La valutazione del paziente complesso/fragile

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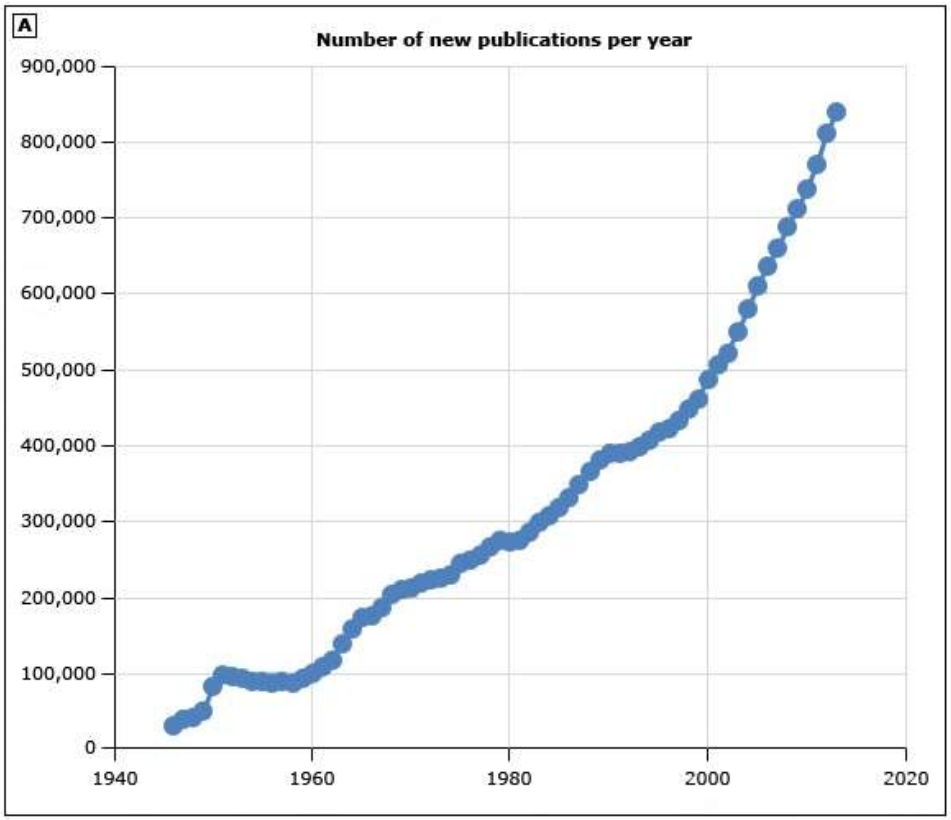
Complessità ≠ Complicato

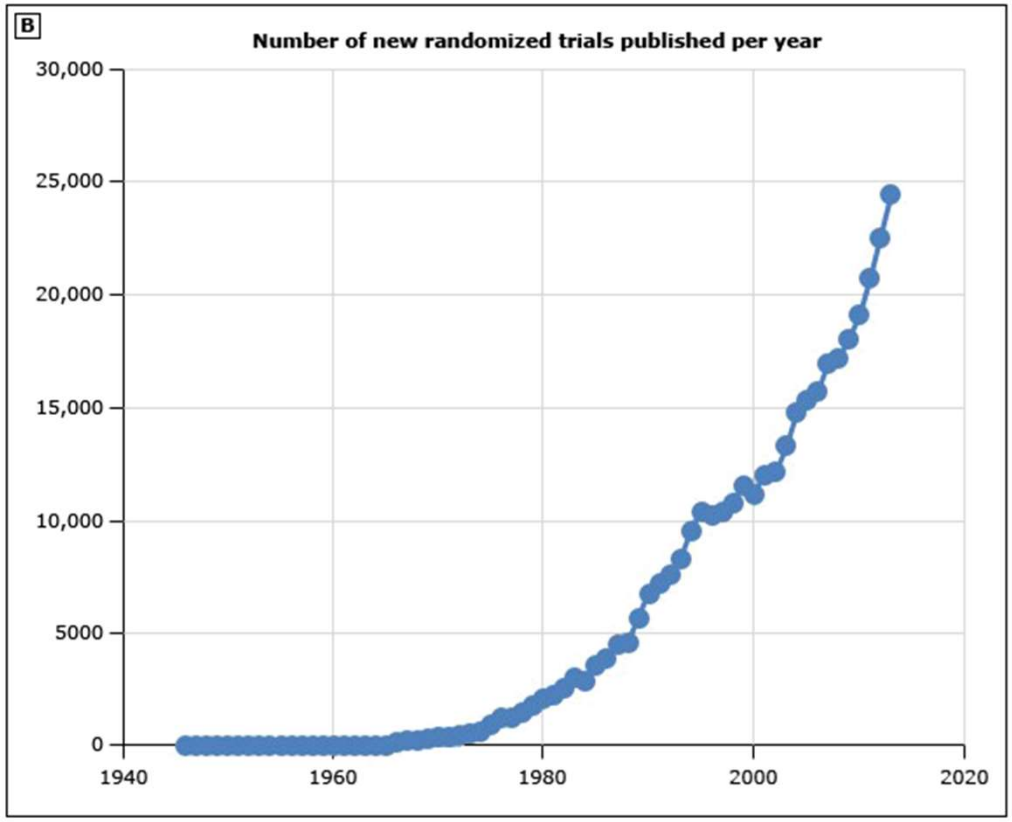
Complicato = cum plicum ..con pieghe

Complessità

cum plexum ..con nodi ..intrecciato

Exponential growth of the medical literature from 1946 to 2015





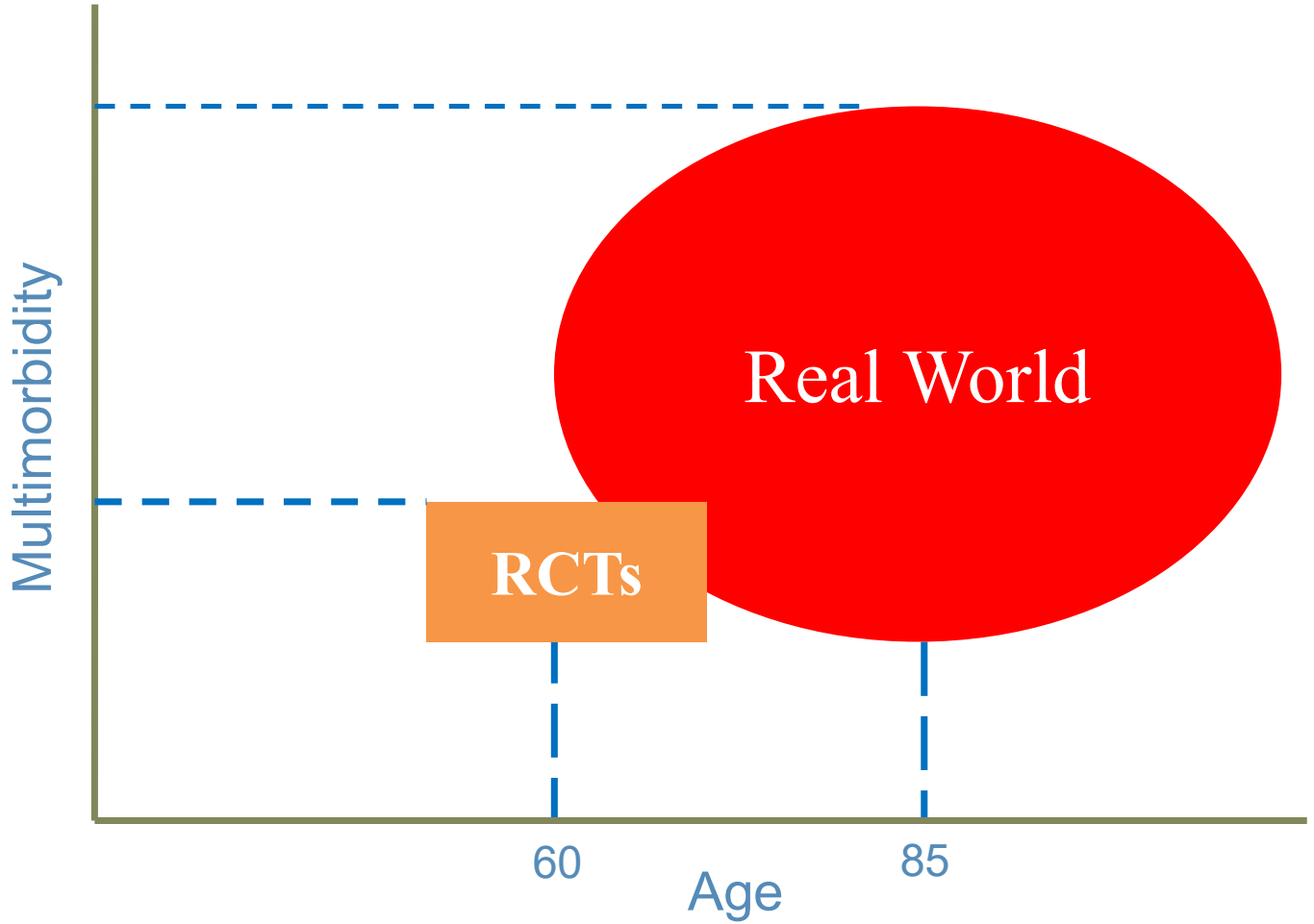
SCIENCEINSIDER | HEALTH

FDA pushes cancer trials to include more elderly people

New guidance aims to improve understanding of drug safety, effectiveness in older adults

3 MAR 2022 · 1:10 PM · BY JENNIFER COUZIN-FRANKEL

A missed target: frail and complex patient



Treatment regimen for a 79-year-old with hypertension, diabetes, osteoporosis, osteoarthritis, and COPD

Time	Medications†	Other
7:00 AM	Ipratropium metered dose inhaler 70 mg/wk of alendronate	Check feet Sit upright for 30 min on day when alendronate is taken Check blood sugar
8:00 AM	500 mg of calcium and 200 IU of vitamin D 12.5 mg of hydrochlorothiazide 40 mg of lisinopril 10 mg of glyburide 81 mg of aspirin 850 mg of metformin 250 mg of naproxen 20 mg of omeprazole	Eat breakfast 2.4 g/d of sodium 90 mmol/d of potassium Low intake of dietary saturated fat and cholesterol Adequate intake of magnesium and calcium Medical nutrition therapy for diabetes‡ DASH‡
12:00 PM		Eat lunch 2.4 g/d of sodium 90 mmol/d of potassium Low intake of dietary saturated fat and cholesterol Adequate intake of magnesium and calcium Medical nutrition therapy for diabetes‡ DASH‡
1:00 PM	Ipratropium metered dose inhaler 500 mg of calcium and 200 IU of vitamin D	
7:00 PM	Ipratropium metered dose inhaler 850 mg of metformin 500 mg of calcium and 200 IU of vitamin D 40 mg of lovastatin 250 mg of naproxen	Eat dinner 2.4 g/d of sodium 90 mmol/d of potassium Low intake of dietary saturated fat and cholesterol Adequate intake of magnesium and calcium Medical nutrition therapy for diabetes‡ DASH‡
11:00 PM	Ipratropium metered dose inhaler	
As needed	Albuterol metered dose inhaler	

Boyd, C. M. et al. JAMA 2005;294:716-724.

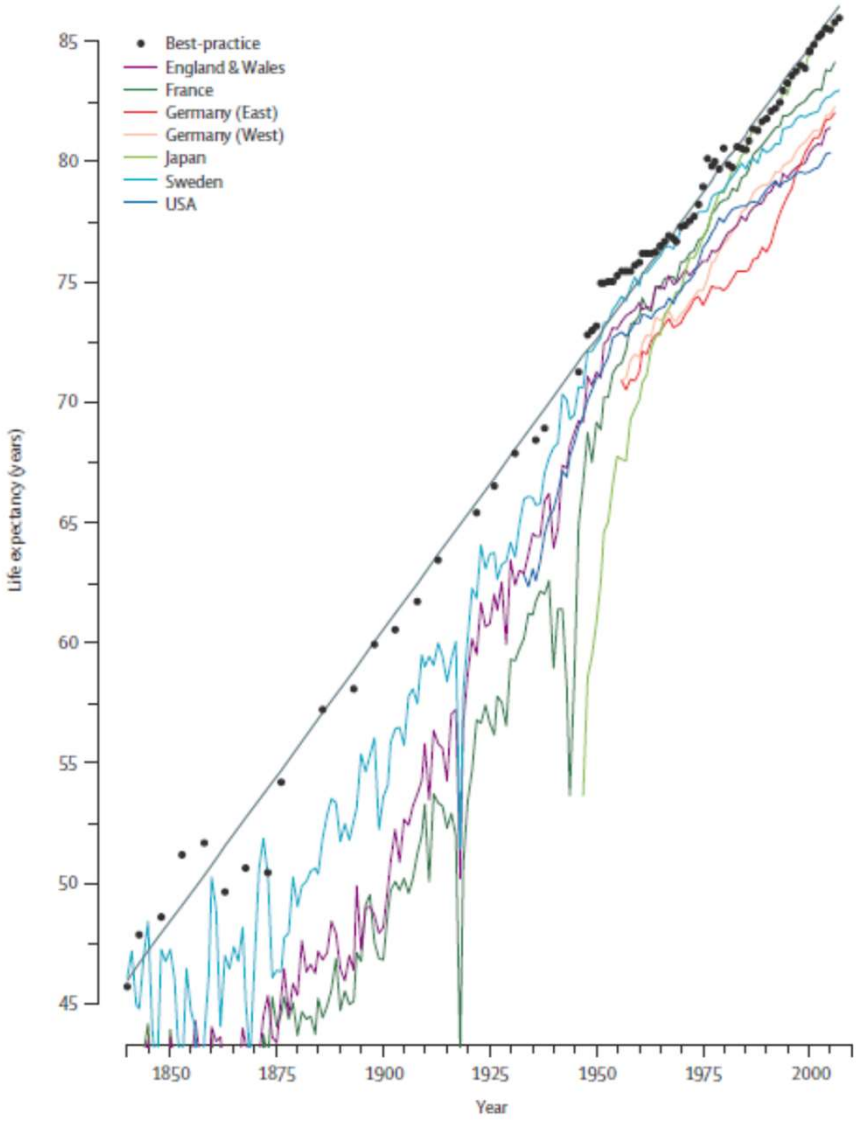
Potential medical interactions

Type of Disease	Medications With Potential Interactions	Type of Interaction: Medication and Other Disease	Type of Interaction: Medications for Different Diseases	Type of Interaction: Medication and Food
Hypertension	Hydrochlorothiazide, lisinopril	Diabetes: diuretics increase serum glucose and lipids*	Diabetes medications: hydrochlorothiazide may decrease effectiveness of glyburide	NA
Diabetes	Glyburide, metformin, aspirin, and atorvastatin	NA	Osteoarthritis medications: NSAIDs plus aspirin increase risk of bleeding Diabetes medications: glyburide plus aspirin may increase the risk of hypoglycemia; aspirin may decrease effectiveness of lisinopril	Aspirin plus alcohol: increased risk of gastrointestinal tract bleeding Atorvastatin plus grapefruit juice: muscle pain, weakness Glyburide plus alcohol: low blood sugar, flushing, rapid breathing, tachycardia Metformin plus alcohol: extreme weakness and heavy breathing Metformin plus any type of food: medication absorption decreased
Osteoarthritis	NSAIDs	Hypertension: NSAIDs: raise blood pressure†; NSAIDs plus hypertension increase risk of renal failure	Diabetes medications: NSAIDs in combination with aspirin increase risk of bleeding Hypertension medications: NSAIDs decrease efficacy of diuretics	NA
Osteoporosis	Calcium, alendronate	NA	Diabetes medications: calcium may decrease efficacy of aspirin; asprin plus alendronate can cause upset stomach Osteoporosis medications: calcium may lower serum alendronate level	Alendronate plus calcium: take on empty stomach (>2 h from last meal) Alendronate: avoid orange juice Calcium plus oxalic acid (spinach and rhubarb) or phytic (bran and whole cereals): eating these foods may decrease amount of calcium absorbed (>2 h from last meal)
Chronic obstructive pulmonary disease	Short-acting β-agonists	NA	NA	NA

Boyd, C. M. et al. JAMA 2005;294:716-724.

WHEN SHOULD ONE BE CONSIDERED OLD?

- 65 years
- 75 years
- 85 years
- It depends on…
- I am uncertain



Ageing populations: the challenges ahead

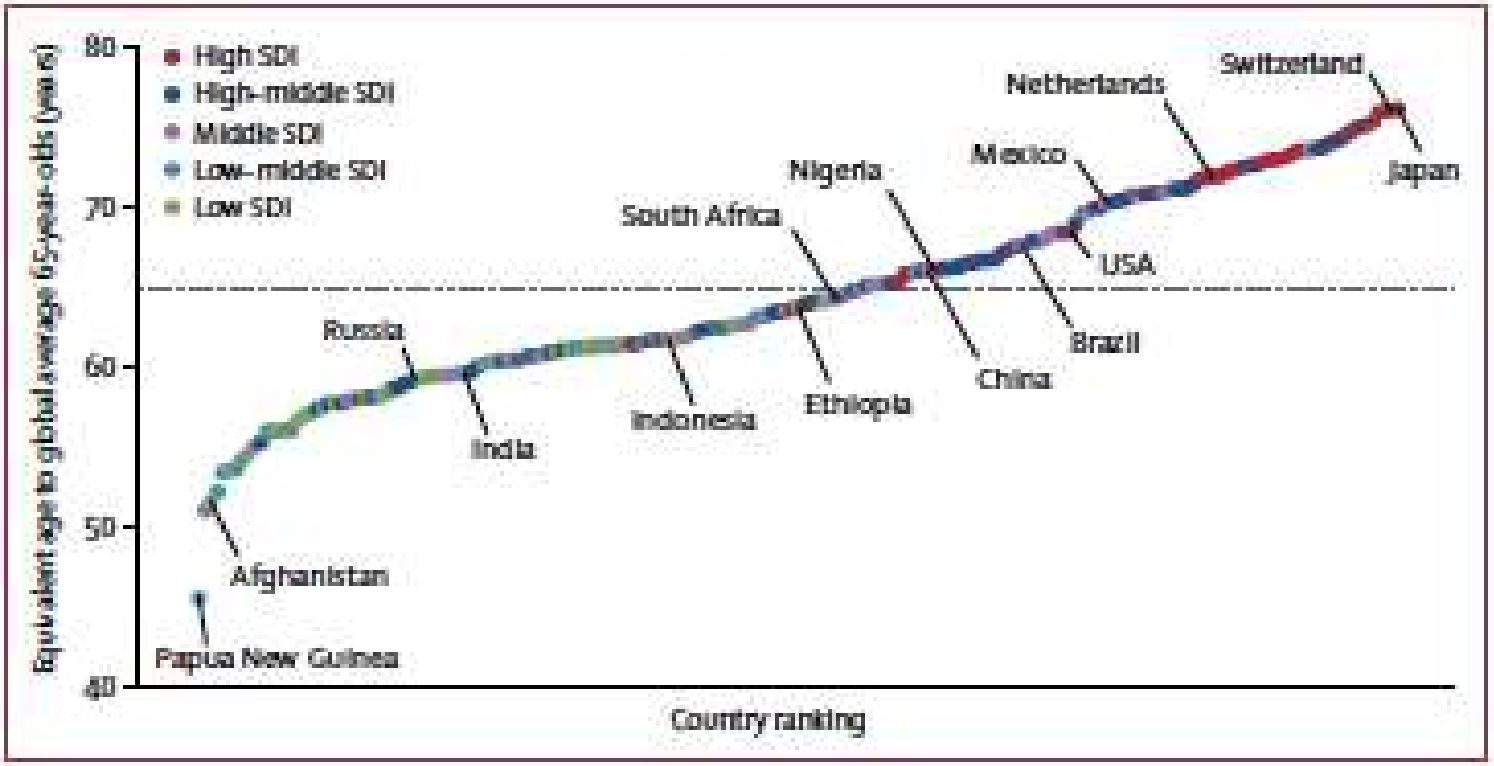
Lancet 2009; 374: 1196-208

	2000	2001	2002	2003	2004	2005	2006	2007
Canada	102	102	103	103	103	104	104	104
Denmark	99	99	100	100	101	101	101	101
France	102	102	103	103	103	104	104	104
Germany	99	100	100	100	101	101	101	102
Italy	102	102	102	103	103	103	104	104
Japan	104	105	105	105	106	106	106	107
UK	100	101	101	101	102	102	103	103
USA	101	102	102	103	103	103	104	104

Data are ages in years. Baseline data were obtained from the Human Mortality Database and refer to the total population of the respective countries.

Table 1: **Oldest age at which at least 50% of a birth cohort is still alive in eight countries**

Measuring population ageing: an analysis of the global burden of disease study 2017



Lancet Public Health 2019; 4: e159–67

Annals of internal medicine

Table 3. Estimated Life Expectancy, by Comorbidity Groups*

Age, y	Life Expectancy in Men, y							Life Expectancy in Women, y						
	Average U.S. Population†	Comorbidity						Average U.S. Population†	Comorbidity					
		None	Low/ Medium	High	Diabetes‡	COPD§	CHF‖		None	Low/ Medium	High	Diabetes‡	COPD§	CHF‖
All races														
66	15.4	18.5	15.7	9.9	14.7	12.2	7.4	18.4	22.5	18.4	12.0	16.1	15.4	8.0
70	12.8	16.3	13.5	8.9	13.1	11.0	7.0	15.4	19.3	15.7	10.8	14.7	13.3	8.0
75	9.9	12.7	11.0	7.4	10.3	8.9	5.8	12.0	15.3	12.4	8.5	11.4	10.8	7.1
80	7.4	9.8	8.2	5.8	7.4	7.0	4.8	9.0	11.6	9.4	6.6	8.5	8.0	5.8
85	5.5	7.2	5.8	4.2	5.5	5.1	3.7	6.6	8.7	7.0	5.1	6.2	6.2	4.7
90	3.9	5.1	3.9	3.0	3.7	3.7	3.0	4.7	5.7	4.7	3.5	4.4	4.4	3.5
White persons														
66	15.5	18.6	16.1	9.9	14.8	12.2	7.9	18.5	22.6	18.5	12.0	16.2	14.7	8.5
70	12.9	16.3	13.9	8.9	13.2	11.0	7.0	15.5	19.4	15.8	10.8	14.0	12.7	8.0
75	9.9	12.8	10.7	7.4	10.3	8.9	5.8	12.0	15.3	12.4	8.5	11.4	10.2	7.0
80	7.4	9.9	8.2	5.4	7.4	6.6	4.8	9.0	11.7	9.0	6.6	8.5	8.0	5.8
85	5.4	7.2	5.8	4.2	5.4	4.8	3.6	6.6	8.2	6.6	5.0	6.2	6.2	4.7
90	3.9	5.0	3.9	3.0	3.6	3.6	3.0	4.7	5.7	4.7	3.8	4.3	4.3	3.5
Black persons														
66	13.5	16.3	14.2	9.1	13.5	11.9	7.1	17.0	21.3	17.8	10.9	17.0	17.0	8.1
70	11.4	14.7	12.4	7.9	11.4	9.5	6.4	14.4	18.7	15.3	9.9	14.7	13.8	8.1
75	9.1	11.9	10.0	6.4	9.4	7.9	5.2	11.5	15.3	12.5	8.5	11.5	11.8	7.2
80	7.1	9.8	8.0	5.2	7.7	6.8	4.5	9.0	12.1	10.0	6.9	9.3	9.0	6.1
85	5.5	7.3	6.3	4.5	5.5	5.2	3.8	6.9	9.0	7.5	5.5	6.5	6.9	5.2
90	4.2	5.7	4.7	3.6	4.5	3.1	3.4	5.2	6.7	5.7	4.1	5.2	5.2	4.1

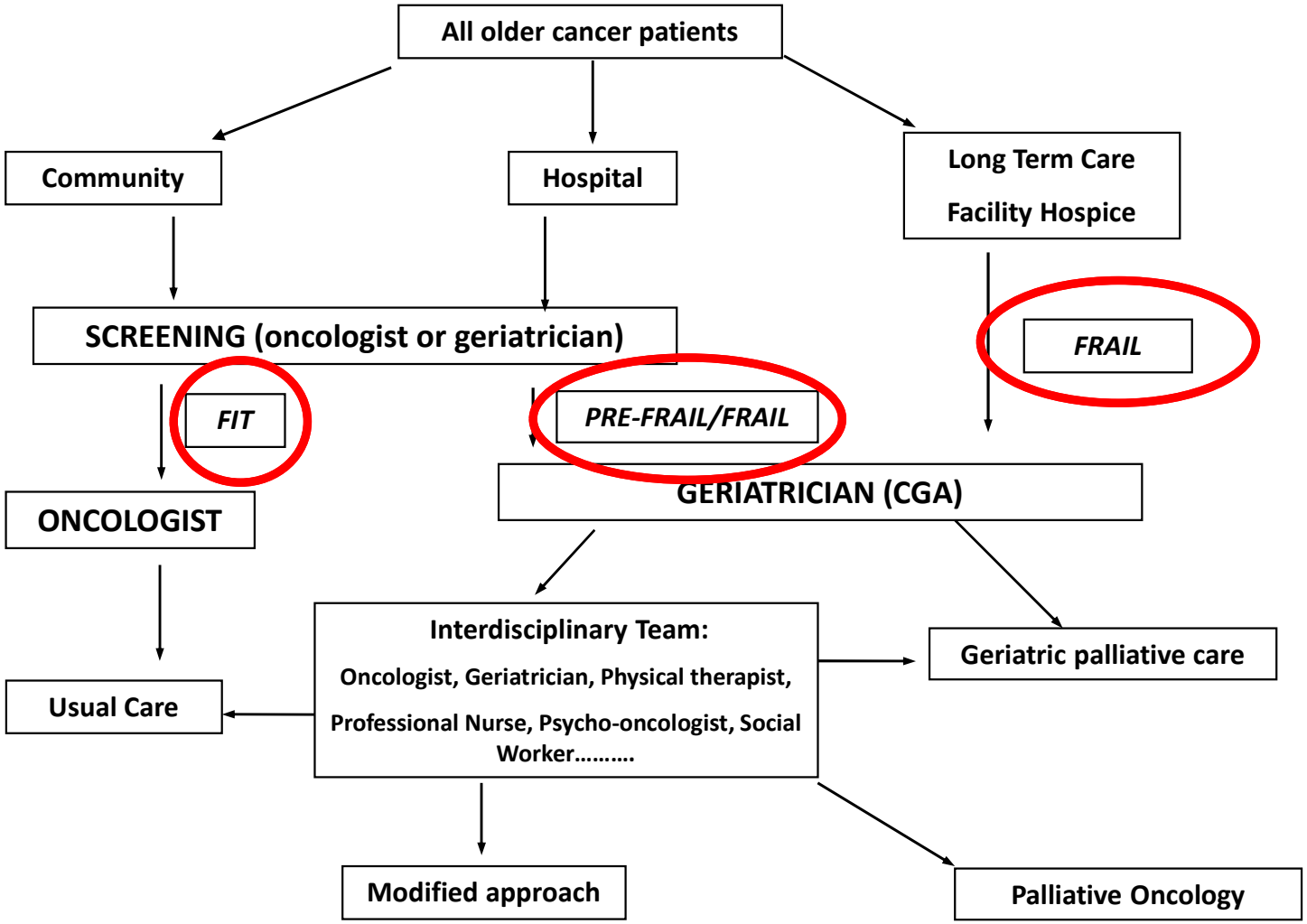
CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease.
* Rounded to the nearest tenth.
† From the 2000 U.S. decennial life table at the chronological age.
‡ Includes diabetes only or diabetes with other conditions except COPD and CHF.
§ Includes COPD only or COPD with other conditions except CHF.
‖ Includes CHF only or CHF with other conditions.

Boomers Turn 70

How this generation has influenced us all ... and how it will change the world again

by **Bill Newcott**, **AARP Bulletin**, January 2016 | Comments: 16

CHI È FRAGILE?

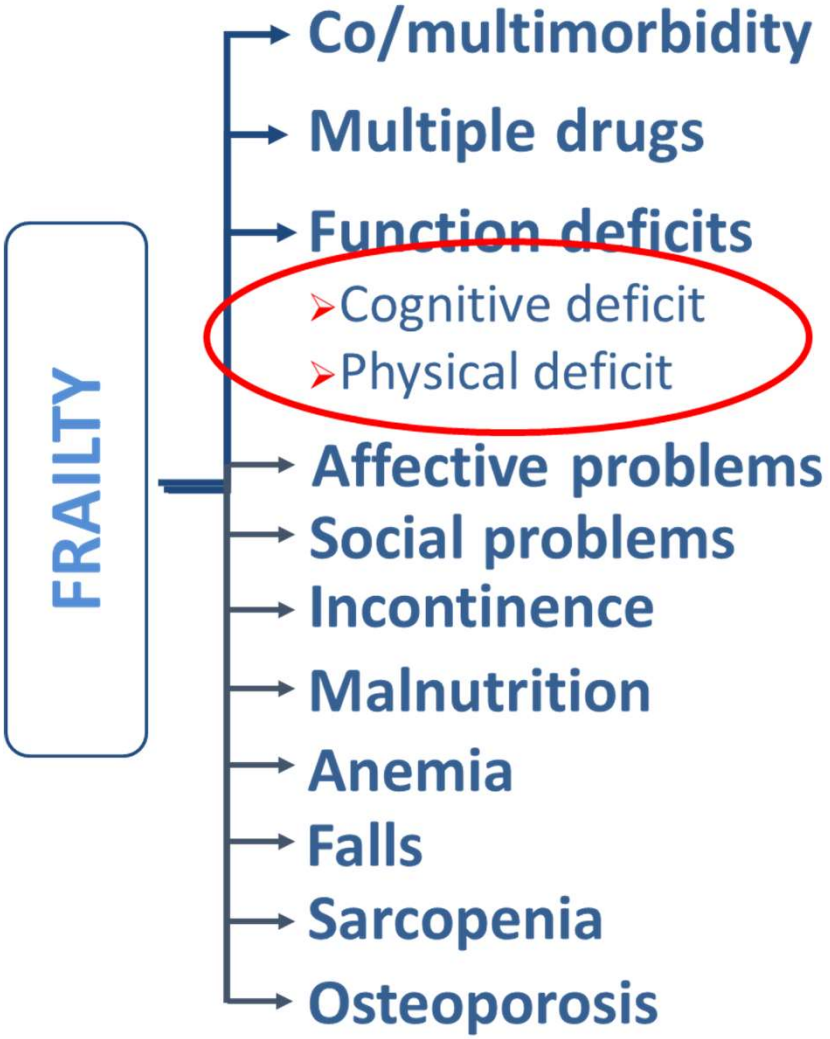


Balducci L, Colloca G et all. Surg Oncol. 2010 Sep;19(3):117-23

The «complex» patient

Researchers have largely shied away from the complexity of multiple chronic conditions

— avoidance that results in expensive, potentially harmful care of unclear benefit.



NEJM FREE FULL TEXT *Tinetti M. NEJM 2011*

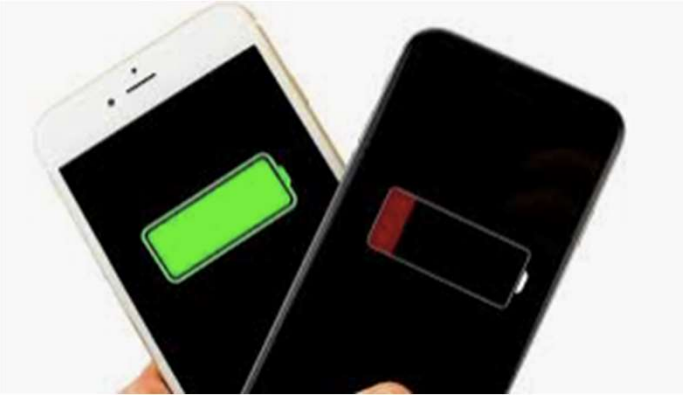
Frailty and stress

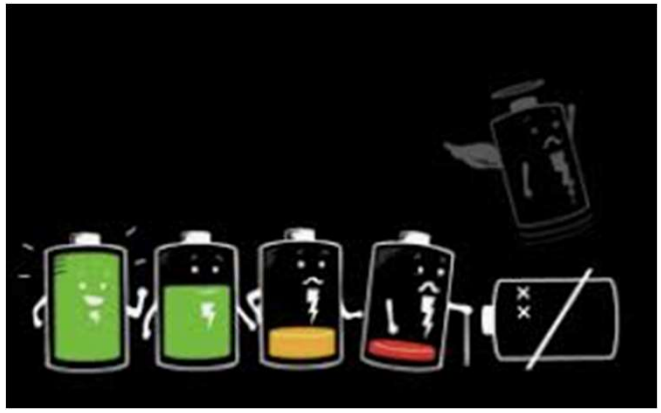
Frailty is most obvious under “stress”

- acute illness
- new medications
- surgery
- pain
- change in environment or support

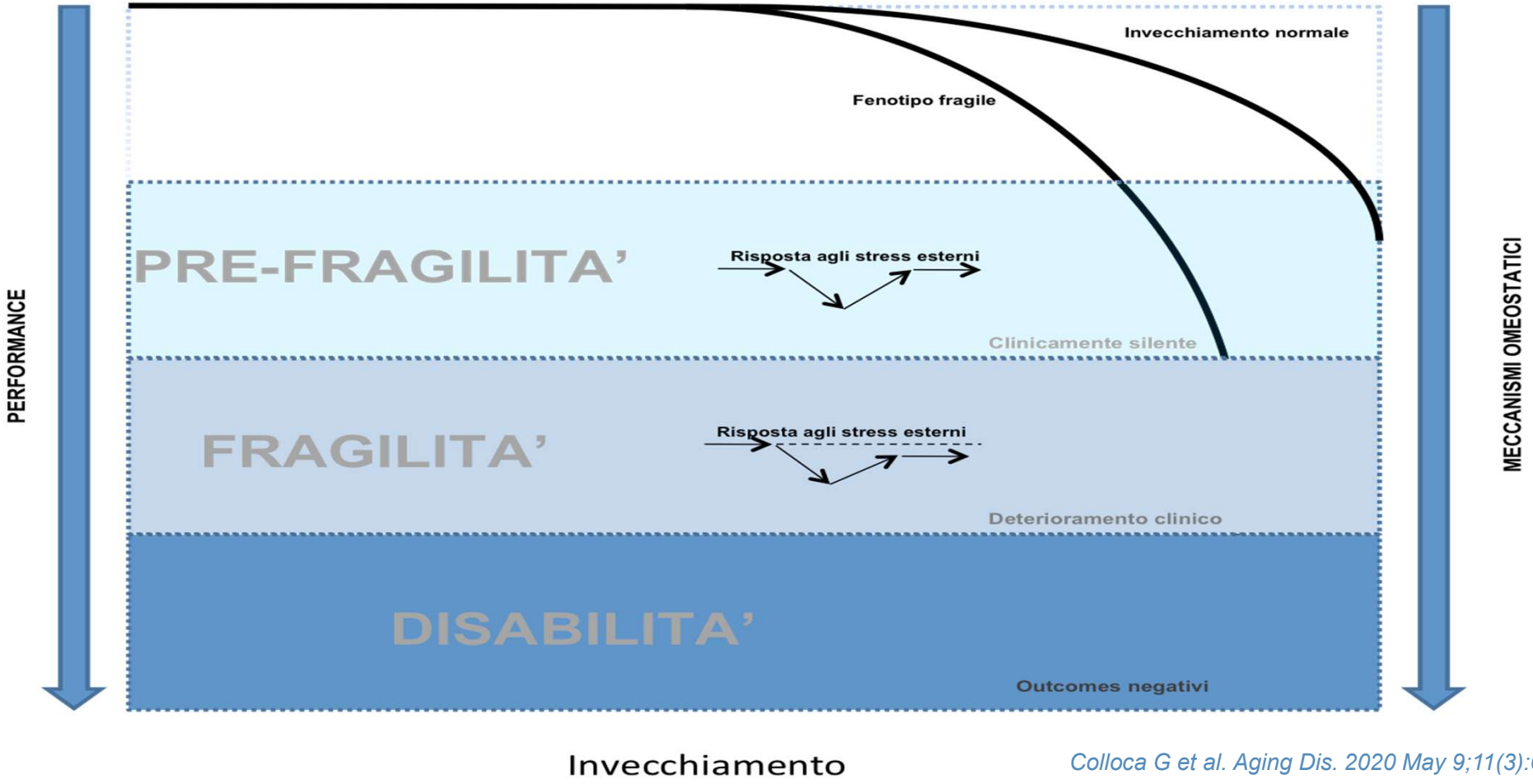
ONCOLOGICAL FRAILTY

"Fragilità" come sindrome, espressione di una ridotta riserva omeostatica e resistenza agli stress di qualunque natura (fisica – malattia-, psicologica, sociale, economica) risultante da un declino cumulativo nei vari sistemi fisiologici e correlata ad outcomes negativi.





Development of frailty with advancing age



Colloca G et al. Aging Dis. 2020 May 9;11(3):649-657.

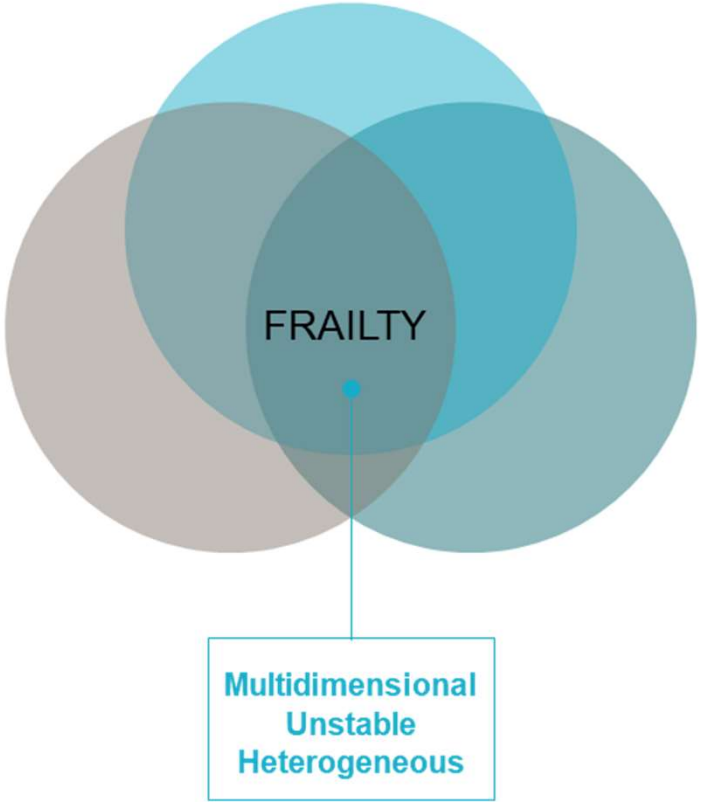
Frailty – an overlapping concept

AGING

Increased vulnerability to disease and accidents over time

DISABILITY

Functional limitations resulting from impairments



COMORBIDITY

Disease processes resulting from biology and exposures

Colloca G et al. Aging Dis. 2020 May 9;11(3):649-657.

Assessing the older patient for cancer treatment

Fitness does not mean you can all do the same exercise

PHYSIOLOGICAL CHANGES IN THE ELDERLY

Pharmacodynamics mechanisms of drug action

- Increased sensitivity to drugs
- Increased adverse effects
- Reduced capacity to respond to physiological challenges and the adverse side effects

Colloca G Surg Onc. 2010 Sep;19(3):124-30.

Pharmacokinetics time course of drug concentration

- Solubility (changes of distribution, protein binding)
- Therapeutic window (hydrophilic vs. lipophilic drugs)
- Adverse drug reactions
- Increased target organ sensitivity

Colloca G Surg Onc. 2010 Sep;19(3):124-30.

Physiological changes in the elderly

Parameter	Changes	Consequences
Absorption	Absorptive surface decreases Splanchnic blood flow decreases Drug-drug interaction may alter absorption Acid production generally unchange	Reduced bioavailability of oral drugs
Decreased renal function	Reduced glomerular filtration rate Decreased blood flow to the kidneys Decreased tubular secretion Reduced creatinine clearance	Reduced: Removal of drug from the body by excretion
Drug distribution	*Reduced for hydrophilic agents:* Decrease in total body water Hemoglobin Decrease in serum albumin levels *Increased for lipophilic agents:* Decreased ratio of lean body mass and increase in fat compartment	Increased toxicity of hydrosoluble agents Reduced effectiveness of liposoluble agents
Decreased liver function	*Reduced:* Hepatocyte mass Hepatic blood flow First pass effect Phase II metabolism generally preserved	Phase I metabolism decreased

Colloca G Surg Onc. 2010 Sep;19(3):124-30.

POLIPHARMACY

Arenas for polypharmacy

In the US 12.5% of the population is over 65 years of age but consume 32% of all prescription medications and account for 25 % of drug expenditure and 30 % of total national healthcare expenditure.

KaufmanDW, et al. JAMA, 2002; 287, 337.

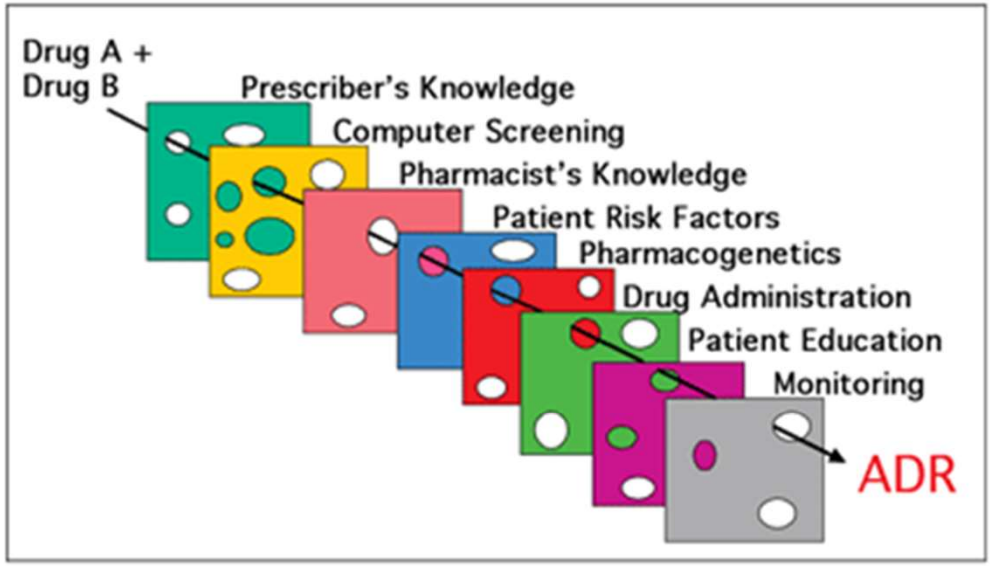
Patients taking two drugs face a 13% risk of adverse drug interactions, rising to 38% when taking four drugs and to 82% if seven or more drugs are given simultaneously

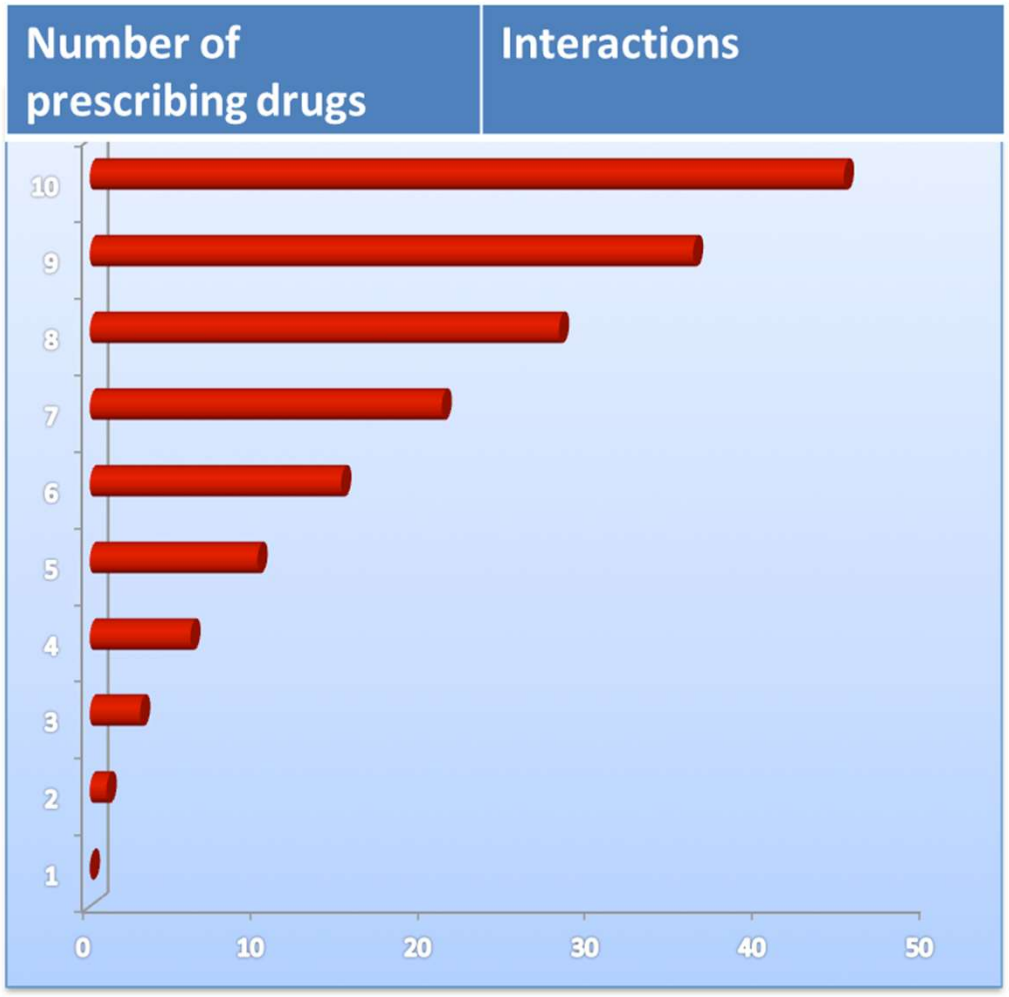
JuurlinkDN, MamdamiM, et al. JAMA, 2003; 289, 1652

If medication-related problems were ranked as a disease by cause of death, it would be the fifth leading cause of death in the United States.

KlarinI, WimoA, FastbomJ Drugs and Aging, 2005; 22, 69–82.

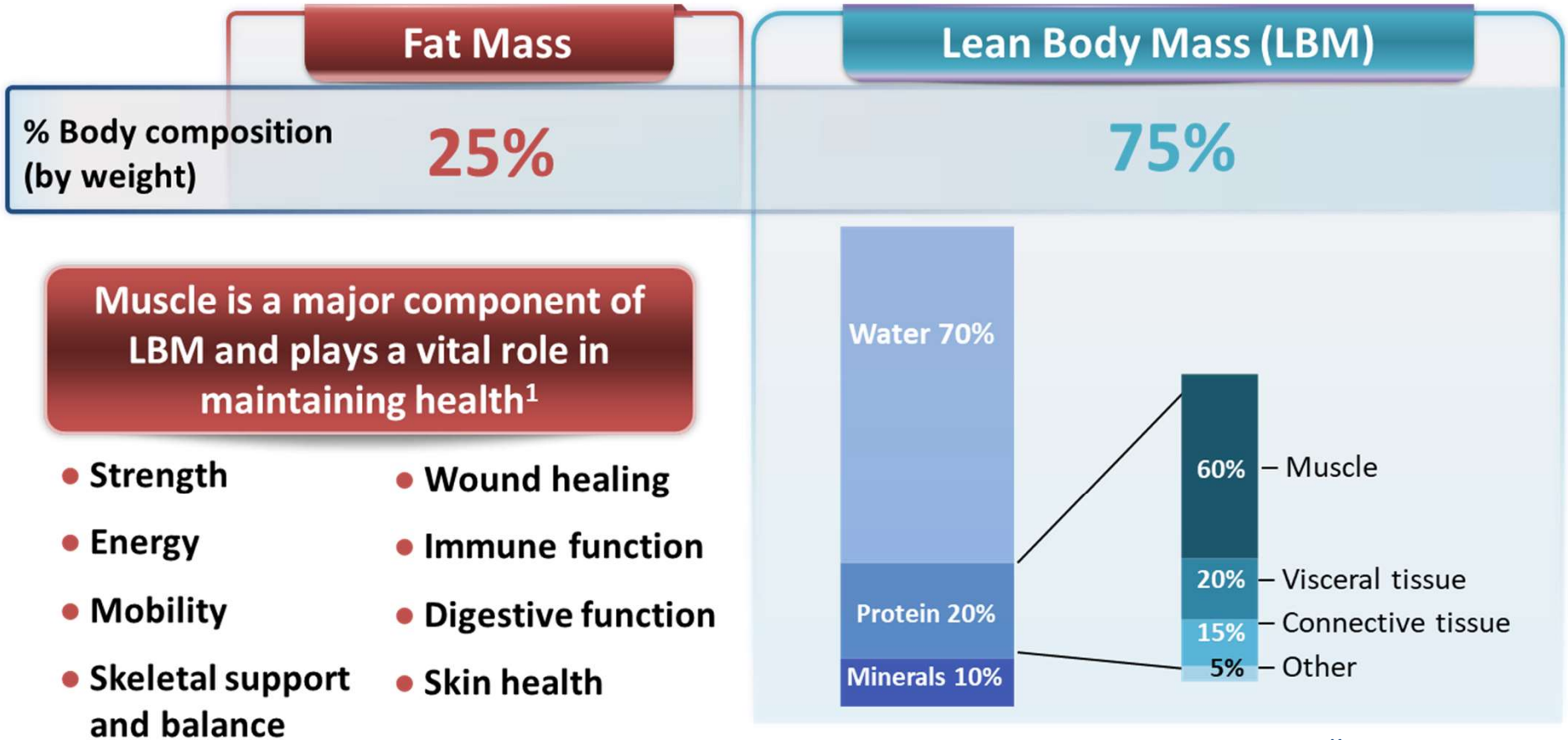
Adrs and drug interactions





Colloca G Surg Onc. 2010 Sep;19(3):124-30.

Body composition



Muscle is a major component of LBM and plays a vital role in maintaining health[1]

- Strength
- Energy
- Mobility
- Skeletal support and balance
- Wound healing
- Immune function
- Digestive function
- Skin health

Colloca G, JGO. 2019

Sarcopenia

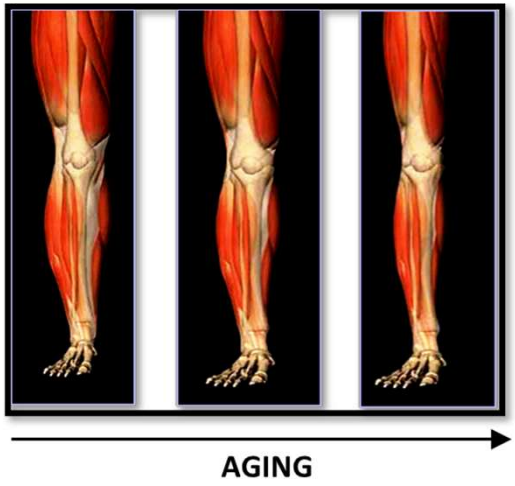
REPORT

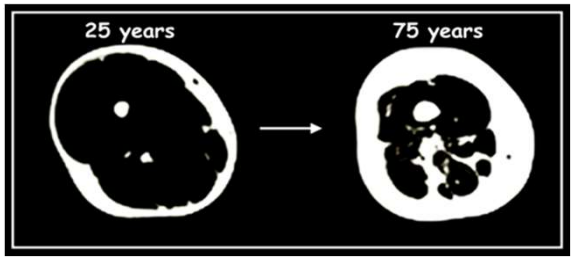
Sarcopenia: European consensus on definition and diagnosis

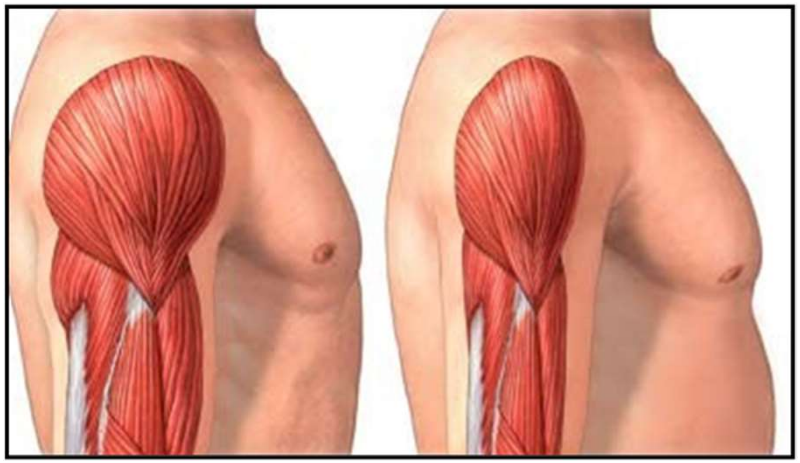
Report of the European Working Group on Sarcopenia in Older People

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]

"Sarcopenia is a (geriatric) syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength (and/or function) with a risk of adverse outcomes such as physical disability, poor quality of life and death"

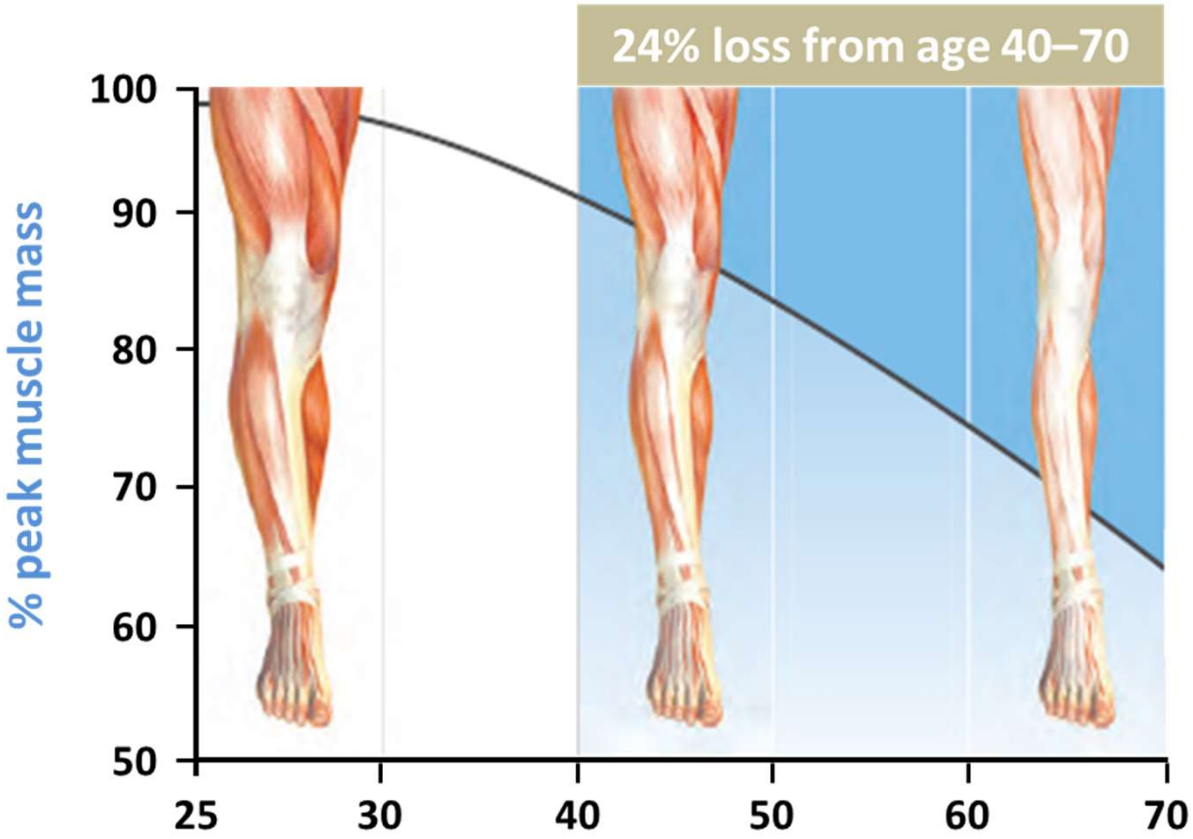






International Journal of Urology, 45-53, 2017, DOI: (10.1111/iju.13473)

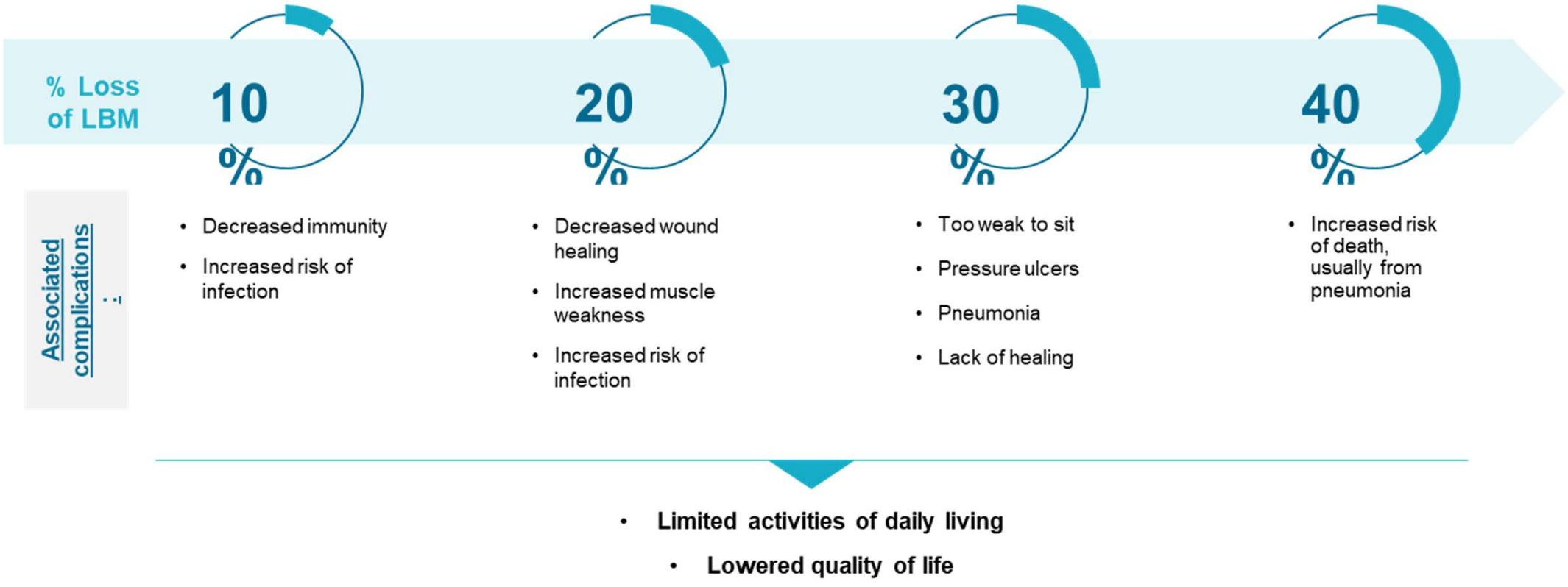
Loss of muscle mass and strength, a natural part of aging



15%
Loss each decade after age 70

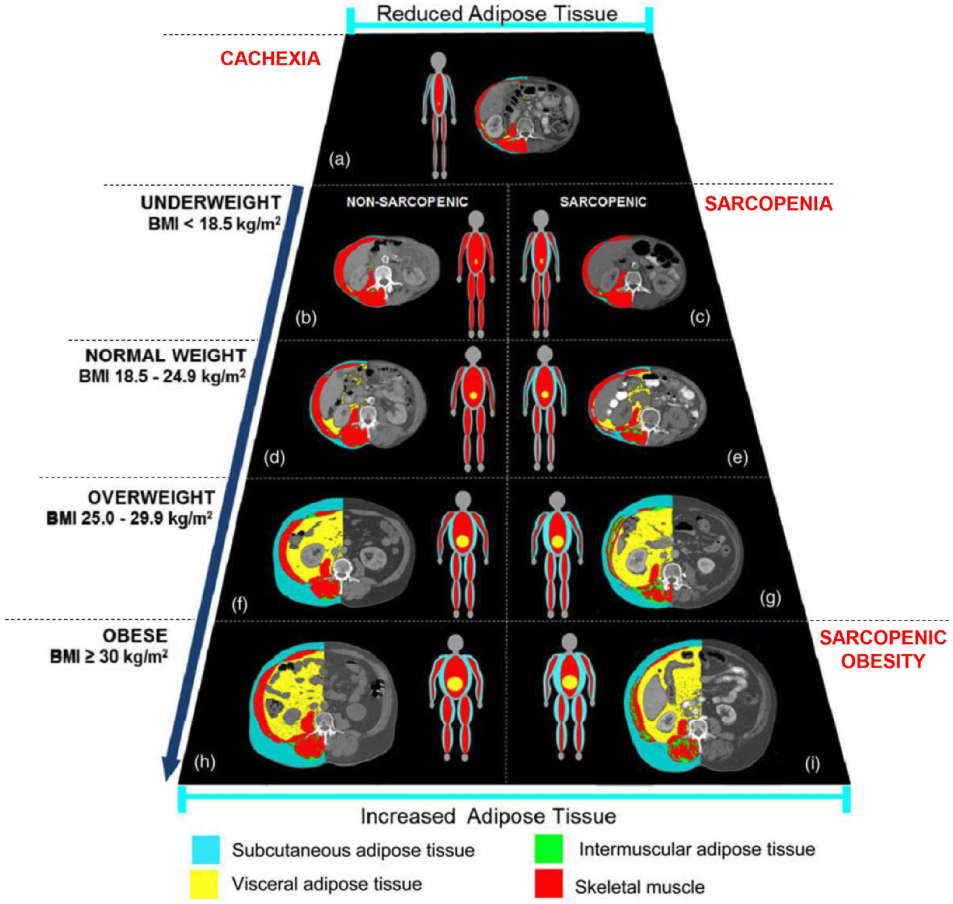
Colloca G, JGO. 2019

Aging and muscle
consequences of losing LBM/muscle



Demling RH. Eplasty 2009;9:e9.

CACHEXIA/SARCOPENIA/SARCOPENIC OBESITY



Prado CM, Cushen SJ, Orsso CE, Ryan AM, Sarcopenia and cachexia in the era of obesity: clinical and nutritional impact, Published online on Cambridge University Press, 08 January 2016.

Take-home message

- THE RIGHT QUESTION

If you do not ask the right questions, you do not get the right answers.

- Un nuovo paziente

- Un nuovo modo di assistere il paziente:
- Età …è relativa
- Le comorbidità ed i farmaci… non si pesano… si gestiscono
- Rischio non è malattia
- La Frailty va scoperta e protetta