

# L'ANZIANO FRAGILE OSPEDALIZZATO E LA BPCO



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*Malattie Respiratorie un Approccio Multidisciplinare*

Milano, 10 Marzo 2018

# ANZIANO FRAGILE

*"... paziente storicamente ignorato dalla medicina tradizionale, in quanto numericamente irrilevante, non gratificante sul piano professionale, perché inguaribile, "scomodo" da gestire da parte delle strutture sanitarie ed assistenziali, anche perché spesso disturbante ..."*

Senin U., 1999

*Quasi tutti i medici sono d'accordo nel dire che l'anziano “fragile” si riconosce ad una prima occhiata anche se quasi nessuno è in grado di fornirne una descrizione adeguata.*

L. Ferrucci et Al  
AIP, 2002; SIGG 2002

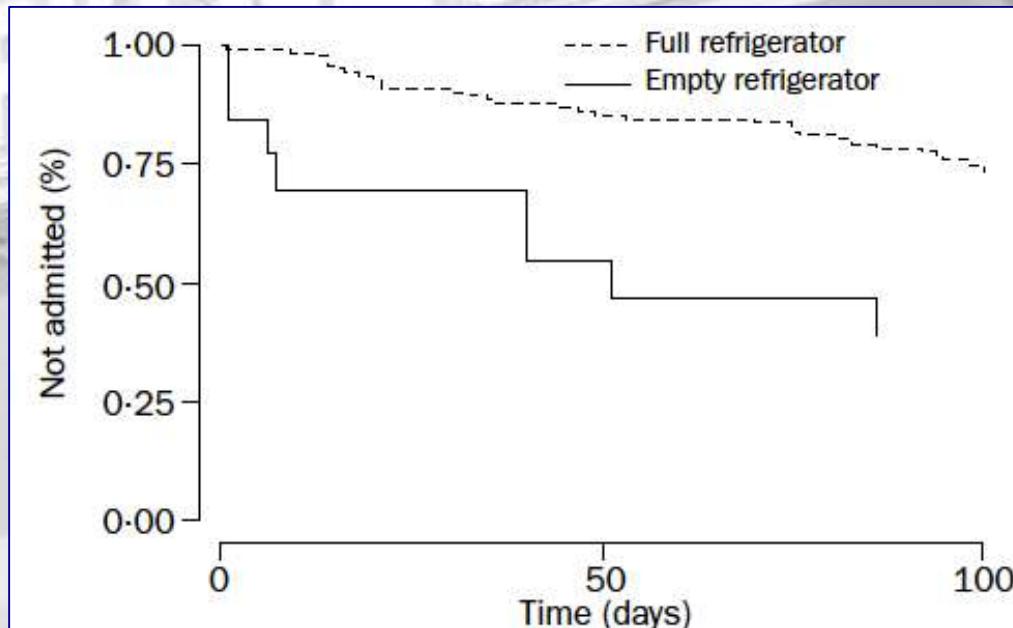
# Refrigerator content and hospital admission in old people

Nadir Boumendjel, François Herrmann, Véronique Girod, Cornel Sieber, Charles-Henri Rapin

We assessed whether the refrigerator contents of elderly people could be related to subsequent admission to hospital.

**132 patients aged over 65 years** had a thorough assessment of their refrigerator contents and the numbers and dates of admission were recorded.

Elderly people with empty refrigerators were **more frequently admitted ( $p=0.032$ )** in the month after assessment and **three times sooner than those who did not have empty refrigerators (34 vs 100 days,  $p=0.002$ ).**



**Kaplan-Meier curves of risk of admission according to refrigerator status**

Log-rank test:  $p=0.006$  at 30 days,  $p=0.812$  at 60 days, and  $p=0.458$  at 90 days.

# Frailty in Older Adults: Evidence for a Phenotype

Linda P. Fried,<sup>1</sup> Catherine M. Tangen,<sup>2</sup> Jeremy Walston,<sup>1</sup> Anne B. Newman,<sup>3</sup> Calvin Hirsch,<sup>4</sup> John Gottdiener,<sup>5</sup> Teresa Seeman,<sup>6</sup> Russell Tracy,<sup>7</sup> Willem J. Kop,<sup>8</sup> Gregory Burke,<sup>9</sup> and Mary Ann McBurnie<sup>2</sup> for the Cardiovascular Health Study Collaborative Research Group

## FRAILTY

*“la fragilità è una sindrome fisiologica caratterizzata dalla riduzione delle riserve funzionali e dalla diminuita resistenza agli stressor, risultante dal declino cumulativo di sistemi fisiologici multipli che causano vulnerabilità e conseguenze avverse ”*

Fried LP, et al. J Gerontol A Biol Sci Med Sci 2001;56A:M146–M156

# CICLO DI INDUZIONE DELLA FRAGILITÀ'

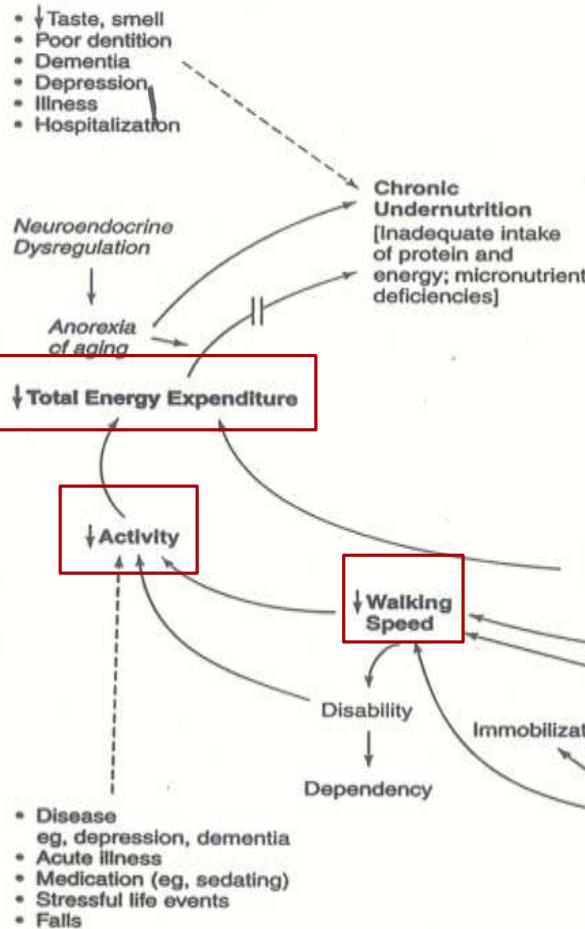
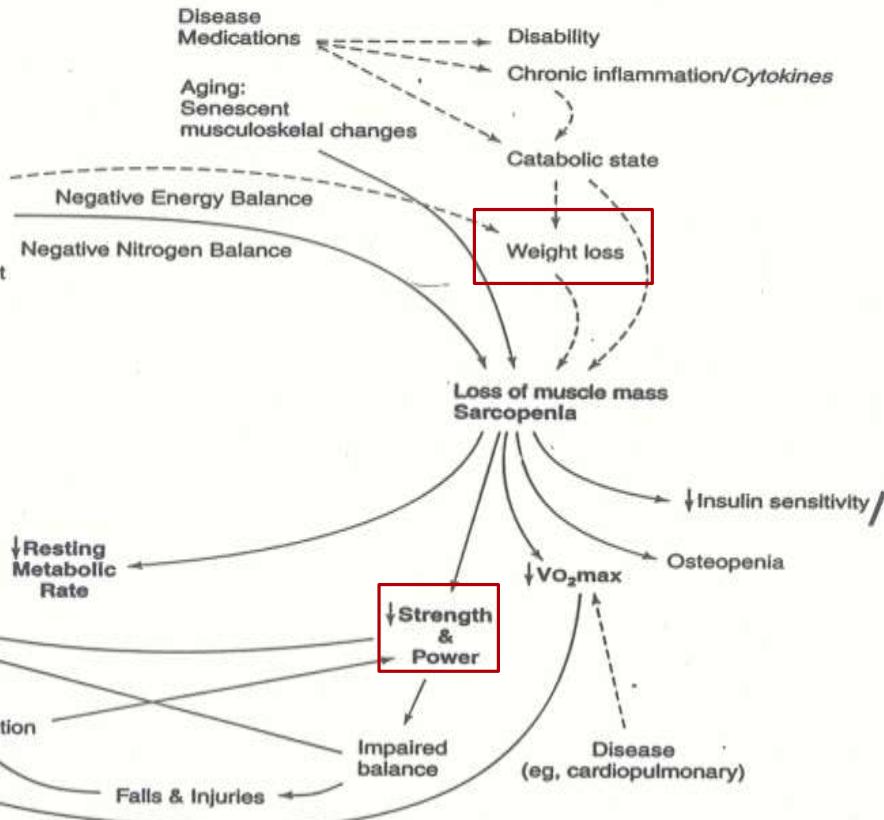


FIGURE 109-5



The cycle of frailty. Key components of frailty that appear to underlie its phenotypic manifestations in a negative cycle are chronic undernutrition; sarcopenia; declines in strength, power, and exercise tolerance; and declines in activity and total energy expenditure. Factors that could precipitate or exacerbate this core cycle are indicated with dashed lines. Factors in which a relationship is hypothesized are indicated in italics.

# MINORE CAPACITA' DI RECUPERO

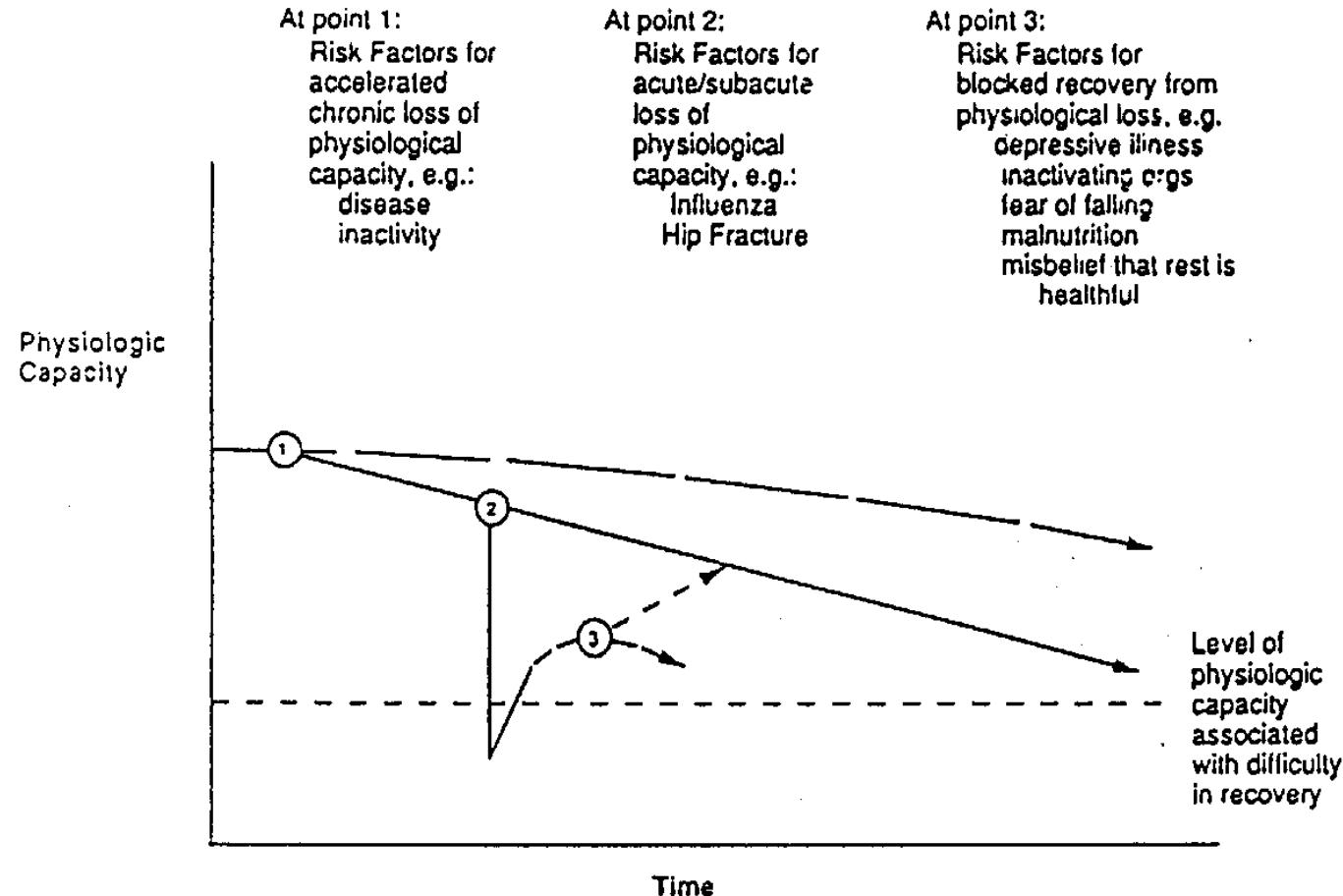


Figure 2. Conceptual model of how risk factors cause frailty.

Buchner and Wagner, 1992

# I PARADIGMI DELLA FRAGILITÀ

Due sono essenzialmente i paradigmi che definiscono la fragilità:

- il **PARADIGMA BIOMEDICO**, secondo il quale la fragilità è una sindrome fisiologica caratterizzata dalla riduzione delle riserve funzionali e dalla diminuita resistenza agli stressor, risultante dal declino cumulativo di sistemi fisiologici multipli che causano vulnerabilità e conseguenze avverse (Fried 2004);
- il **PARADIGMA BIO-PSICO-SOCIALE**, secondo il quale la fragilità è uno stato dinamico che colpisce un individuo che sperimenta perdite in uno o più domini funzionali (fisico, psichico, sociale), causate dall'influenza di più variabili che aumentano il rischio di risultati avversi per la salute (Gobbens 2010).

# FATTORI DI RISCHIO

- Età avanzata
- Stato sociale: dipendenza o necessità di caregivers
- Stato cognitivo: deterioramento, demenza o depressione
- Declino funzionale, disabilità fisica e necessità di aiuto nelle ADL/IADL
- Malnutrizione
- Frequenti cadute e traumi (frattura di femore)
- Stato infiammatorio e disendocrino
- Malattie croniche
- Polifarmacoterapia
- Istituzionalizzazione o ospedalizzazione

# FRAILTY AND ADVERSE OUTCOMES



## Frailty in elderly people

Andrew Clegg, John Young, Steve Iliffe, Marcel Olde Rikkert, Kenneth Rockwood

Year	Country	Participants (n)	Length of follow-up (years)	Falls (HR* / OR† [95% CI])		Worsening disability (HR* / OR† [95% CI])		Hospitalisation (HR* / OR† [95% CI])		Care home admission (HR* / OR† [95% CI])		Mortality (HR* / OR† [95% CI])		
				Inter- mediate frailty	Severe frailty	Inter- mediate frailty	Severe frailty	Inter- mediate frailty	Severe frailty	Inter- mediate frailty	Severe frailty	Inter- mediate frailty	Severe frailty	
Cardiovascular Health Study (CHS) <sup>3</sup>	2001	USA	5317	7	1.12* (1.00–1.26)	1.23* (0.99–1.54)	1.55* (1.38–1.75)	1.79* (1.47–2.17)	1.11* (1.03–1.19)	1.27*, (1.11–1.46)	NA	NA	1.32* (1.13–1.55)	1.63* (1.27–2.08)
Canadian Study of Health and Aging (CSHA) <sup>32</sup>	2004	Canada	9008	5	NA	NA	NA	NA	NA	NA	2.54† (1.67–3.86)	2.60† (1.36–4.96)	2.54† (1.92–3.37)	3.69† (2.26–6.02)
Women's Health and Aging Study (WHAS) <sup>33</sup>	2006	USA	1438	3	0.92* (0.63–1.64)	1.18* (0.63–2.19)	NA	NA	0.99* (0.67–1.47)	0.67* (0.33–1.35)	5.16* (0.81–32.79)	23.98* (4.45–129.2)	3.50* (1.91–6.39)	6.03* (3.00–12.08)
Study of Osteoporotic Fractures (SOF) <sup>34</sup>	2008	USA	6701	4.5	1.23† (1.02–1.48)	2.44† (1.95–3.04)	1.89†, (1.66–2.14)	2.79† (2.31–3.37)	NA	NA	NA	NA	1.54† (1.40–1.69)	2.75* (2.46–3.07)

HR=hazard ratio. NA=not available. OR=odds ratio. \*Hazard ratio. †Odds ratio. The comparator for hazard ratios and odds ratios is people who are not frail.

Table: Covariate-adjusted associations between frailty and adverse outcomes (falls, disability, hospitalisation, care home admission, and mortality) from four large prospective cohort studies

Review

## Frailty assessment instruments: Systematic characterization of the uses and contexts of highly-cited instruments

Brian J. Buta <sup>a,b</sup>, Jeremy D. Walston <sup>a,b</sup>, Job G. Godino <sup>c,d</sup>, Minsun Park <sup>d</sup>, Rita R. Kalyani <sup>a,b</sup>, Qian-Li Xue <sup>a,b</sup>, Karen Bandeen-Roche <sup>a,d</sup>, Ravi Varadhan <sup>a,b,e,\*</sup>

- A total of **67 frailty instruments** available in the literature
- **Nine instruments** are "highly-cited" ( $\geq 200$  citations)
- The most common assessment context was **observational studies of older community-dwelling adults.**

# THE FRAILTY PHENOTYPE

Table 1. Operationalizing a Phenotype of Frailty

A. Characteristics of Frailty	B. Cardiovascular Health Study Measure*
Shrinking: Weight loss (unintentional)	Baseline: >10 lbs lost unintentionally in prior year
Sarcopenia (loss of muscle mass)	
Weakness	Grip strength: lowest 20% (by gender, body mass index)
Poor endurance; Exhaustion	"Exhaustion" (self-report)
Slowness	Walking time/15 feet: slowest 20% (by gender, height)
Low activity	Kcals/week: lowest 20% males: <383 Kcals/week females: <270 Kcals/week
C. Presence of Frailty	
	Positive for frailty phenotype: $\geq 3$ criteria present
	Intermediate or prefrail: 1 or 2 criteria present

\*See Appendix.

## CRITERI DI FRAGILITÀ'

(Fried et al, 2001)

- **Perdita di peso involontaria**
- **Bassa velocità del passo**
- **Scarsi livelli di attività fisica**
- **Facile affaticabilità**
- **Debolezza muscolare (low grip strength)**
  - *3-5: Fragile*
  - *1-2: Intermedio ( "pre-fragile" )*
  - *0: Non fragile*

# Accumulation of Deficits as a Proxy Measure of Aging

Arnold B. Mitnitski<sup>1,2</sup>, Alexander J. Mogilner, and Kenneth Rockwood<sup>2,\*</sup>

<sup>1</sup>*Department of Mechanical Engineering, Ecole Polytechnique, Montreal P.O. Box 6079, Station Centre-ville Montreal, Quebec H3C 3A7;* <sup>2</sup>*Queen Elizabeth II, Health Sciences Centre, Geriatric Medicine Research Unit, Room 1421, 5955 Veterans' Memorial Lane, Halifax, Nova Scotia B3H 2E1*

“...a method for appraising health status in elderly people.

**A frailty index was defined as the proportion of accumulated deficits (symptoms, signs, functional impairments, and laboratory abnormalities). It serves as an individual state variable, reflecting severity of illness and proximity to death...”**

## 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 problems
- Poor muscle tone in neck
- Bradykinesia, facial
- Problems getting dressed
- Problems with bathing
- Problems carrying out personal grooming
- Urinary incontinence
- Toileting problems
- Bulk difficulties
- Rectal problems
- Gastrointestinal problems
- Problems cooking
- Sucking problems
- Problems going to the toilet
- Impaired mobility
- Musculoskeletal problems
- Bradykinesia of the limbs
- Poor muscle tone in limbs
- Poor limb coordination
- Poor coordination, trunk
- Poor standing posture
- Irregular gait pattern
- Falls

- Mood problems
- Feeling sad, blue, depressed
- History of depressed mood
- Tiredness all the time
- Depression (clinical impression)
- Sleep changes
- Restlessness
- Memory changes
- Short-term memory impairment
- Long-term memory impairment
- Changes in general mental functioning
- Onset of cognitive symptoms
- Clouding or delirium
- Paranoid features
- History relevant to cognitive impairment or loss
- Family history relevant to cognitive impairment or loss
- Impaired vibration
- Tremor at rest
- Postural tremor
- Intention tremor
- History of Parkinson's disease
- Family history of degenerative disease

- Seizures, partial complex
- Seizures, generalized
- Syncope or blackouts
- Headache
- Cerebrovascular problems
- History of stroke
- History of diabetes mellitus
- Arterial hypertension
- Peripheral pulses
- Cardiac problems
- Myocardial infarction
- Arrhythmia
- Congestive heart failure
- Lung problems
- Respiratory problems
- History of thyroid disease
- Thyroid problems
- Skin problems
- Malignant disease
- Breast problems
- Abdominal problems
- Presence of snout reflex
- Presence of the palromental reflex
- Other medical history

**NUMBER OF DEFICITS PRESENT**

**NUMBER OF DEFICITS CONSIDERED**

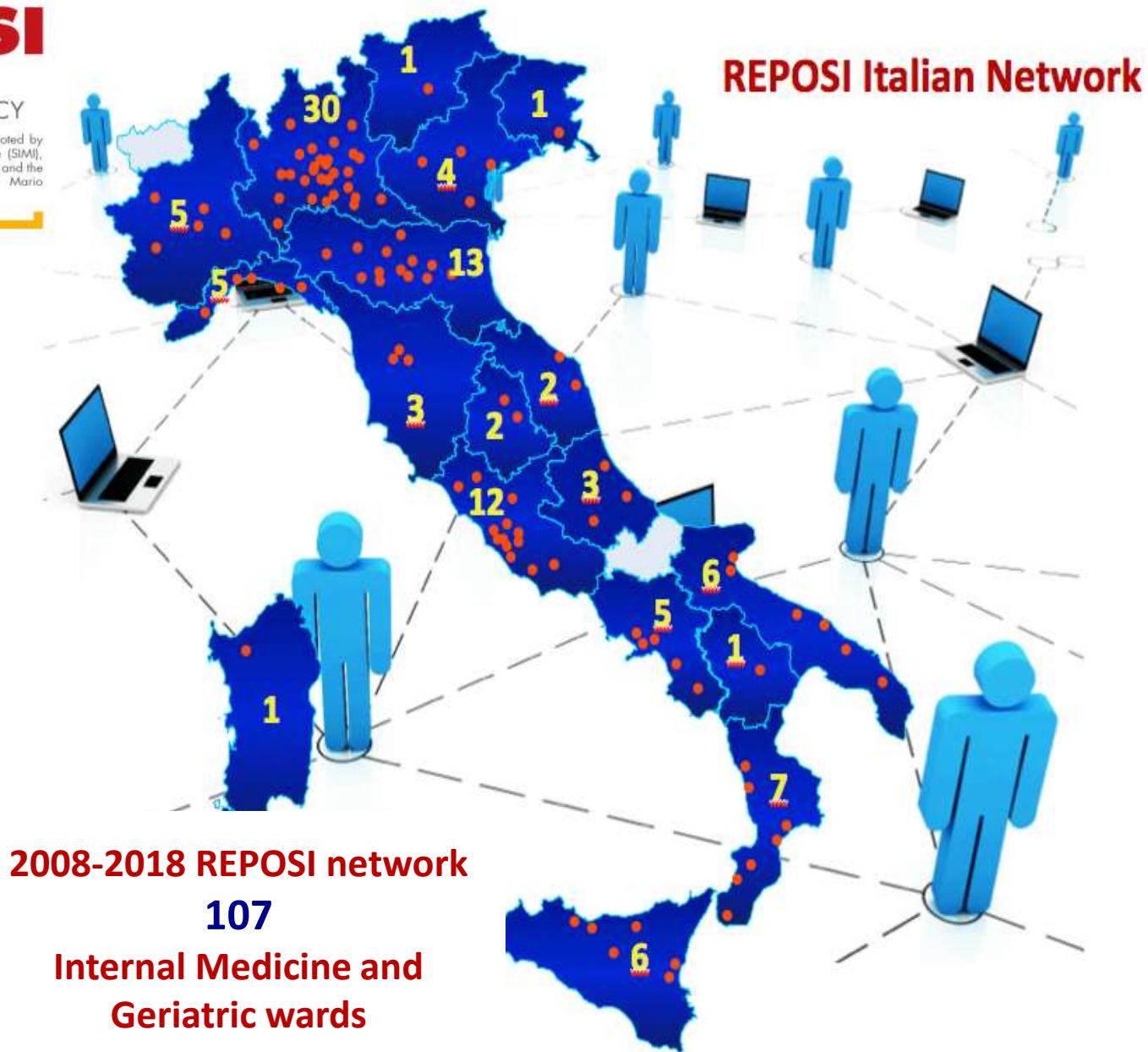


# REPOSI

REGISTER OF  
MULTIMORBIDITY  
AND POLYPHARMACY

**REPOSI** is a collaborative study promoted by the Italian Society of Internal Medicine (SIMI), IRCCS Ca' Granda Foundation Hospital and the Institute of Pharmacological Research Mario Negri of Milan, Italy.

*From 2008  
7,014 patients aged 65  
years or older by 107  
Italian and 15 Spanish  
(only in 2014-2015 )  
internal medicine and  
geriatric wards and  
more than 300 clinical  
investigators*





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## Starting 2008:

- Pre-hospital
- In-hospital

## From 2010

- 2010: 3-months follow-up
- 2012: 12-months follow-up

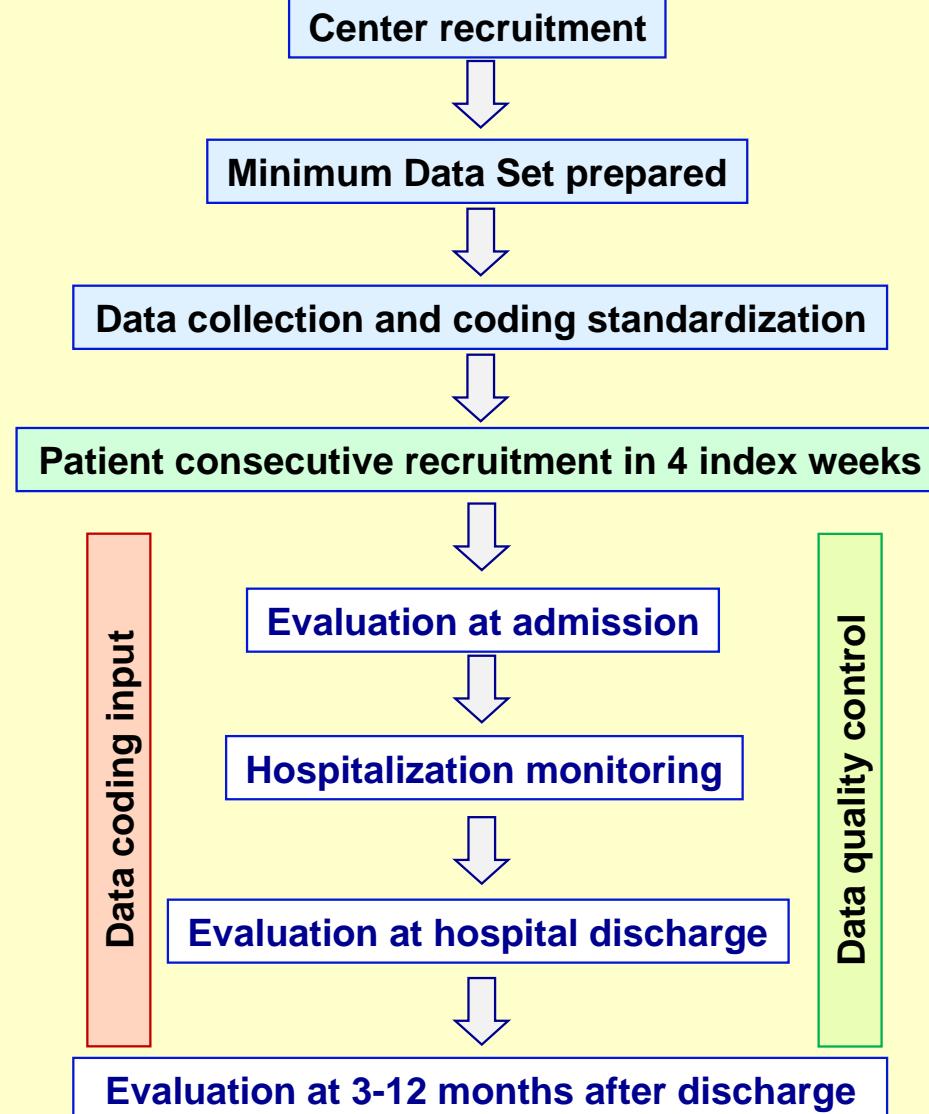
## From 2014

- REPOSI Spanish Network

## Main outcomes

- mortality (in-hospital, 3-12 months);
- re-hospitalization;
- changes in multimorbidity and polypharmacy (at admission, at discharge and at 3-12 months).

## REPOSI FLOW CHART



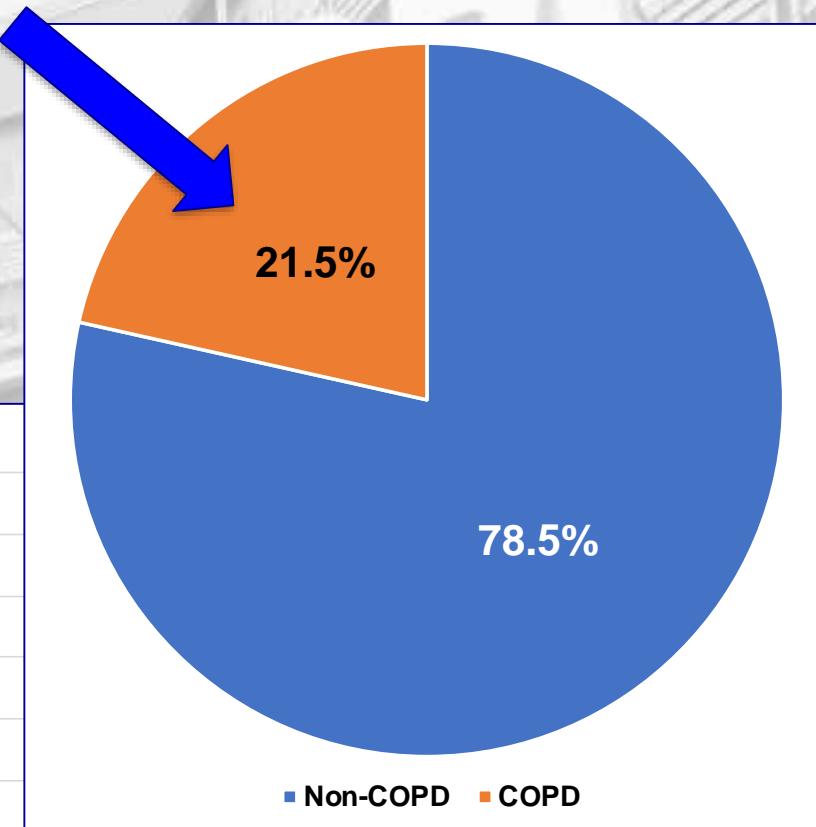
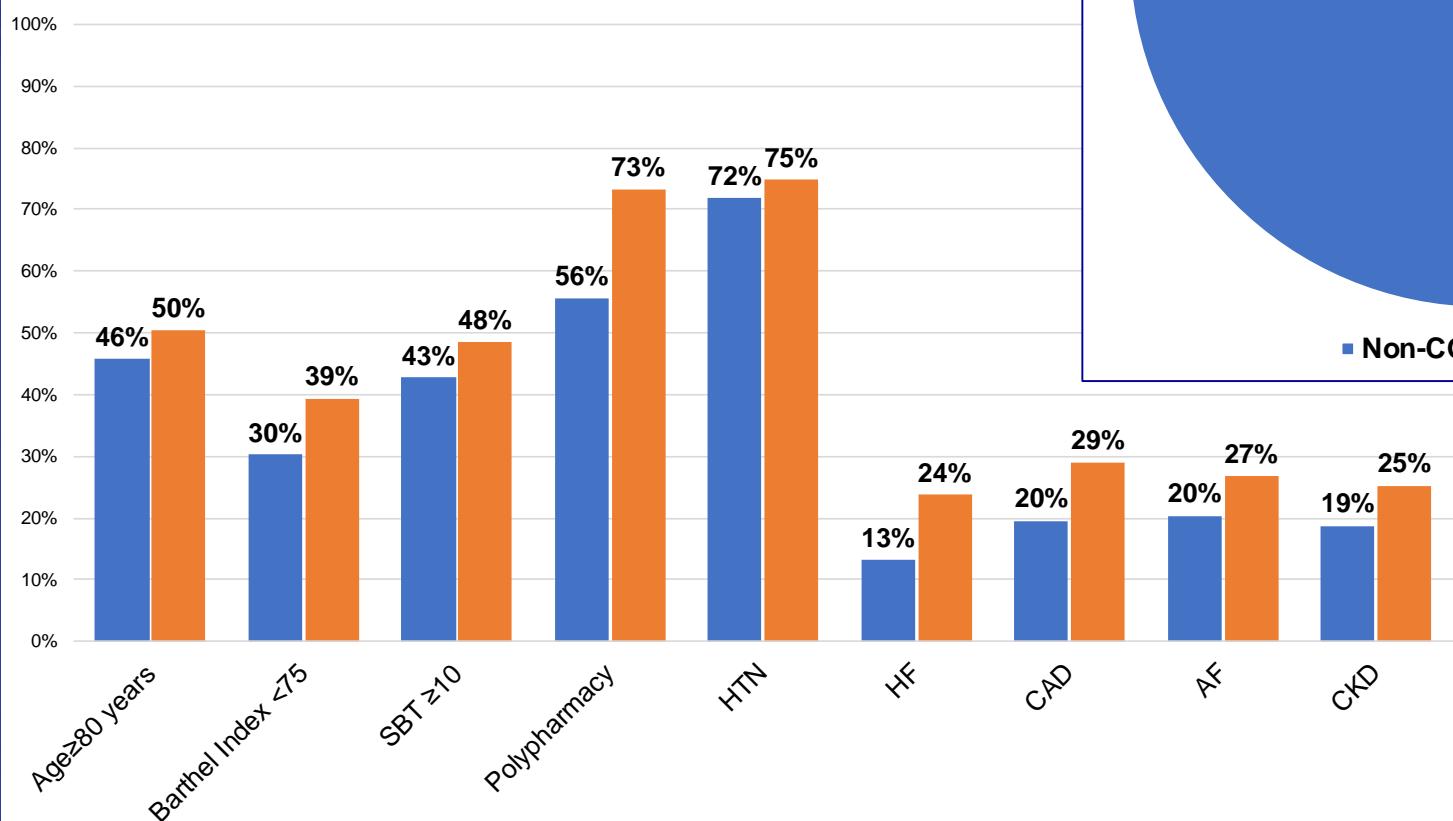
# COPD POPULATION IN THE REPOSI REGISTRY

UOMINI: 61.43%

DONNE: 38,57%

ETA' MEDIA: 80,03 (79.48 - 80.58)

■ Non-COPD ■ COPD

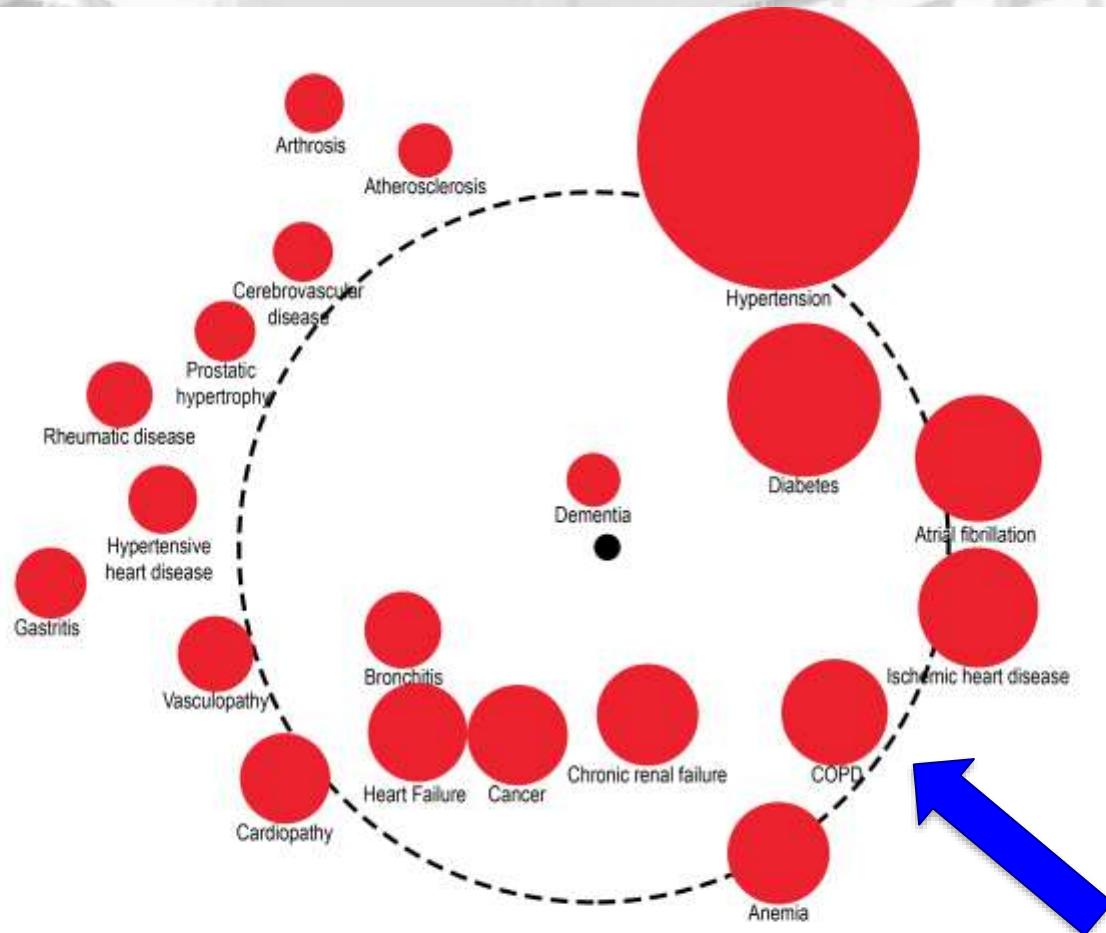


# COPD AND CLINICAL OUTCOMES

## COPD vs. Non-COPD

	Multivariate		
	OR	95% CI	p
Any Death	1.33	0.98-1.81	0.071
CV Death	1.66	1.04-2.67	0.034
Respiratory Death	2.14	1.00-4.59	0.051
Hospitalization	1.50	1.08-2.09	0.016
Hospitalization/Respiratory Death	1.60	1.17-2.18	0.003
Hospitalization/Any Death	1.51	1.17-1.95	0.001

# COMORBIDOMA IN-HOSPITAL MORTALITY



# REPOSI FRAILTY INDEX

## Frailty models:

1. **Phenotype model:** defined by L. Fried as unintentional weight loss, exhaustion, low energy expenditure, slow gait speed and weak grip strength
2. **Cumulative deficit model:** Rockwood frailty index that consist in a cumulative sum of deficits (symptoms, signs, disabilities, and laboratory abnormalities)

## AIM OF THE STUDY

To develop a frailty index for hospitalized older patients and test its association with in-hospital mortality rate in the REPOSI register enrolled patients

Most of the existing frailty tools have been developed and validated in the frame of community-dwelling older adults

Fried et al., 2001; J Gerontol A Biol Sci Med Sci (3):M146-56;  
Rockwood K et al. CMAJ 2005;173:489-95

# REPOSI FRAILTY INDEX

- 65 years or older patients
- Hospitalized in Italian REPOSI wards from 2010 to 2016
- Length of hospital stay  $\geq 5$  days

REPOSI REGISTER  
2010 – 2016:  
**4715 patients**  
in 116 wards

**4488**  
Patients  
enrolled in Italy

**3847**  
Patients  
included in the  
study

Excluded:  
227 patients  
enrolled in Spain

Excluded:  
641 patients with  
 $\leq 5$  days of  
hospital stay

# REPOSI FRAILTY INDEX

**FRAILTY INDEX:** The number of deficits that an individual has  
The total number of deficits considered

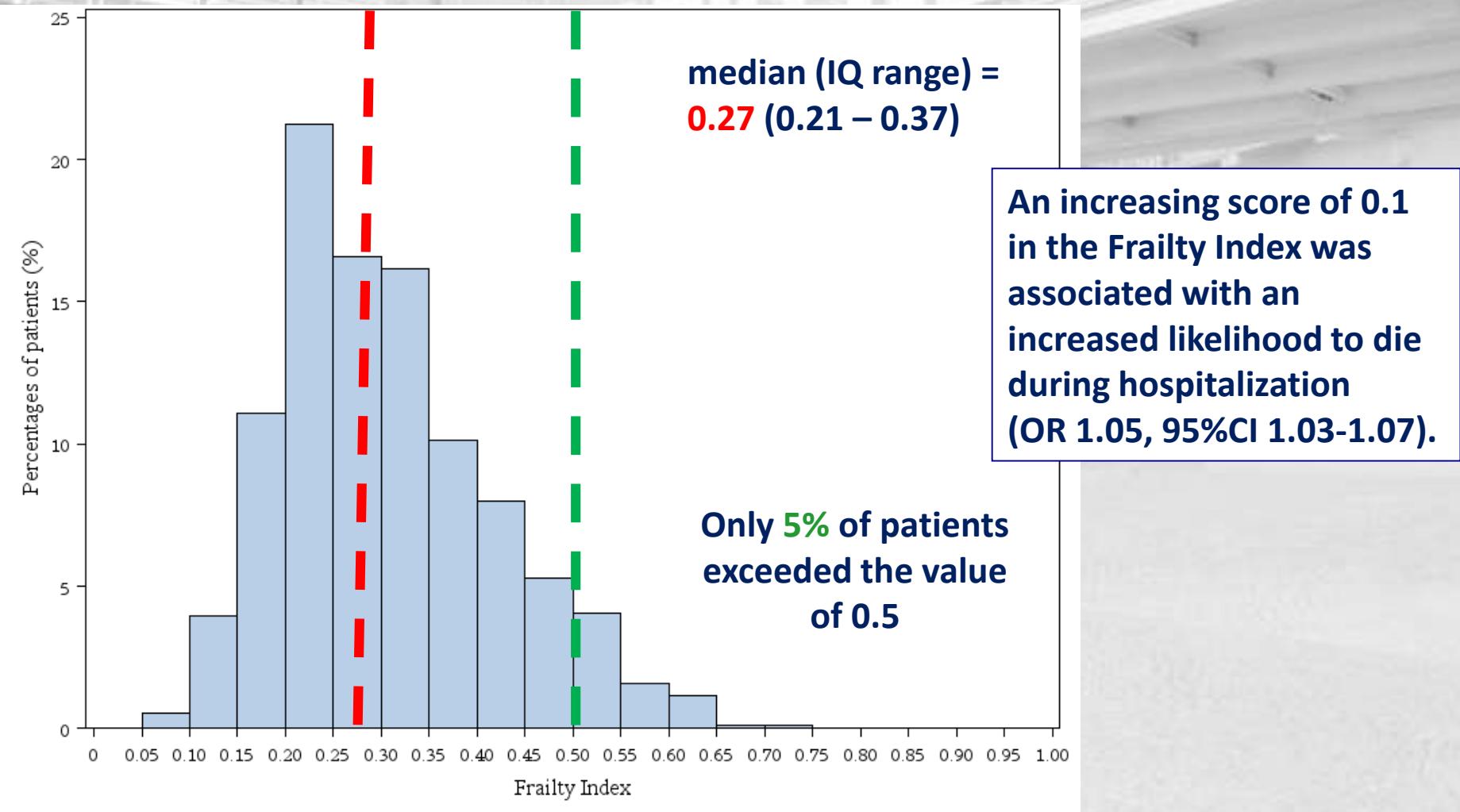
For example, if  $\frac{10}{34} = 0.29$  Individual's Frailty Index

# REPOSI FRAILTY INDEX

Variable/Deficit	Cut Point	Score			
BMI	< 21 Kg/m <sup>2</sup>	1	Hypertension (Severity)	Yes (≥ 3)	1
	≥ 21 Kg/m <sup>2</sup>	0		Yes (2)	0.5
BI - Hygiene (Grooming)	0 - 1	1		No	0
	3 - 4	0.5		Yes	1
	5	0	Diabetes	No	0
BI - Bathing	0 - 1	1	Kidney diseases	Yes	1
	3 - 4	0.5		No	0
	5	0		Yes	1
BI - Eating	0 - 2	1	Respiratory disease	No	0
	5 - 8	0.5		Yes	1
	10	0	Heart failure	No	0
BI - Using Toilet	0 - 2	1	Ischaemic heart disease	Yes	1
	5 - 8	0.5		No	0
	10	0		Yes	1
BI - Climbing (up and down)	0 - 2	1	Tumours	No	0
	5 - 8	0.5		Yes	1
	10	0		No	0
BI - Dressing	0 - 2	1	Tyroid disorders	Yes	1
	5 - 8	0.5		No	0
	10	0	Stroke/TIA/cerebrovascular	Yes	1
BI - Fecal Incontinence	0 - 2	1		No	0
	5 - 8	0.5		Yes	1
	10	0	Upper gastrointestinal	No	0
BI - Urinary Incontinence	0 - 2	1	Lower gastrointestinal	Yes	1
	5 - 8	0.5		No	0
	10	0		Yes	1
BI - Mobility Impairment	0 - 3/0 - 1 - 3 [WheelChair]	1	Liver diseases	No	0
	8 - 12/ 4 - 5 [WheelChair]	0.5		Yes	1
	15	0	Skeletal muscle diseases	No	0
BI - Transferring	0 - 3	1		Yes	1
	8 - 12	0.5		No	0
	15	0	Psychiatric disease	Yes	1
Short Blessed Test (SBT)	20 - 28	1		No	0
	10 - 19	0.7	Neurologic	Yes	1
	5-9	0.3		No	0
	0-4	0	Dyslipidemias	Yes	1
Anemia (Hb)	< 11 g/dL	1		No	0
	≥ 11 g/dL	0	Depression	Yes	1
Platelet Count	< 100 or ≥ 320 [F] < 150 or ≥ 250	1		No	0
	≥ 100 & < 320 [F] ≥ 150 & < 250	0	Anxiety	Yes	1
White Blood Cells	< 4000 or > 10000 10 <sup>3</sup> /µL	1		No	0
	≥ 4000 & ≤ 10000 10 <sup>3</sup> /µL	0	Total	34 Deficits	
Clearance	< 30 g/dL	1			
	≥ 30 g/dL	0			

# REPOSI FRAILTY INDEX

The frailty index was initially calculated on the complete case of 3200 (83.2%) patients.



# REPOSI FRAILTY INDEX\* IN PATIENTS WITH COPD vs NO COPD

Variables	COPD (N=601)	No COPD (N=2599)
Frailty Index (mean $\pm$ SD)	<b>0.34 (0.13)</b>	0.29 (0.12)
Frailty Index $\leq$ 25	<b>28.1</b>	46.1
Frailty Index >25	<b>71.9</b>	53.9

\*At hospital admission

# PATIENTS WITH COPD

## Frailty vs No Frailty

Variables	Frailty (FI $\geq 25$ )	No Frailty (FI $< 0.25$ )
Age (mean $\pm$ SD)	<b>80.1 (6.8)</b>	77.5 (7.0)
Sex		
- Male	<b>61.3%</b>	65.1%
- Female	<b>38.7%</b>	34.9%
Barthel Index*		
- 91-100	<b>27.1%</b>	85.8%
- 75-90	<b>26.9%</b>	13.0%
- <75	<b>46.0%</b>	1.2%
Short Blessed Test*		
- Normal	<b>31.0%</b>	44.4%
- Possible cognitive impairment	<b>14.8%</b>	22.5%
- Moderate cognitive impairment	<b>37.7%</b>	29.0%
- Severe cognitive impairment	<b>16.5%</b>	4.1%

\*At hospital admission

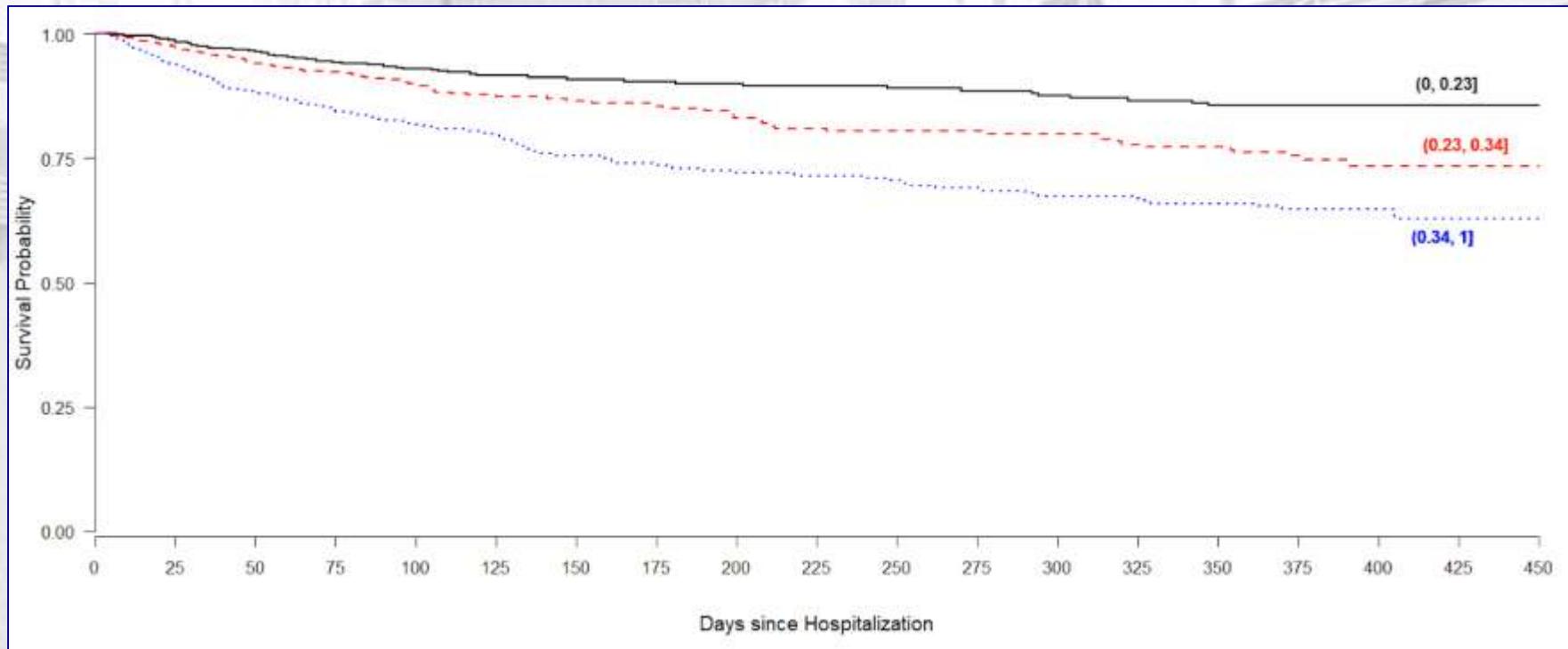
# COMORBIDITY\* IN PATIENTS WITH COPD

## Frailty vs No Frailty

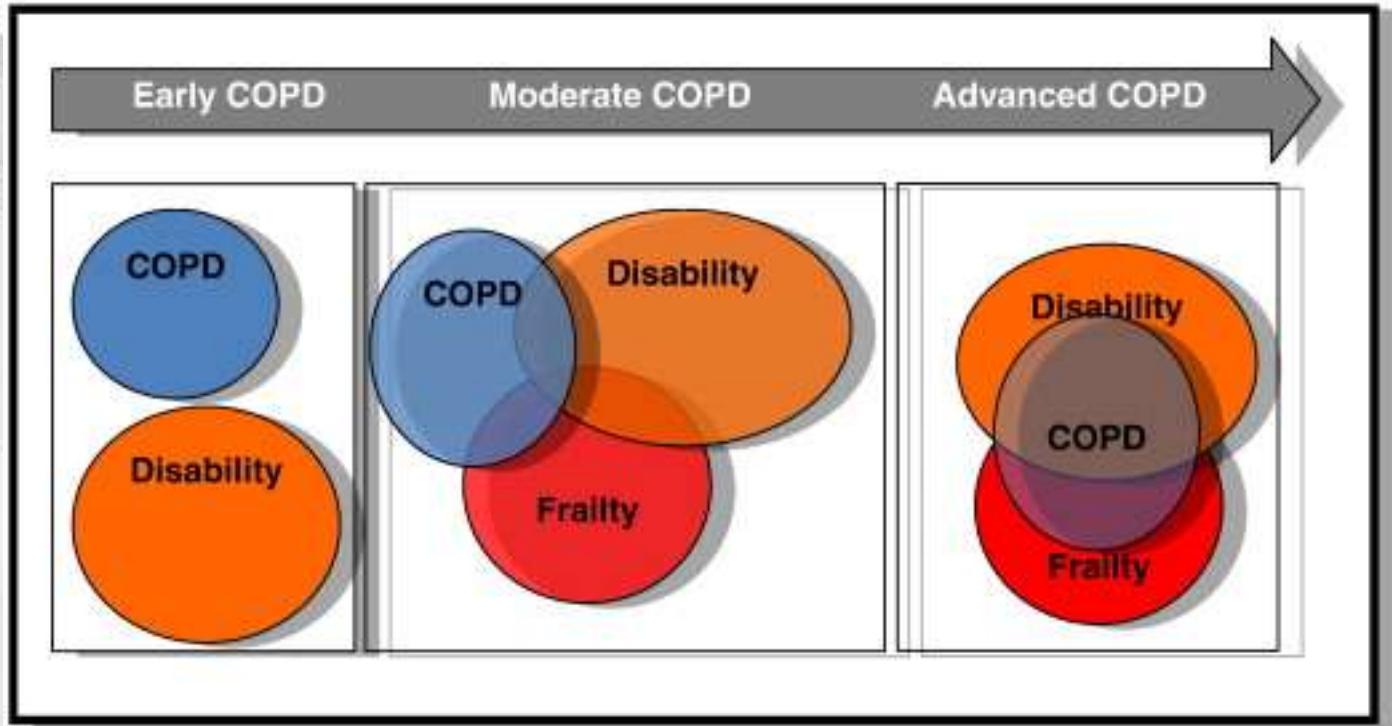
Variables	Frailty (FI $\geq 25$ )	No Frailty (FI < 0.25)
Diabetes	41.0%	21.9%
Ischemic Heart Disease	40.2%	14.2%
Heart Failure	32.2%	8.9%
Cerebrovascular Diseases	25.5%	7.7%
Neurologic Disorders	28.9%	8.9%
Psychiatric Disorders	22.0%	7.7%
Depression	15.7%	3.5%
Chronic Kidney Disease	38.2%	13.6%
Musculoskeletal Diseases	32.9%	17.8%

\*At hospital admission

## Kaplan and Meier survival curves according to 33<sup>rd</sup> and 67<sup>th</sup> percentiles of the frailty index



The frailty index was associated with in-hospital mortality (Odds Ratio [OR] 1.605; 95% CI: 1.375 – 1.873 for each 0.1 FI increment), when adjusting for age and gender. The frailty index was also associated with overall mortality (HR = 1.46, 95% CI: 1.32 – 1.62).



# COSA FARE?

- Il punto critico dell' assistenza ai pazienti fragili è lo **straordinario numero di variabili** che intervengono a **determinare l' aumento della vulnerabilità individuale, interagenti** tra loro con **effetti spesso imprevedibili**.
- La sua **prevenzione**, allo stato attuale, consiste nello **stabilizzare il sistema stesso nel suo insieme**.
- La semplice **correzione di uno dei fattori** implicati nel fenomeno fragilità **può non essere sufficiente** per correggere il fenomeno.
- **L'attività fisica** aumenta la forza, la massa muscolare, abbassa la pressione sanguigna, migliora la sensibilità all'insulina e la tolleranza al glucosio, può modulare i fattori responsabili dell'infiammazione, alcune funzioni ormonali e la funzione mitocondriale.
- Quindi, se si volesse scegliere un' intervento per stabilizzare i diversi sistemi coinvolti nella fragilità, **l'attività fisica potrebbe costituire un buon modello**.



*Linda P. Fried, epidemiologist and geriatrician at Columbia University*

# FOCUS

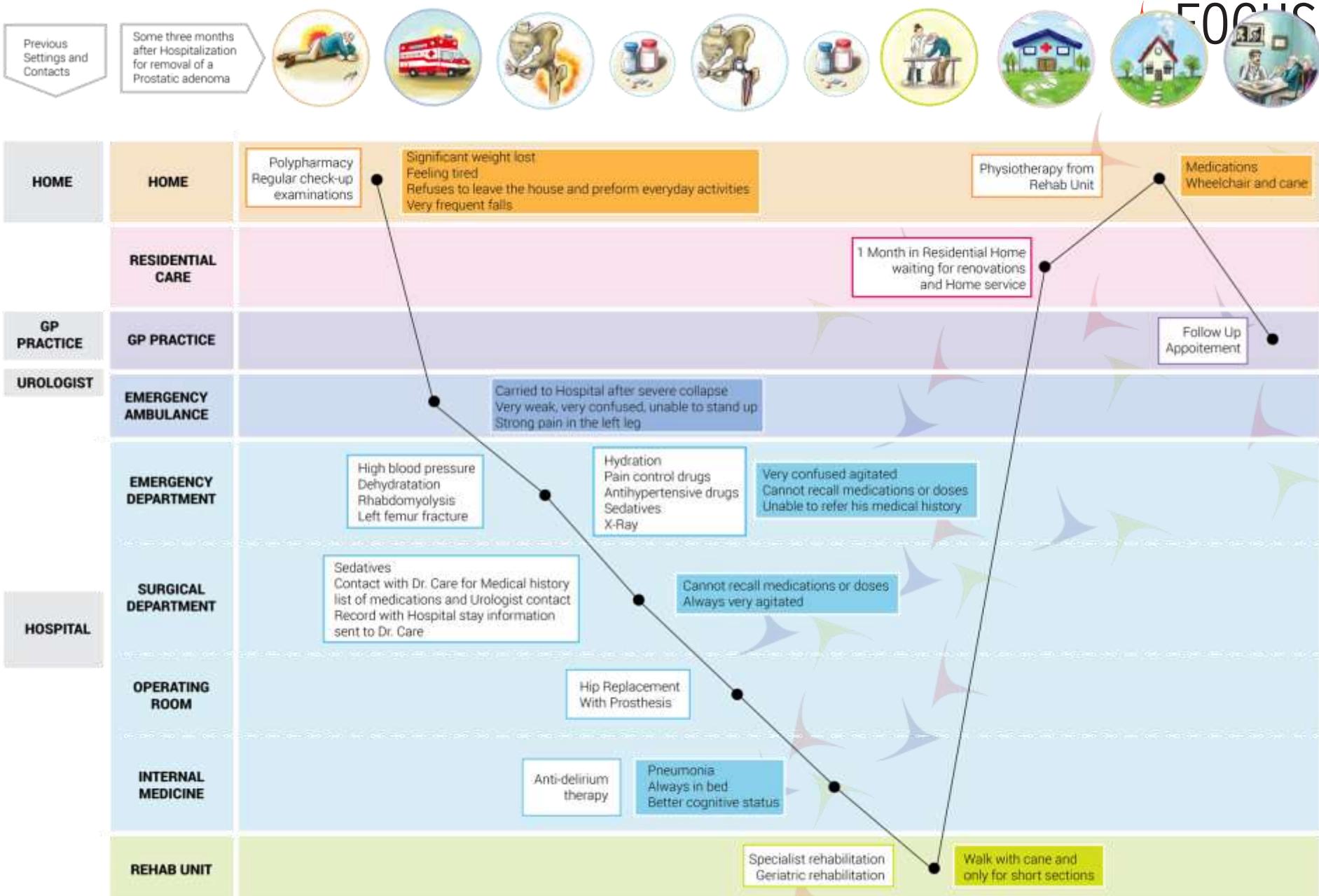
<http://focus-aha.eu/about>

## Interventions reducing frailty / postponing its progress

- Exercise programs delivered in group with (GRADE B) or without (GRADE A) home-based practice
- Nutritional supplementation (GRADE A)
- Exercise and nutritional supplementation (GRADE B)
- Combined treatment (GRADE B)
- Cognitive training (GRADE B)



Frailty management  
Optimisation through EIP  
AHA Commitments and  
Utilisation of  
Stakeholders input



# QUALE APPROCCIO?

**Table 4.3. Conventional care versus older-person-centred and integrated care**

Conventional care	Older-person-centred and integrated care
Focuses on a health condition (or conditions)	Focuses on people and their goals
Goal is disease management or cure	Goal is maximizing intrinsic capacity
Older person is regarded as a passive recipient of care	Older person is an active participant in care planning and self-management
Care is fragmented across conditions, health workers, settings and life course	Care is integrated across conditions, health workers, settings and life course
Links with health care and long-term care are limited or non-existent	Links with health care and long-term care exist and are strong
Ageing is considered to be a pathological state	Ageing is considered to be a normal and valued part of the life course

# Grazie per l'attenzione .



Aiutando  
la Ricerca  
**Aiuti la Vita**



Sostieni l'Istituto con il tuo **5 per mille**

Dal 1961 il Mario Negri, con oltre 11.000 ricerche a livello internazionale, ha dato il suo prezioso contributo alla lotta contro:

- tumori e dolore
- malattie neurodegenerative
- patologie cardiovascolari e renali
- rigetto dei trapianti d'organo
- malattie pediatriche
- malattie rare
- dipendenza dalle droghe
- inquinamento ambientale

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Finanziamento della ricerca scientifica  
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*Insanity: doing the same thing over and over again and expecting different results.*

Albert Einstein

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