.
BMI, body mass index; CC, calf circumference.

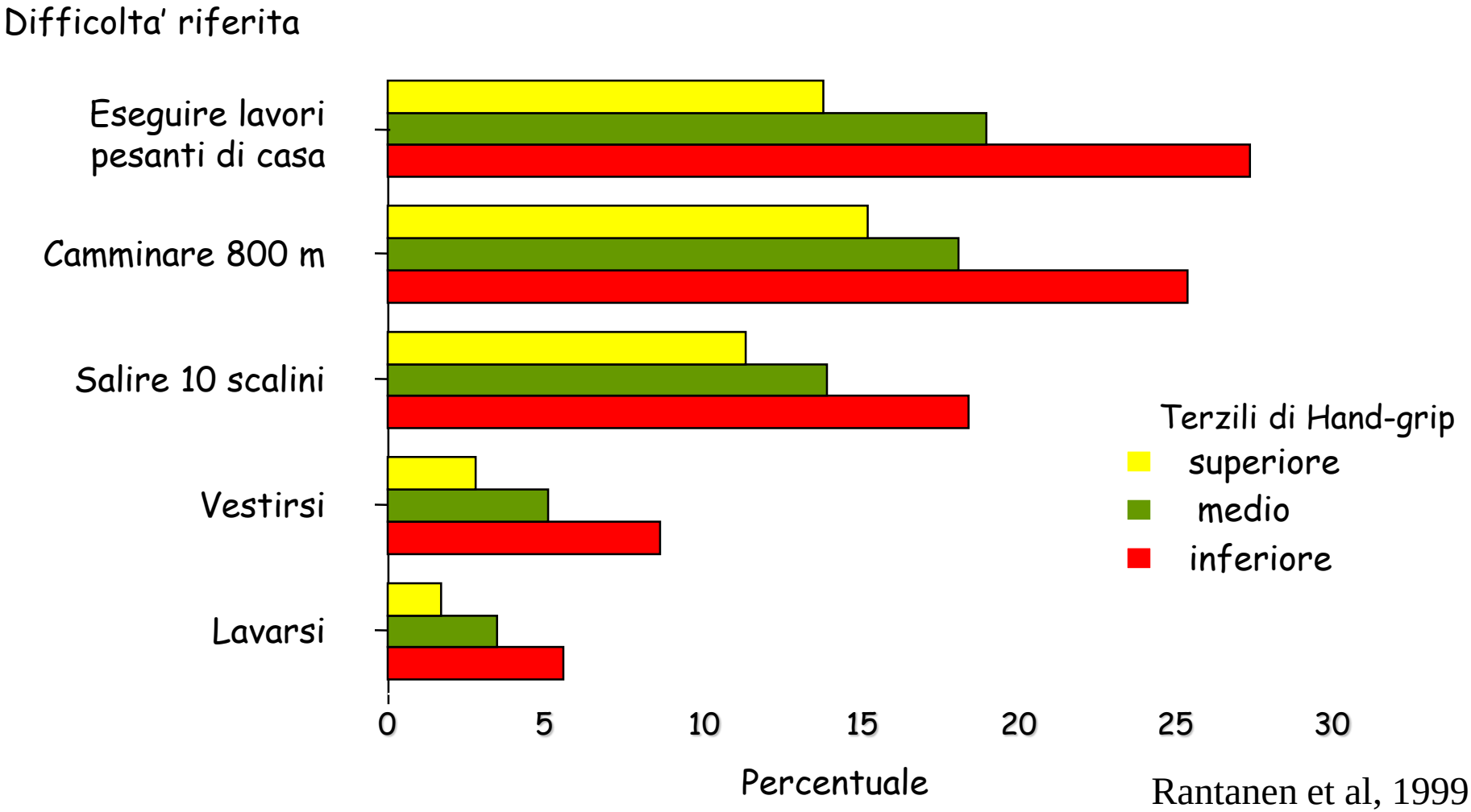
Journal of Cachexia, Sarcopenia and Muscle 2017; 8: 251–258

Stato funzionale e test del cammino dei 6 minuti, in relazione a terzili di forza muscolare della gamba dopo aggiustamento per BMI in 141 donne anziane



Zamboni et al, JAGS 1999

Prevalenza di limitazione funzionale nel 1991-93 in relazione ai terzili di forza muscolare misurata con Hand-grip 25 anni prima (3,218 uomini sani 45-68 anni al basale)



Rantanen et al, 1999

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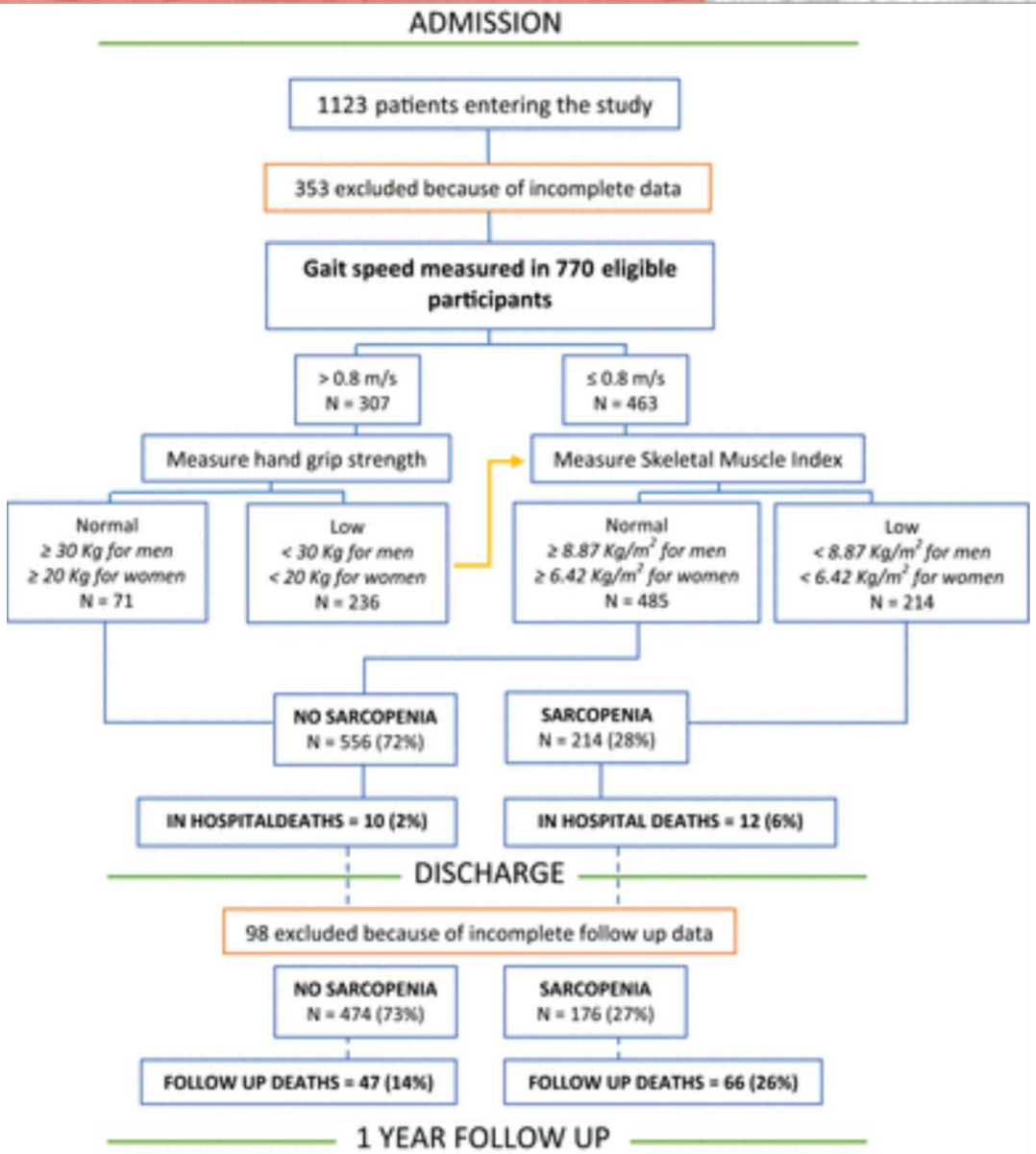

Vetrano J Gerontol A Biol Sci Med Sci. 2014;69(9):1154-1161

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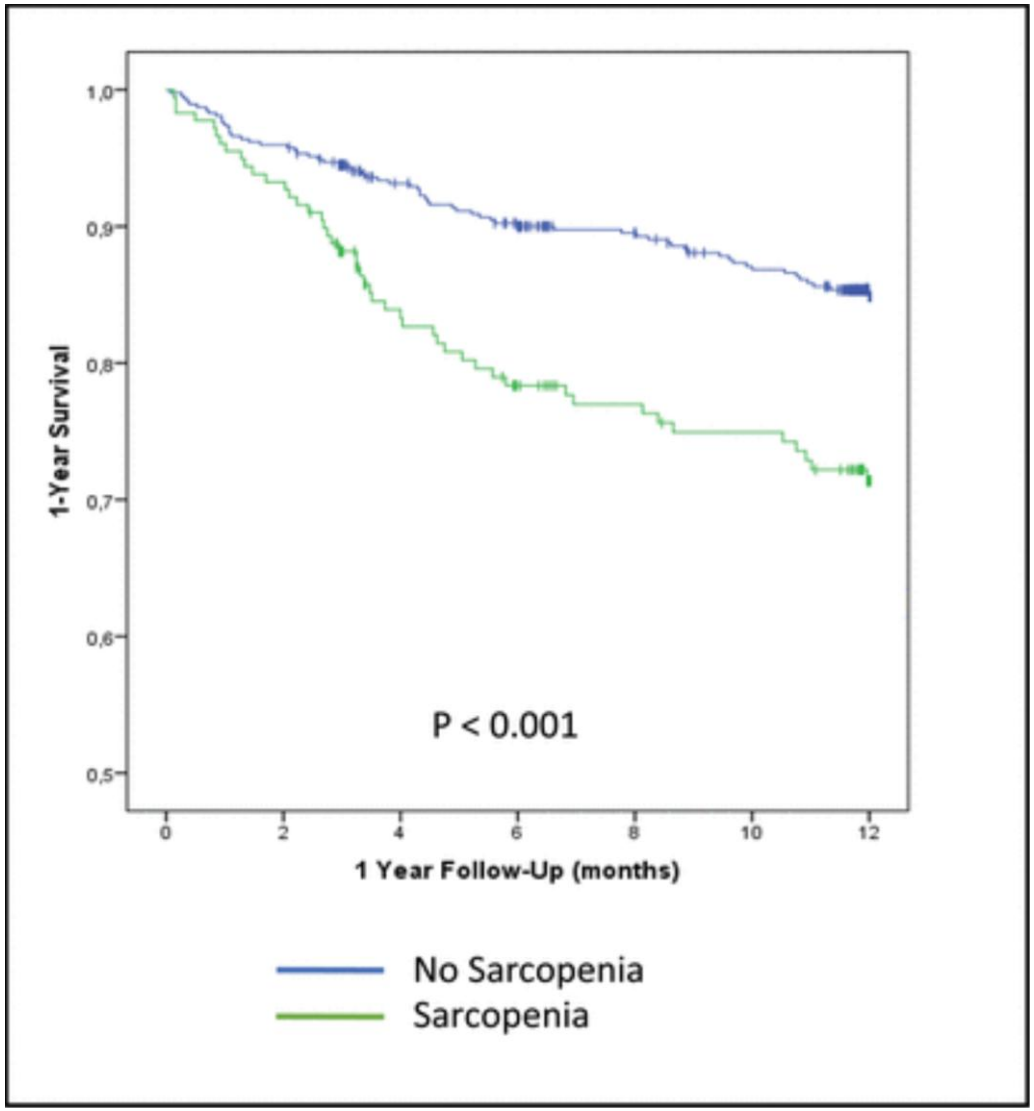
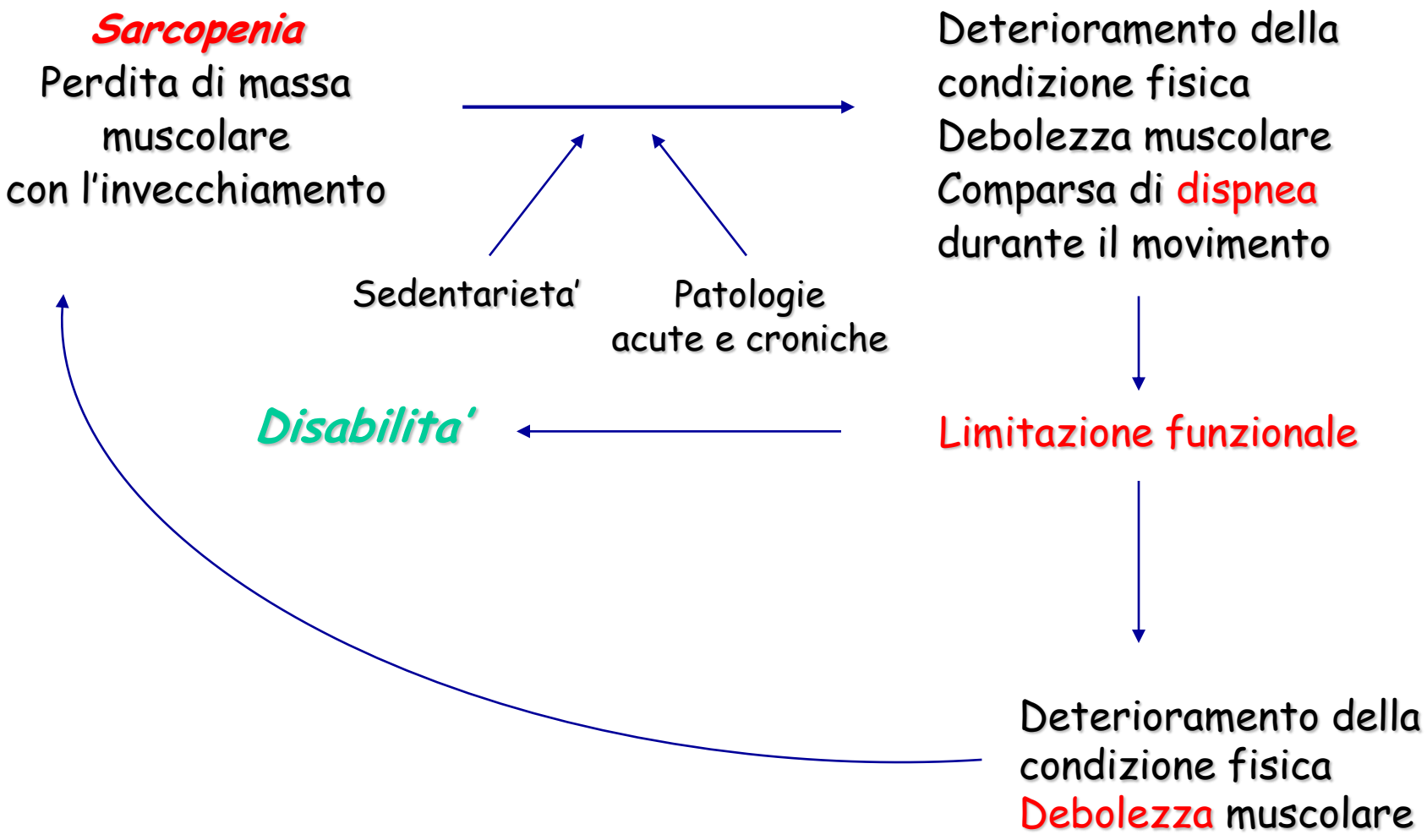


Vetrano J Gerontol A Biol Sci Med Sci. 2014;69(9):1154-1161


Sarcopenia
Perdita di massa muscolare con l'invecchiamento
Deterioramento della condizione fisica
Debolezza muscolare
Comparsa di dispnea durante il movimento
Sedentarieta'
Patologie acute e croniche
Disabilita'
Limitazione funzionale
Deterioramento della condizione fisica
Debolezza muscolare

ICD-10 code: M62.84

Vi ringrazio per l'attenzione

healthy aging center verona

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