UNIVERSITÀ CATTOLICA del Sacro Cuore

Politerapia: per una deprescrizione ragionata

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Ortopediche e della Testa-Collo
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Paziente moderno

Fragilità

- **Multimorbidità** > 75 aa ♀
- Polifarmacoterapia
- Incontinenza
- Cadute
- Problemi nutrizionali
- Osteoporosi
- Anemia
- Sarcopenia

=

Deficit funzionale

→

- Stato cognitivo
- Funzione fisica
- Tono dell'umore
- Condizione socio-economica

Fragilità: "... perdita progressiva della capacità omeostatica"

- **"being in a weakened state"**
- **"ailing, sickly, and infirm, as well as feeble, and lack of energy."**
- **"being in a delicate state.."**
- **the opposite of hardiness**
- **"excess demand imposed on reduced capacity.."**
- **"a precarious balance easily perturbed"**
- **"at risk for adverse health outcomes"**
- **"sarcopenia"**
- **"underweight"**
- **"failure to thrive"**
- **"tendency to fall"**
- **"slowing mentation"**

Definizione operativa di fragilità in popolazione generale anziana – *Cardiovascular Health Study*

1. Forza (handgrip) nel quintile inferiore
2. Velocità del cammino nel quintile inferiore
3. Perdita di peso non intenzionale ≥4,5 kg nell'ultimo anno
4. Facile esauribilità
5. Livello di attività fisica nel quartile inferiore

PHENOTYPE FRAILTY INDEX (PFI)

Fragile: ≥3 componenti

Intermedio (prefragile): 1 o 2 componenti

Non fragile (robusto): 0 componenti

L Fried, et al. *J Gerontol* 2001

European Geriatric Medicine 7 (2016) 197–200

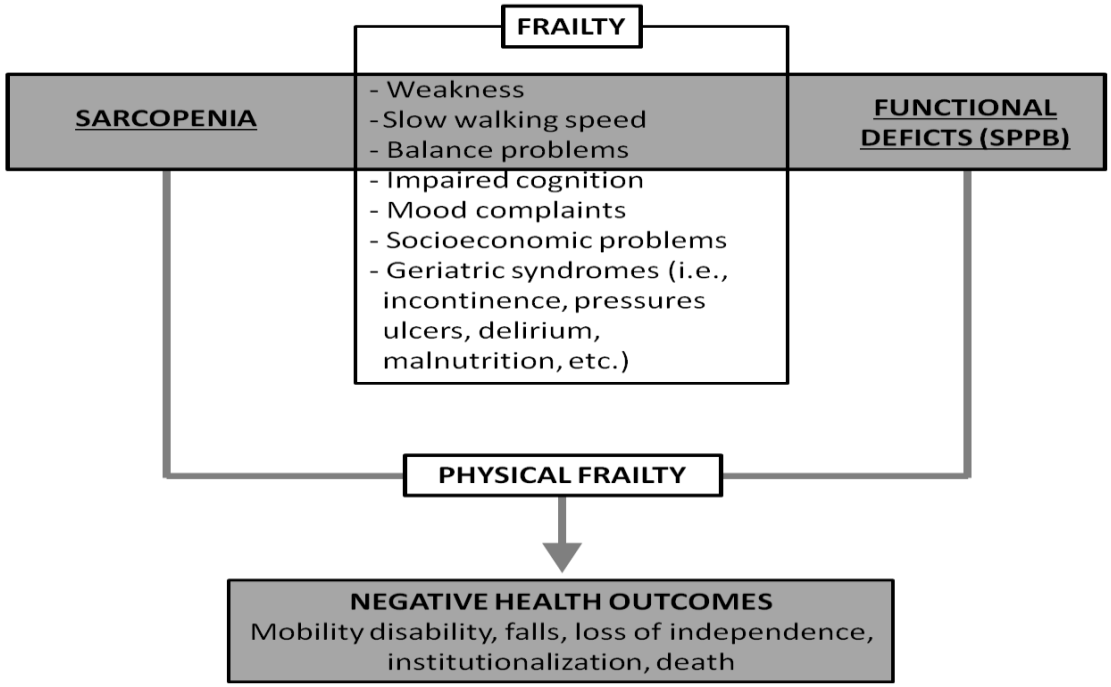
Available online at ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com/en

Research paper

Sarcopenia and frailty: From theoretical approach into clinical practice

F. Landi [a,*], A. Cherubini [b], M. Cesari [c], R. Calvani [a], M. Tosato [a], A. Sisto [a], A.M. Martone [a], R. Bernabei [a], E. Marzetti [a]



Identifying an at-risk older population

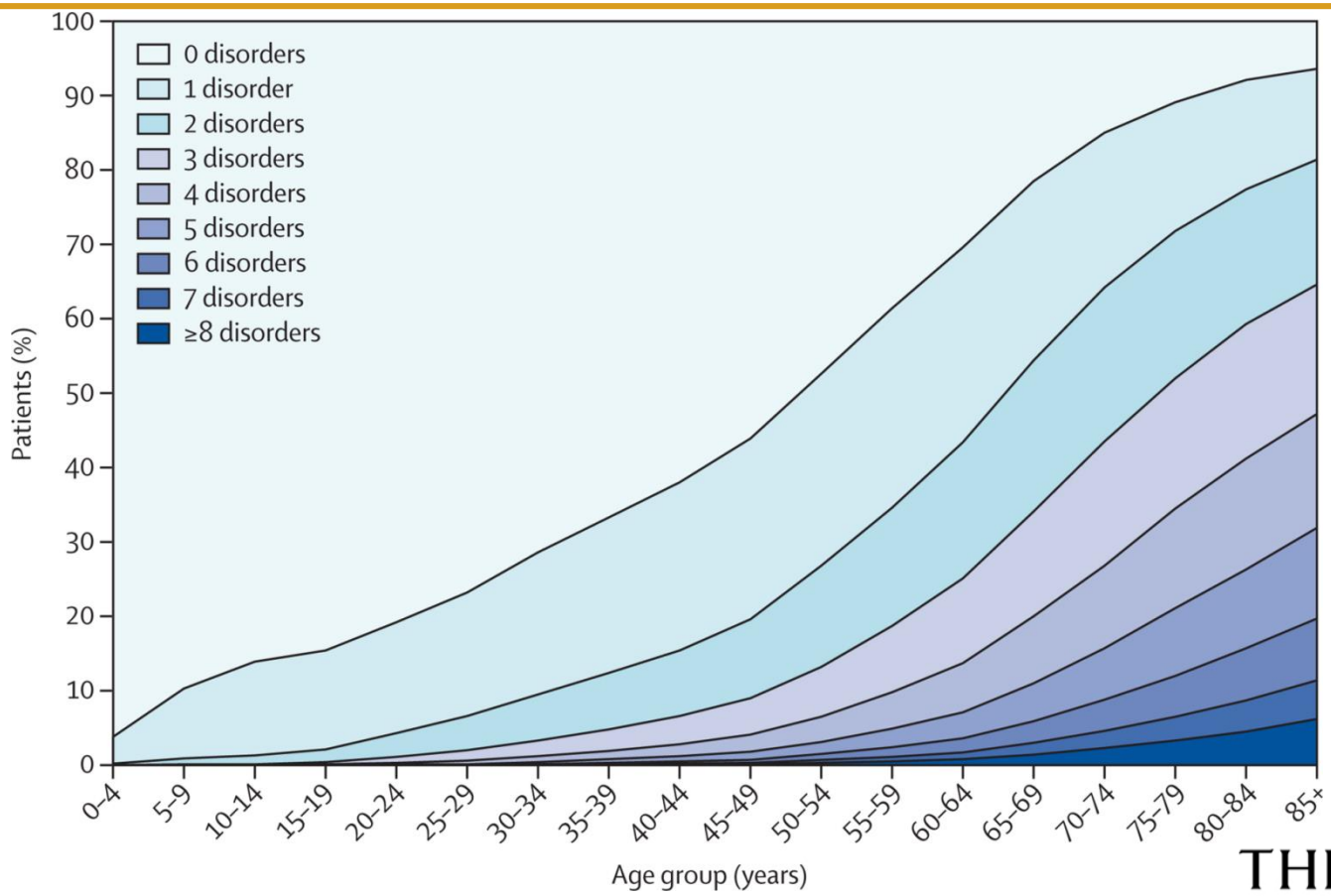
The target population is comprised of individuals with target organ damage (low muscle mass), specific clinical phenotype, and impaired physical performance

Conceptual framework of physical frailty and sarcopenia—resemblance to common conditions of advanced age			
Condition	**Measurable Biological Substrate**	**Measurable Clinical Manifestations**	**Measurable Function**
CHF	Myocardial dysfunction (echocardiography)	• Shortness of breath • Fatigue	6-min walking test
COPD	Airways destructive changes (spirometry)	• Dyspnoea • Cough • Sputum	6-min walking test
PAD	Arterial stenosis (Doppler ultrasonography)	• Intermittent claudication • Numbness • Ulcers	Treadmill walking distance
PF&S	Reduced muscle mass (DXA)	• Slow walking speed • Poor balance • Weakness	SPPB

Landi et al., Clin Geriatr Med 2015;31:367-74

Multimorbidity

Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study



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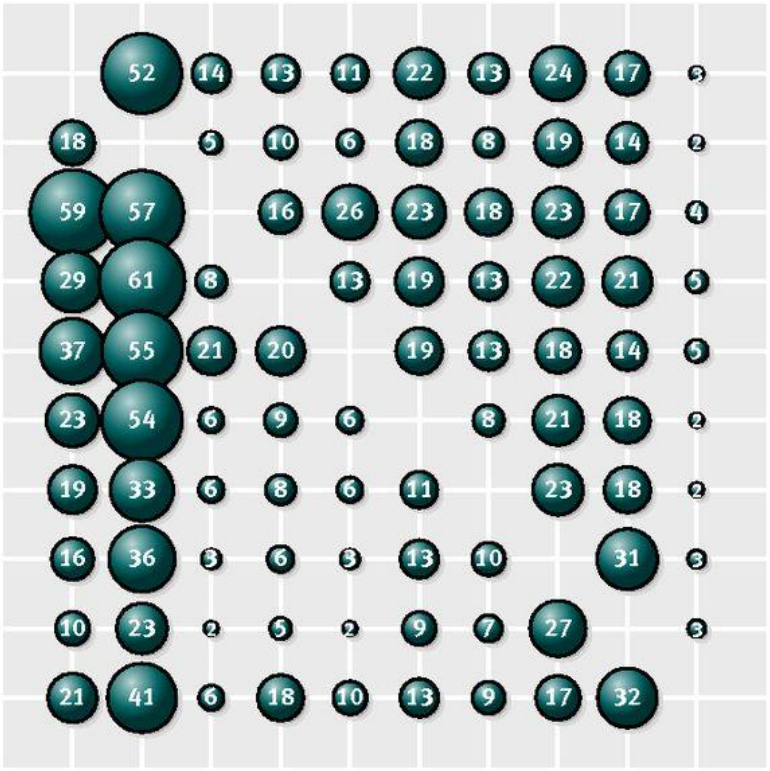
THE LANCET
Vol 380 July 7, 2012

Comorbidity of 10 common conditions



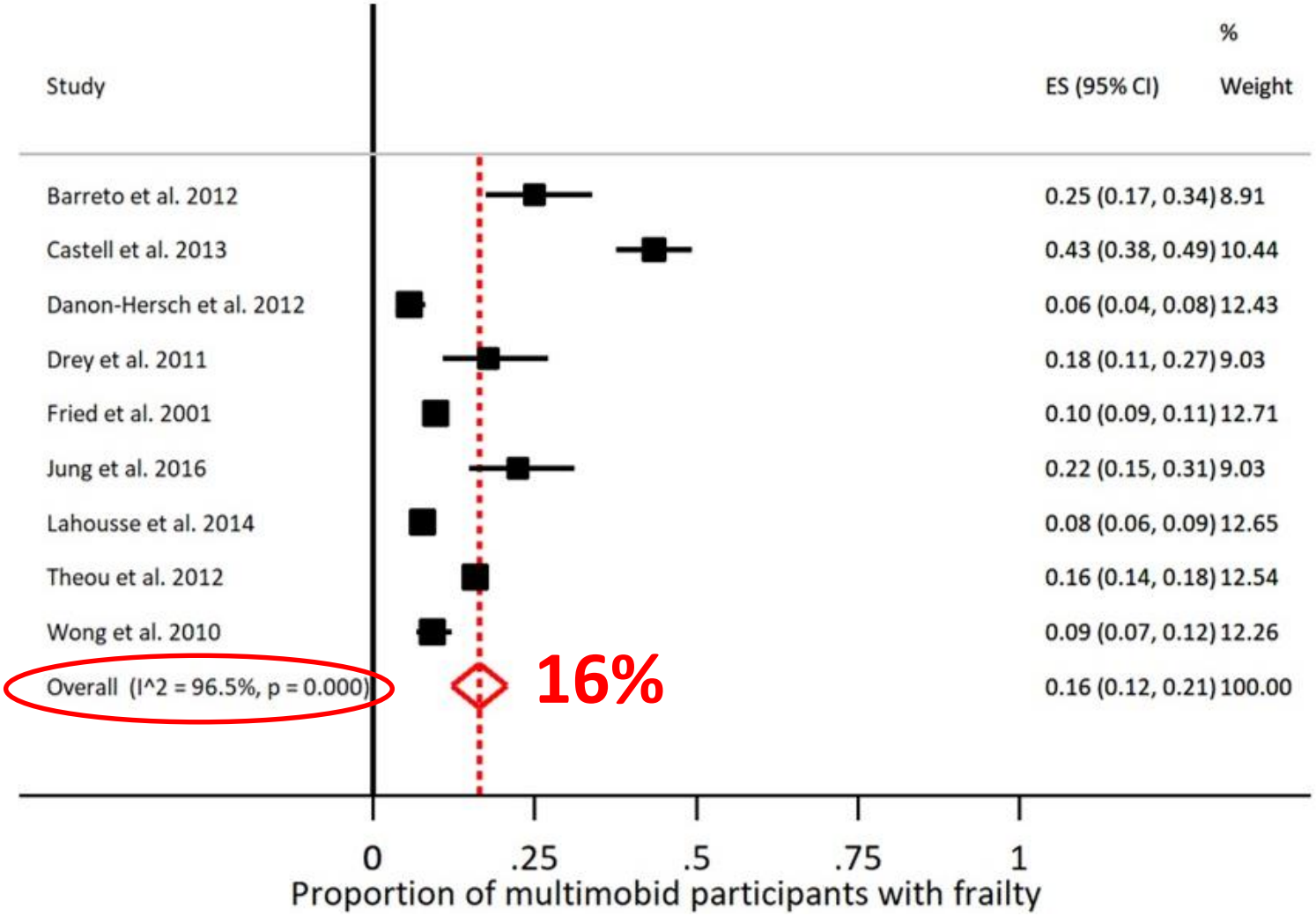
	Percentage who only have the row condition*	Mean No of conditions in people aged <65 years with row condition	Mean No of conditions in people aged ≥65 years with row condition
Coronary heart disease	8.8	3.4	4.4
Hypertension	21.9	2.5	3.6
Heart failure	2.8	3.9	5.6
Stroke/transient ischaemic attack	6.0	3.6	4.8
Atrial fibrillation	6.5	3.3	5.0
Diabetes	17.6	2.9	6.5
Chronic obstructive pulmonary disease	14.3	2.8	4.5
Painful condition	12.7	3.1	4.3
Depression	25.4	2.6	4.9
Dementia	5.3	4.1	4.6

* Percentage who do not have one of 39 other conditions in the full count

Guthrie B et al. BMJ 2012;345:bmj.e6341

BMJ

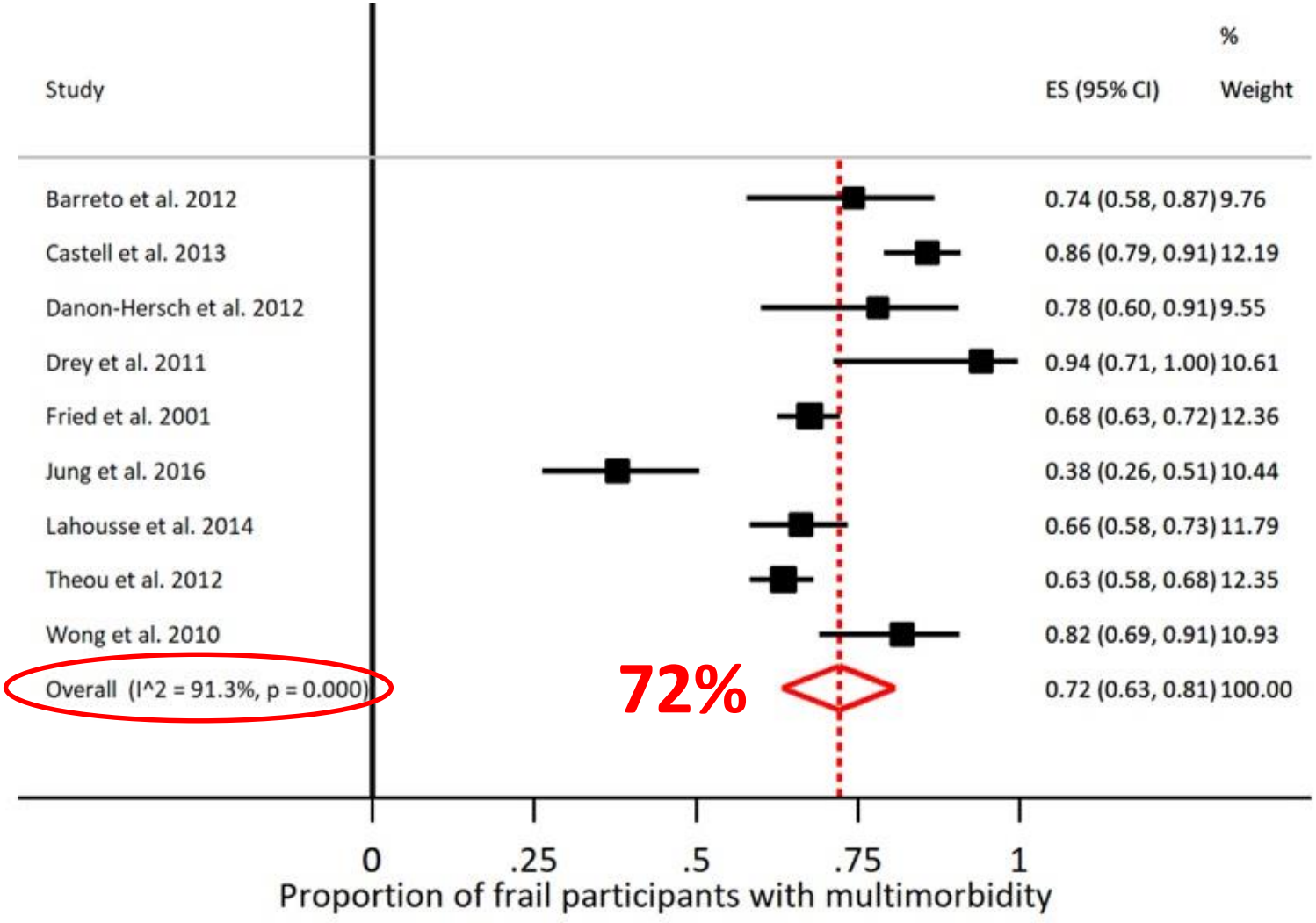
Proportion of multimorbid people with frailty



Vetrano DL et al. J Geront Med Sci (in press)

Multimorbidity → 2+ diseases
Frailty → CHS criteria

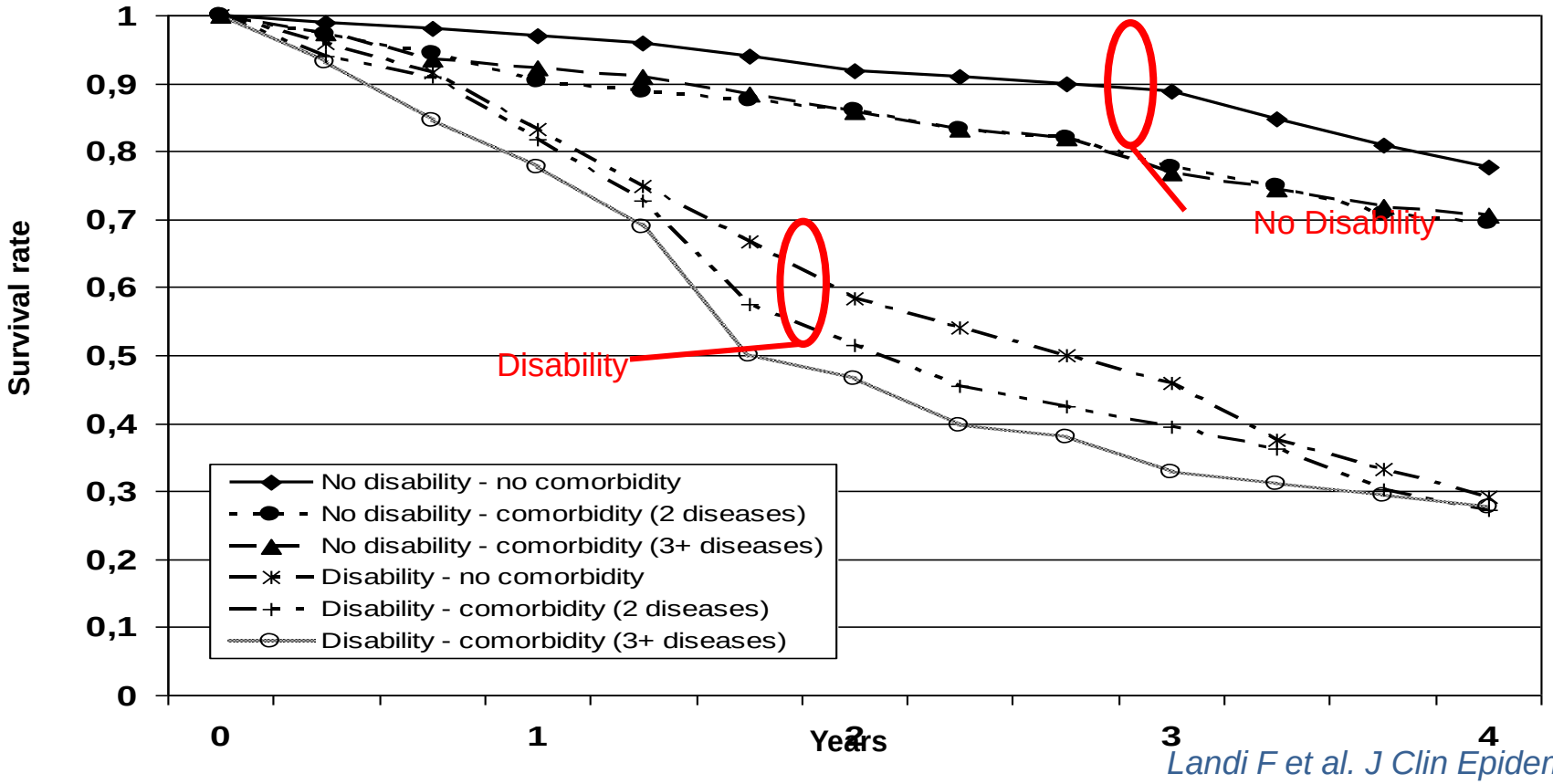
Proportion of frail people with multimorbidity



Vetrano DL et al. J Geront Med Sci (in press)

Multimorbidity → 2+ diseases
Frailty → CHS criteria

Disability, more than multimorbidity, was predictive of mortality among older persons aged 80 years and older.



Landi F et al. J Clin Epidemiol. 2010

Older adults and polypharmacy

Italy

	All age groups (≥ 65 y) n=12.301.537	**65-74 y n=6.154.421**	**75-84 y n=4.474.887**	**≥85 y n= 1.672.229**
Polypharmacy				
5-9 drugs	6.024.383 (49.0%)	2.681.639 (43.6%)	2.462.378 (55.0%)	880.366 (52.6%)
≥10 drugs	**1.389.591 (11.3%)**	529.506 (8.6%)	629.043 (14.1%)	231.042 (13.8%)

Onder G et al. J Gerontol A Biol Sci Med Sci. 2013

US

… The highest prevalence of medication use was among persons aged at least 65 years, of whom **12% took at least 10 medications**

Kaufman et al. JAMA 2002

Sweden

… mean number of drugs was 7.9 for age group 70-79 y, 9.3 for age group 80-89 y and 9.7 for age group 90 y or older

Hovstadius B et al. BMC Clin Pharmacol. 2009

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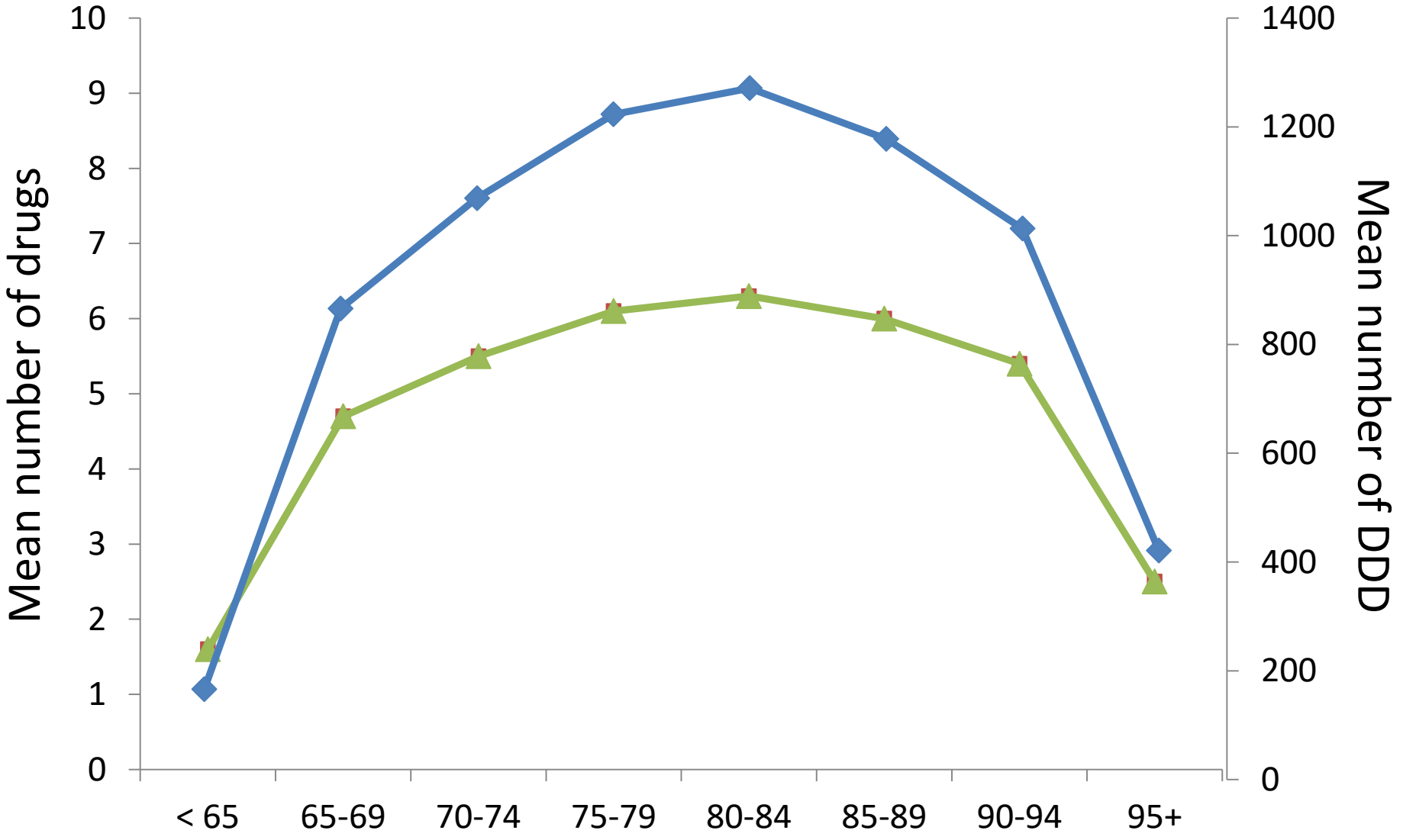
Numero medio di sostanze per età e sesso (2017) – dati Osmed

Fascia d'età	Numero medio di sostanze		
	Uomini	Donne	Totale
65-69	7,6	7,8	7,7
70-74	9,1	9,3	9,2
75-79	10,1	10,3	10,2
80-84	11,4	11,4	11,4
85-89	12,1	11,7	11,8
90-94	12,2	11,6	11,7
≥95	12,0	11,0	11,2
Totale	**9,6**	**9,9**	**9,7**

Drug use in Italy (n=15,931,642)



Onder G et al. JAMDA 2015

Esposizione a farmaci nella popolazione di età ≥65 anni per ATC al III livello

ATC III livello	Categoria	Prevalenza d'uso (%)		
		Uomini	Donne	Totale
A02B	Antiulcera peptica e malattia da reflusso gastroesofageo	47,0	49,2	48,3
B01A	Antitrombotici	45,2	38,6	41,5
C10A	Sostanze modificatrici dei lipidi, non associate	36,9	32,6	34,4
M01A	Farmaci antiinfiammatori ed antireumatici non steroidei	28,6	35,9	32,8
C07A	Betabloccanti	29,3	29,7	29,5
A11C	Vitamine A e D, comprese le loro associazioni	10,7	37,4	25,9
J01C	Antibatterici beta-lattamici, penicilline	23,9	23,2	23,5
J01M	Antibatterici chinolonici	22,8	20,4	21,4
C09A	Ace inibitori non associati	21,8	16,8	18,9
C08C	Calcio-antagonisti selettivi con preval.effetto vascolare	19,3	17,3	18,2

Esposizione a farmaci nella popolazione di età ≥90 anni per ATC al III livello (prime 30 categorie, 2017)

ATC III livello	Categoria	Prevalenza d'uso (%)		
		Uomini	Donne	Totale
B01A	Antitrombotici	73,6	63,1	65,8
A02B	Antiulcera peptica e malattia da reflusso gastroesofageo	69,0	62,0	63,8
C03C	Diuretici ad azione diuretica maggiore	45,9	40,9	42,2
C07A	Betabloccanti	34,8	34,2	34,3
J01M	Antibatterici chinolonici	34,0	24,5	26,9
M01A	Farmaci antiinfiammatori ed antireumatici non steroidei	26,1	27,1	26,8
J01D	Altri antibatterici beta-lattamici	28,1	24,1	25,1
C09A	ACE-inibitori non associati	28,4	23,3	24,6
A11C	Vitamine A e D, comprese le loro associazioni	16,4	26,4	23,8
J01C	Antibatterici beta-lattamici, penicilline	25,8	22,5	23,4
N06A	Antidepressivi	19,8	24,2	23,1

The Example of Heart Failure

	ACE-i Metanalysis Pts 12763	ACE-i vs AR-AT1 ELITE II Pts 3150	AR-AT1 VAL-HeFT Pts 5011	ß-block. Metanalysis Pts 9711	Anti-Aldost. RALES Pts 822	Digoxin DIG Pts 3397	Anti Aldost. TOPCAT Pts 3445
Age	**61**±11	**71**±7	**67**±10	**61**±10	**65**±12	**63**±11	**68**
Males (%)	81%	70%	71%	73%	73%	78%	48%
NYHA III-IV	no IV	48%	40% (III)	46%	95%	33%	34%
Comorbidity	**no**	**no**	**no**	**no**	**no**	**no**	**no**
Disability	**no**	**no**	**no**	**no**	**no**	**no**	**no**

The Trial:

International, multi-centre, randomised double-blind placebo controlled

Inclusion Criteria:

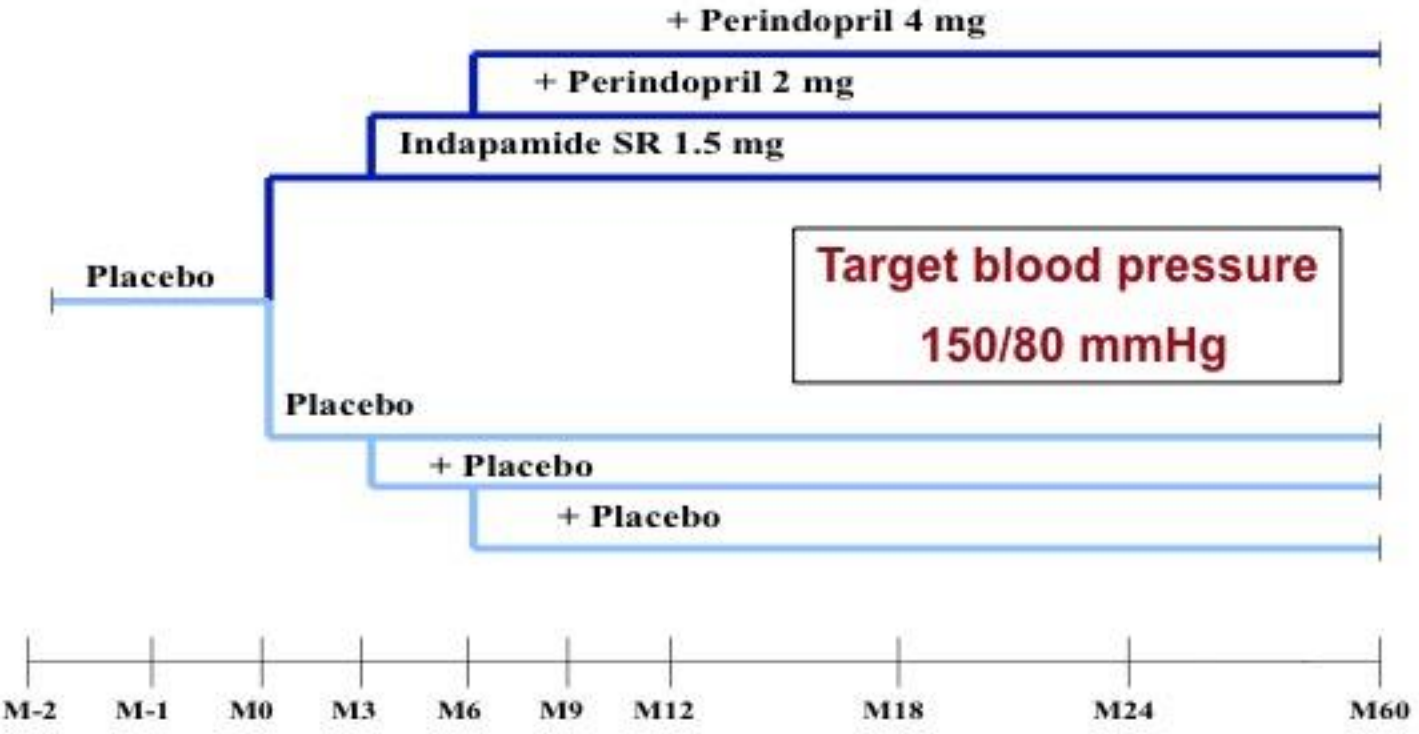
Aged 80 or more,
Systolic BP; 160 -199mmHg
+ diastolic BP; <110 mmHg,
Informed consent

Exclusion Criteria:

Standing SBP < 140mmHg
Stroke in last 6 months
Dementia
Need daily nursing care

Primary Endpoint:

All strokes (fatal and non-fatal)



EBM and Geriatrics

- ✓ Frail elderly are systematically excluded from RCTs
- ✓ Those included are “superfit”, “young-old” randomized patients
- ✓ A new form of EBM is in place

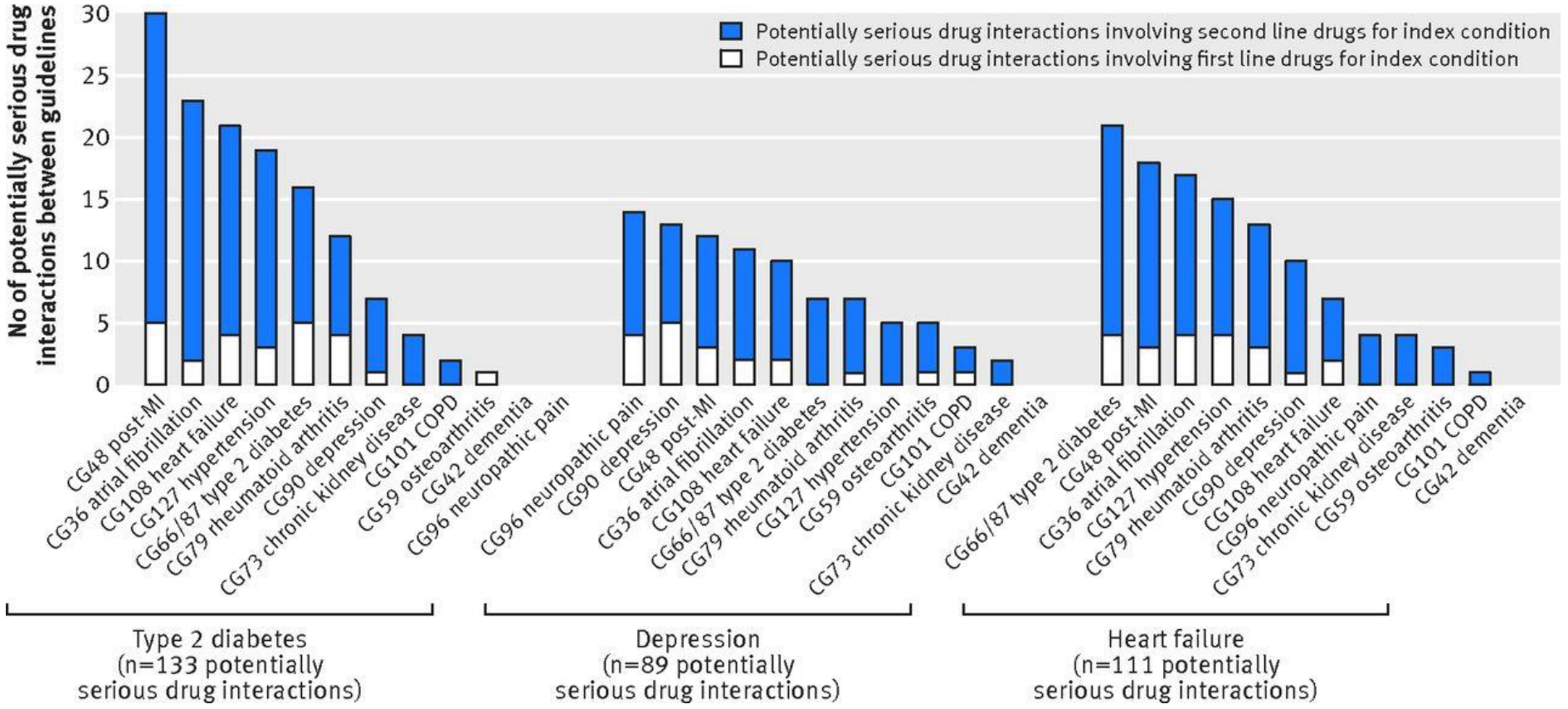
EVIDENCE BIASED MEDICINE

Treatment Regimen for a 79-Year-Old Woman With Hypertension, Diabetes Mellitus, 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.

Potentially serious drug-drug interactions between drugs recommended by clinical guidelines for 3 index conditions and drugs recommended by each of other 11 other guidelines



Dumbreck et al BMJ 2015

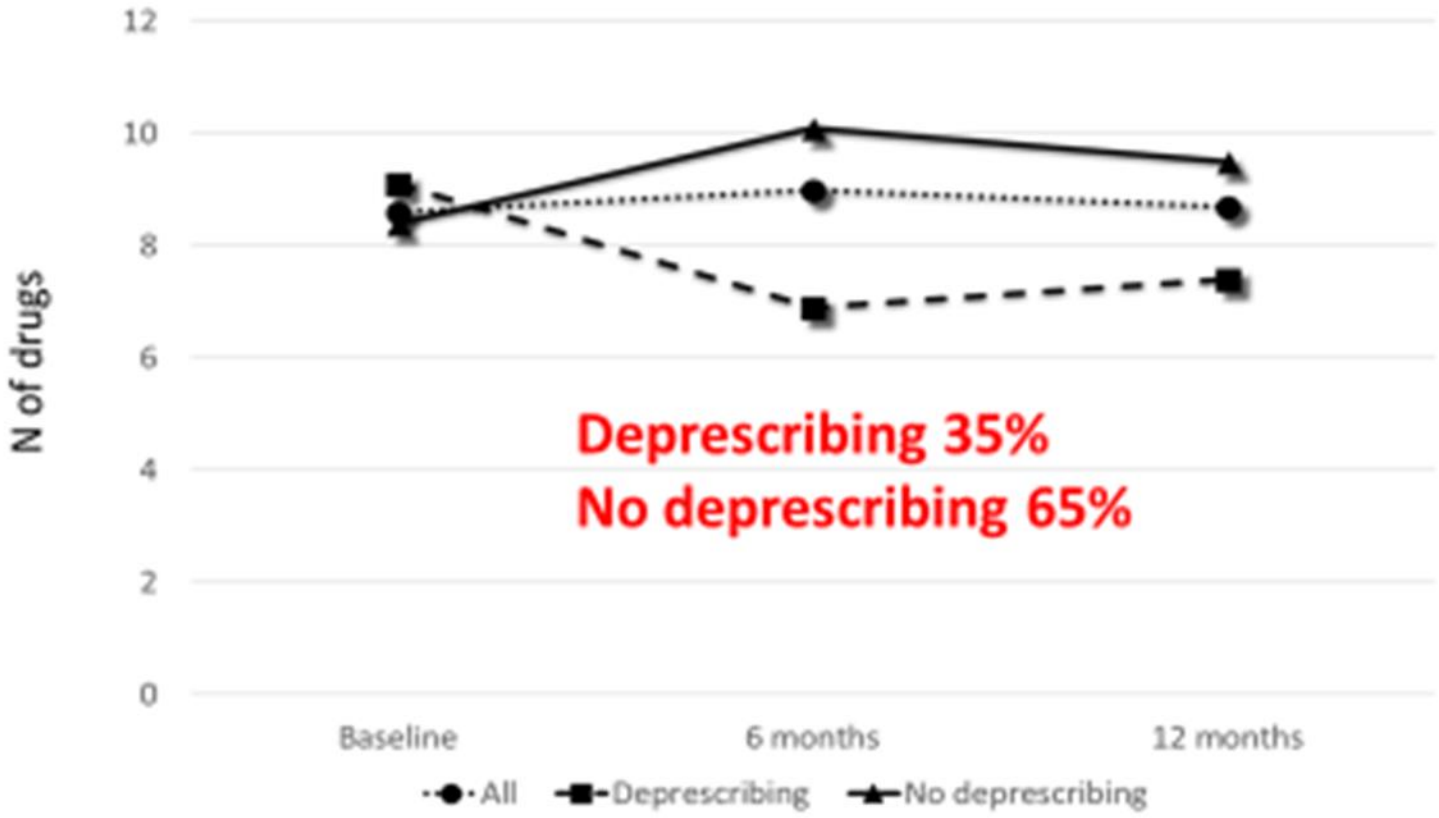
Indicatori di rischio di interazione nella popolazione di età ≥65 anni (2017)

	Totale (≥65 anni) n=7.437.376 (%)	65-74 anni n=3.683.354 (%)	75-84 anni n=2.662.145 (%)	≥85 anni n=1.091.877 (%)
1. Utilizzo di Diuretici risparmiatori di potassio tra gli utilizzatori di Ace inibitori o Sartani*	103.881 (2,7)	34.237 (2,0)	46.408 (3,0)	23.231 (4,0)
2. Utilizzo di Cortisonici tra gli utilizzatori di Chinoloni*	57.667 (7,0)	24.210 (6,6)	22.175 (7,0)	11.268 (7,7)
3. Utilizzo di Cortisonici tra gli utilizzatori di Fans o ASA*	175.088 (6,6)	75.288 (6,4)	70.241 (6,7)	29.546 (6,9)
4. Utilizzo di Chinoloni tra gli utilizzatori di Sulfaniluree*	12.367 (5,4)	5.053 (5,0)	5,320 (5,5)	1.983 (6,0)
5. Utilizzo di PPI tra gli utilizzatori di Clopidogrel*	179.403 (58,0)	60.419 (56,4)	80.110 (58,9)	38.759 (58,9)

* L'uso concomitante è stato calcolato per gli utilizzatori prevalenti nel periodo 1 aprile-30 giugno 2017:

- Indicatore 1 (Ace inibitori o Sartani): n=3.858.754;
- Indicatore 2 (Chinoloni): n=829.551;
- Indicatore 3 (Fans o ASA):
- Indicatore 4 (Sulfaniluree): n=229.519;
- Indicatore 5 (Clopidogrel): n=309.185.

DEPRESCREBING IN NH - SHELTER

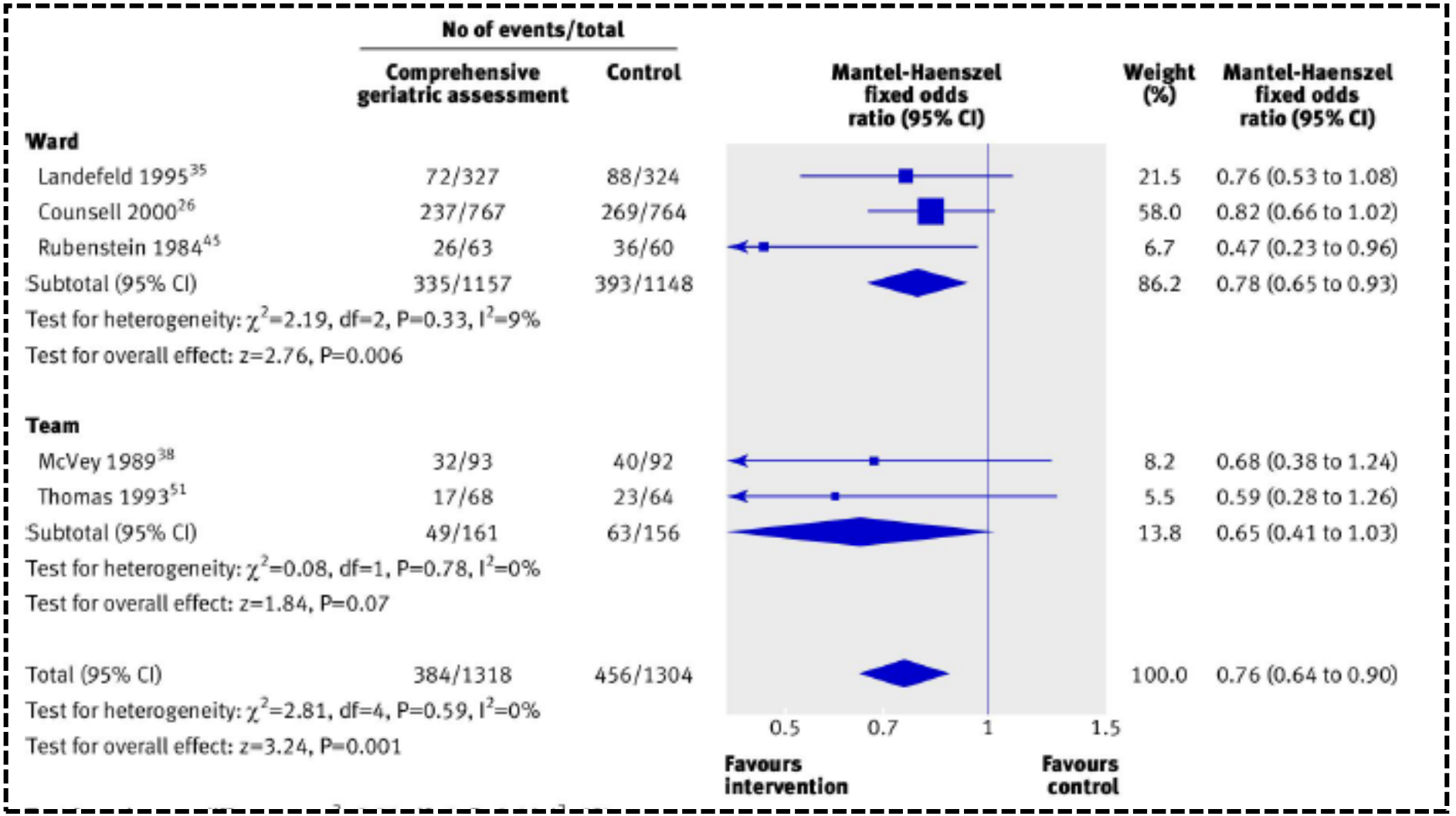


Onder G et al JAMDA in press

DEPRESCRIBING IN NH - SHELTER

	Odds Ratio	95% C.I.	P
Genere (femmine)	1.04	0.82-1.32	0.739
Età (anni)			
65-75	Ref.	-	-
75-85	0.78	0.57-1.06	0.115
85-95	0.60	0.44-0.82	0.001
95+	0.86	0.54-1.35	0.502
Cardiopatia ischemica	0.99	0.79-1.23	0.923
Ictus	0.93	0.73-1.19	0.570
Diabete	0.96	0.76-1.22	0.759
Insufficienza Cardiaca	0.79	0.61-1.03	0.080
Cancro	0.73	0.52-1.02	0.061
COPD	0.75	0.52-1.08	0.125
Demenza	1.08	0.85-1.36	0.535
Costipazione	0.86	0.68-1.08	0.194
Dolore	1.12	0.89-1.42	0.319
Dispnea	0.78	0.48-1.24	0.288
Disabilità ADL*			
Independenza	Ref.	-	-
Necessità di assistenza	1.00	0.75-1.34	0.984
Dipendenza	0.91	0.66-1.26	0.589
Deterioramento cognitivo†			
Intatto	Ref.	-	-
Leggero/moderato	1.40	1.06-1.85	0.016
severo	1.59	1.13-2.23	0.008
Depressione‡	1.04	0.84-1.28	0.733
Geriatri	1.25	1.01-1.56	0.046
Farmacisti	0.85	0.65-1.11	0.221

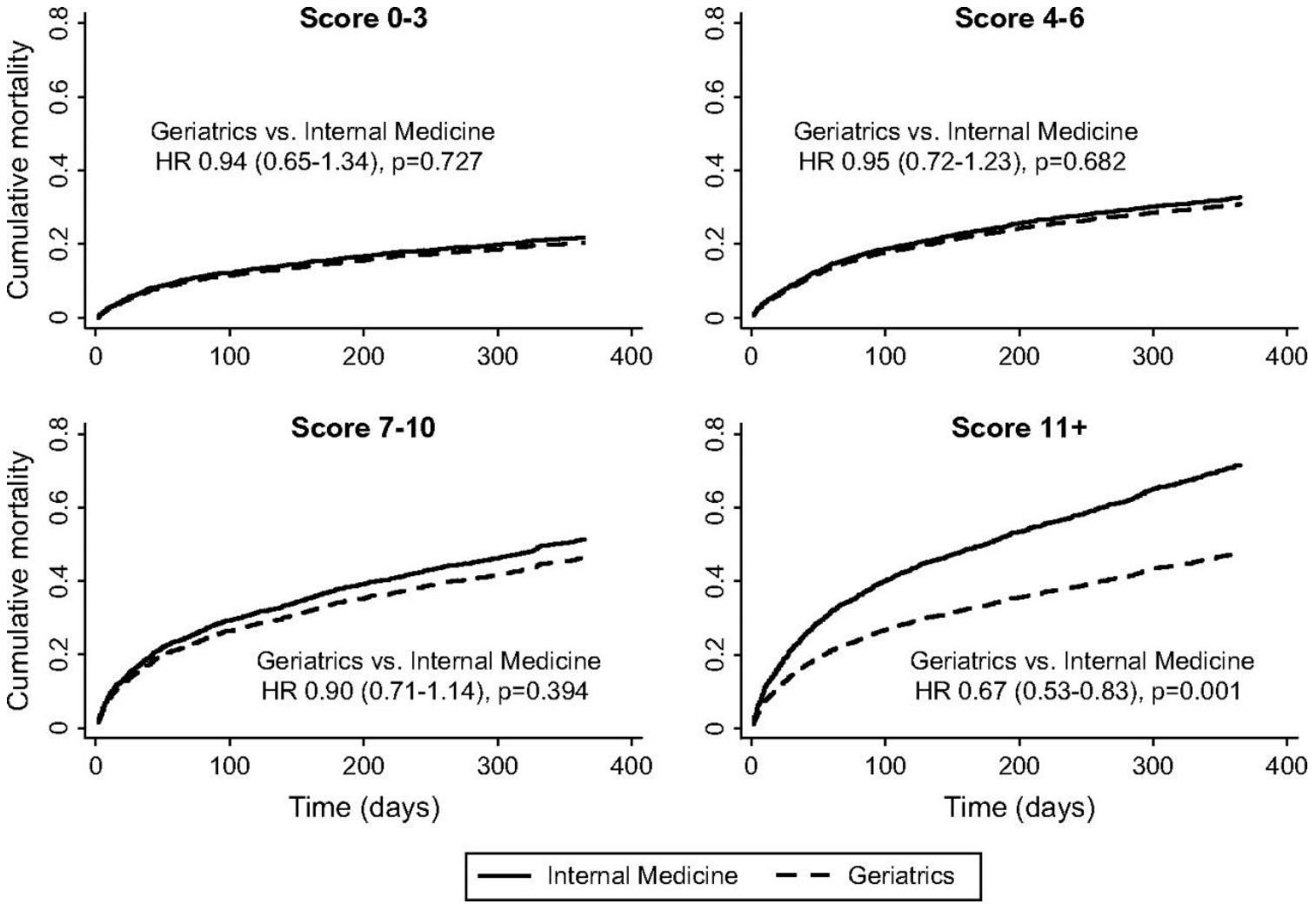
CGA for older adults admitted to hospital: meta-analysis of RCTs



Odds ratios for death or deterioration at the end of follow-up (median 12 months) in elderly patients according to comprehensive geriatric assessment (ward, team) after emergency admission at baseline

BMJ 2011;343:d6553

One-year survival as a function of hospital admission to an acute geriatrics or internal medicine ward, after stratification by risk of death score



J Gerontol A Biol Sci Med Sci 2009;65A:159-164

SPECIAL ARTICLES

Patient-Centered Care for Older Adults with Multiple Chronic Conditions: A Stepwise Approach from the American Geriatrics Society

American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity*

Guiding Principles:

1. Recognizing the **limitations of the evidence base**, interpret and apply the medical literature specifically to older adults with multimorbidity.
2. Frame clinical management decisions within the context of risks, burdens, benefits, and **prognosis** for older adults with multimorbidity.

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4. Use strategies for choosing **therapies that optimize benefit, minimize harm, and enhance quality of life** for older adults with multimorbidity.

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4. Use strategies for choosing therapies that optimize benefit, minimize harm, and enhance quality of life for older adults with multimorbidity.
5. Elicit and incorporate **patient preferences** into medical decision-making for older adults with multimorbidity.

The NEW ENGLAND JOURNAL of MEDICINE

Goal-Oriented Patient Care — An Alternative Health Outcomes Paradigm

David B. Reuben, M.D., and Mary E. Tinetti, M.D.

… focus on a patient's individual health goals within or across a variety of dimensions (e.g., symptoms; physical functional status, including mobility; and social and role functions) and determine how well these goals are being met…

NEJM FREE FULL TEXT Rubern DB NEJM 2012

GOAL ORIENTED CARE

1. Individually desired rather than universally applied health states;
2.It simplifies decision making for patients with multiple conditions by focusing on outcomes that span conditions and aligning treatments toward common goals
3. It prompts patients to articulate which health states are important to them and their relative priority

NEJM FREE FULL TEXT Rubern DB NEJM 2012

GOAL ORIENTED CARE

Comparison of Traditional Disease-Specific and Goal-Oriented Outcomes.*

Measurement Domain	Examples of Diseases	Traditional Outcomes	Goal-Oriented Outcomes
Survival	Cancer, heart failure	Overall, disease-specific, and disease-free survival	None if survival not a high-priority goal; survival until personal milestones are met (e.g., grandchild's wedding)
Biomarkers	Diabetes, COPD	Change in indicators of disease activity (e.g., glycated hemoglobin level, CRP level, and pulmonary-function tests)	None (not a meaningful outcome observed or felt by patient)
Signs and symptoms	Heart failure, COPD, arthritis	Inventory of disease-specific signs and symptoms (e.g., dyspnea, edema, and back pain)	Symptoms that have been identified as important by the patient (e.g., control of dyspnea or pain sufficient to perform an activity such as bowling or walking grandchild to school)
Functional status, including mobility	Cancer, heart failure, COPD	Usually none or disease-specific (e.g., Karnofsky score, NYHA functional classification, and 6-minute walk test)	Ability to complete or compensate for inability to complete specific tasks identified as important by the patient (e.g., ability to get dressed without help)

NEJM FREE FULL TEXT

Rubern DB NEJM 2012

SPRINTT

Sarcopenia & Physical fRailty IN older people:
multi-componenT Treatment strategies

A private - public partnership – will be a good approach to answer these complex questions

"Developing innovative therapeutic interventions against physical frailty and sarcopenia (ITI-PF&S) as a prototype geriatric indication"

Innovative Medicines Initiative

efpia

SANOFI

GlaxoSmithKline

NOVARTIS

Lilly

SERVIER

IMI Call n.9 (call for interest) was published on July 9th, 2013

Eligibility criteria

INCLUSION CRITERIA

Demographic characteristics

Age ≥70 years

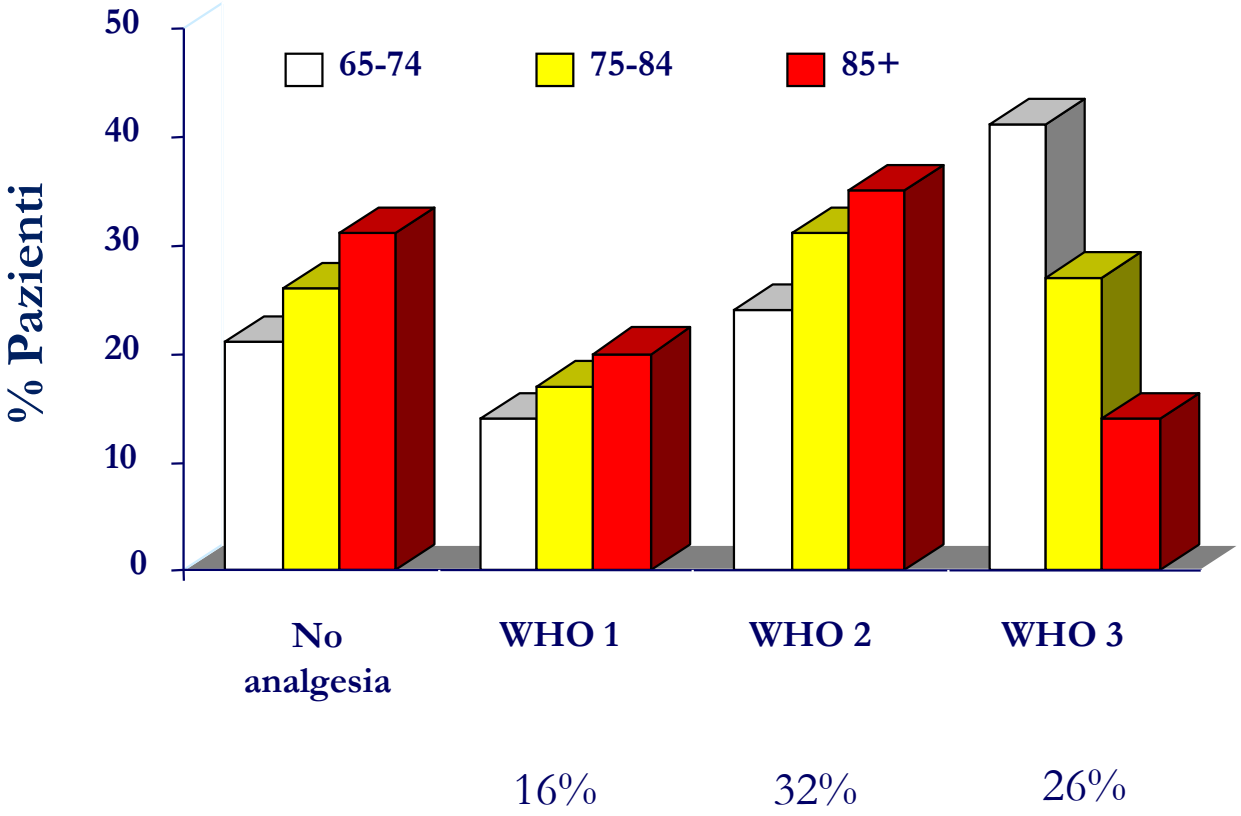
Physical function, body composition, and lifestyle criteria

- Able to complete the 400-meter walk test
- SPPB score between 3 and 9
- Presence of low muscle mass (DXA) according to FNIH
- Sedentary lifestyle
- Willingness to be randomized to either intervention group

Implementation of physical frailty in clinical practice

Condition	Measurable biological substrate	Measurable clinical manifestations	Measurable function
CHF	Myocardial dysfunction (echocardiography)	- Shortness of breath - Fatigue	6-min walking test
COPD	Airways destructive changes (spirometry)	- Dyspnoea - Cough - Sputum	6-min walking test
PAD	Arterial stenosis (Doppler echocardiography)	- Intermittent claudication - Numbness - Ulcers	Treadmill walking distance
PF	Reduced muscle mass (DXA)	- Slow walking speed - Poor balance - Weakness	SPPB

Management of pain in elderly patients with cancer. Systematic Assessment of Geriatric drug use via Epidemiology (SAGE)



38%

Morphin

4 out of 10 patients 65-74

1 out of 10 patients 85+

13%

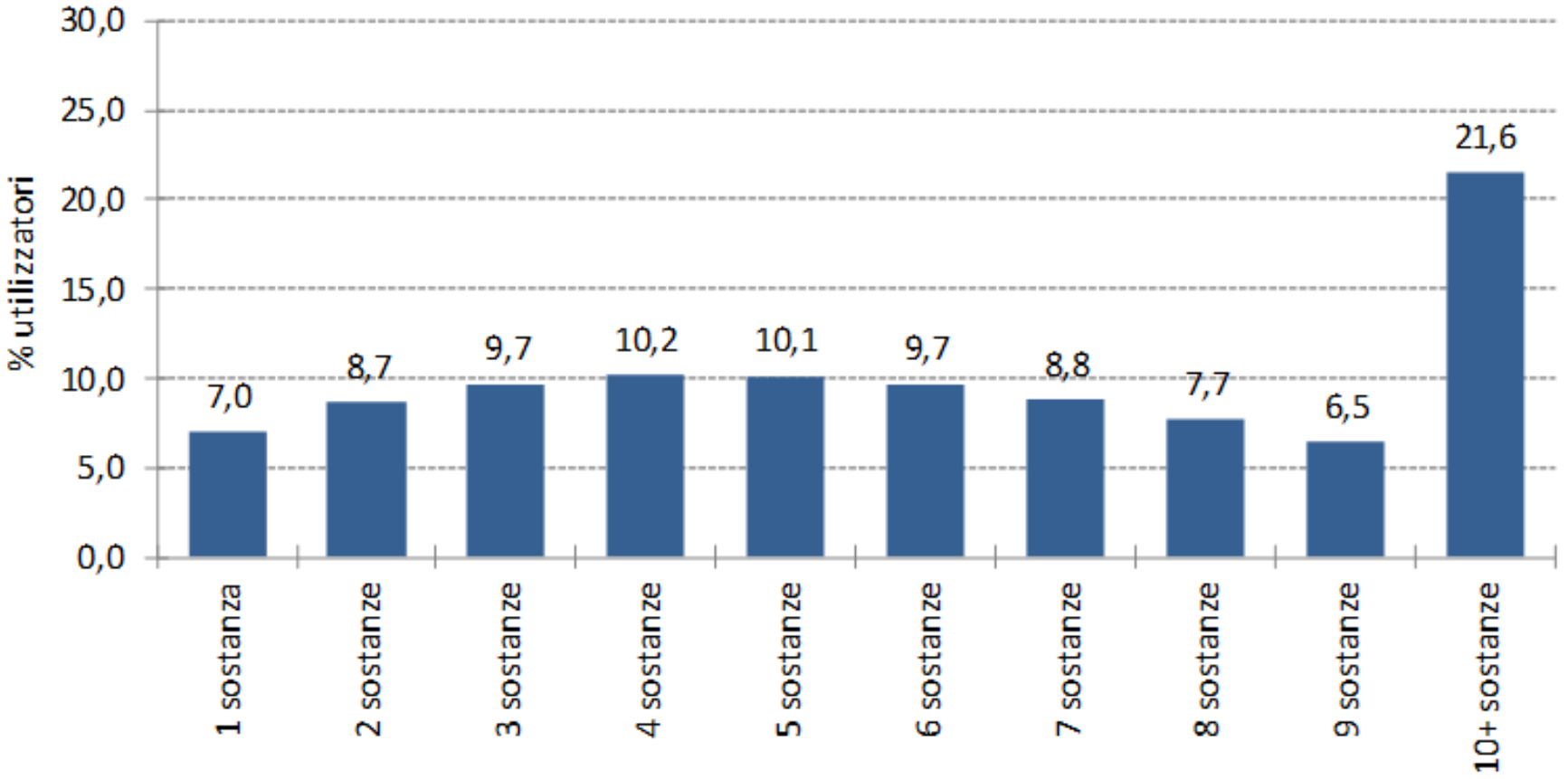
No analgesia

2 out of 10 patients 65-74

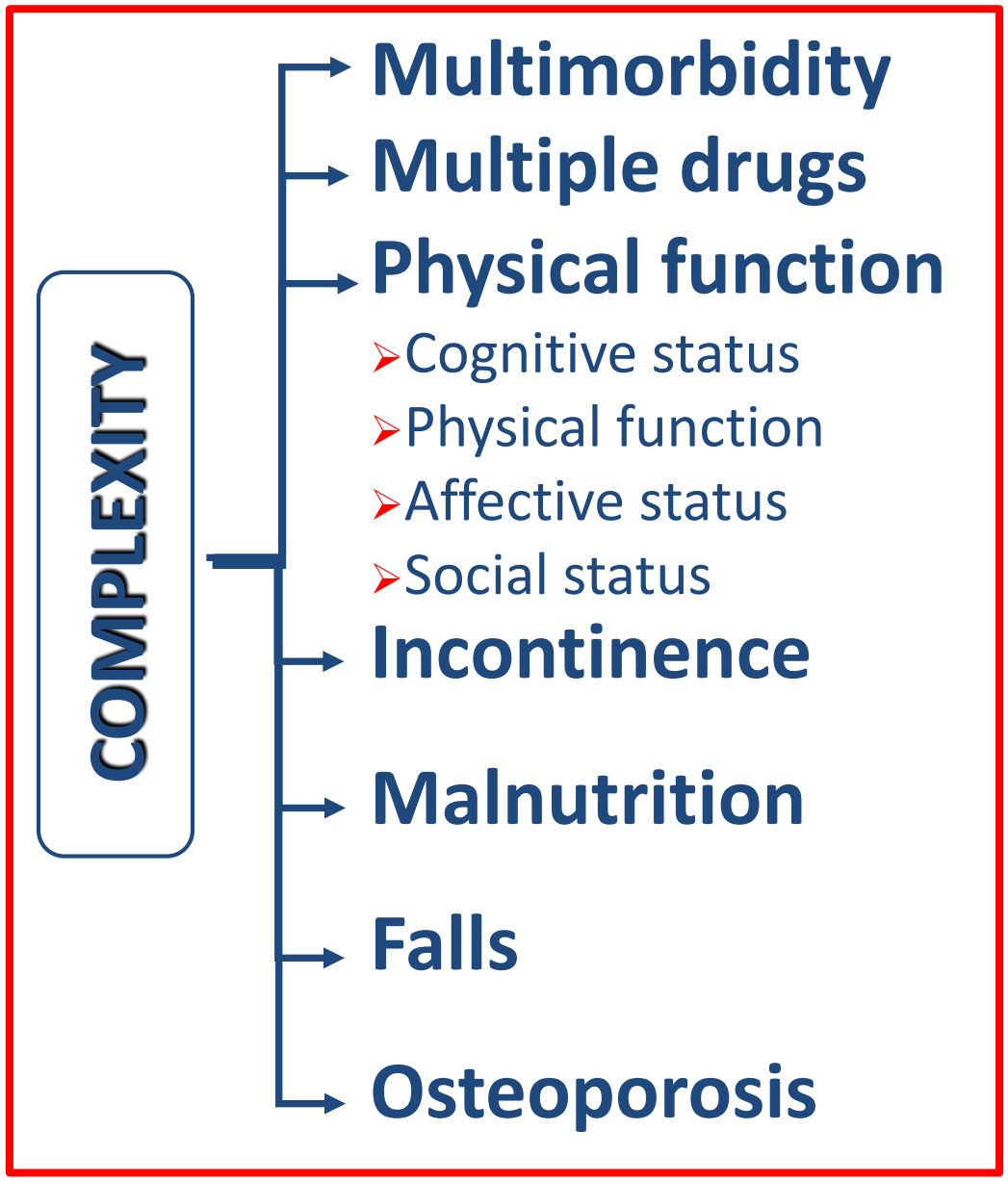
3 out of 10 patients 85+

Bernabei R. et al., JAMA 1998

Distribuzione degli utilizzatori nella popolazione di età ≥65 anni per numero di sostanze diverse (2017) – dati Osmed



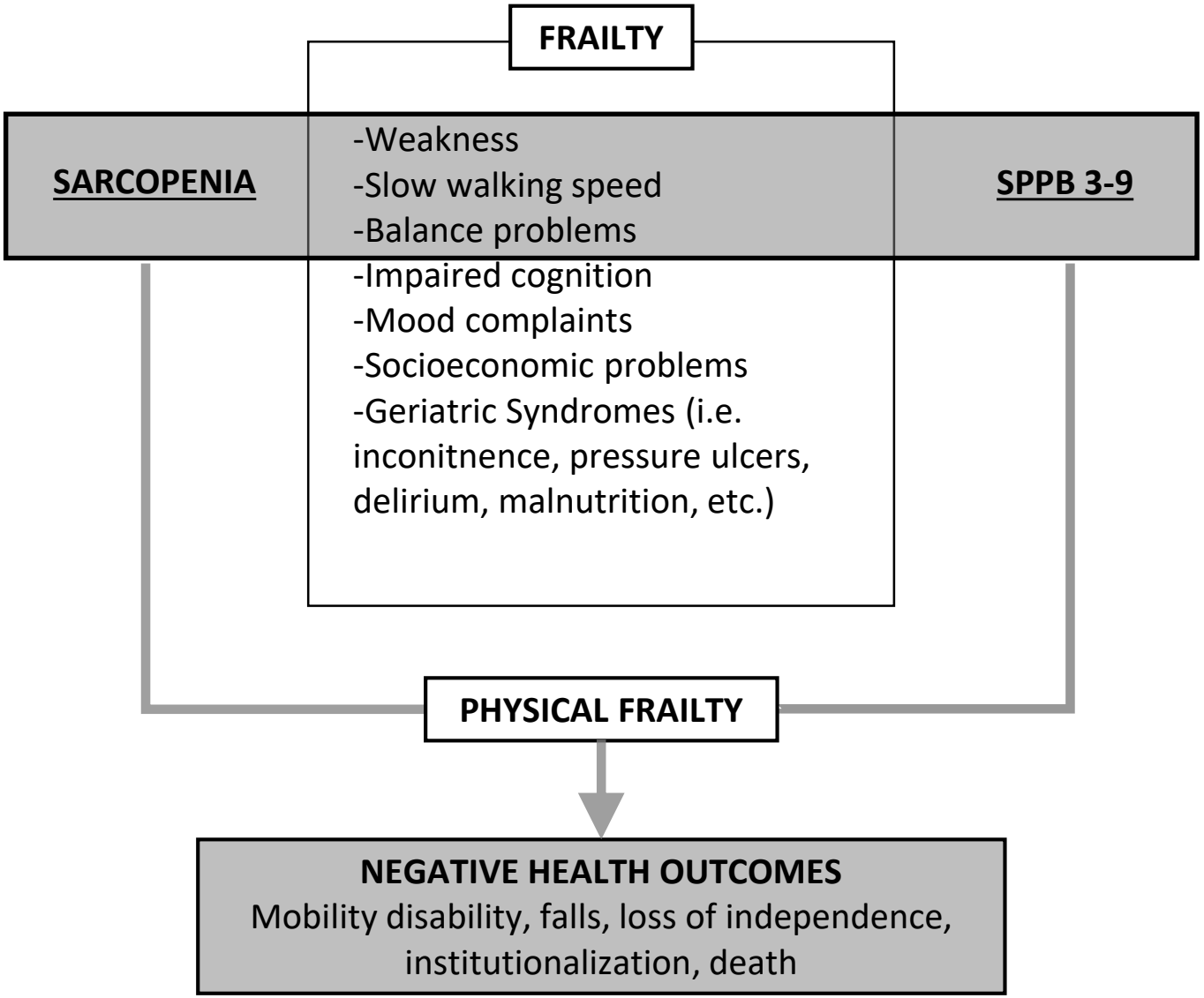
The «up-to-date» patient



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. NEJM2011

Identification of a target population and operationalization of frailty



Fragilità: definizione

- Sindrome multifattoriale, determinata dalla riduzione della fisiologica riserva funzionale e della capacità di resistere a eventi stressanti ambientali (capacità di omeostasi)
- Comporta un aumentato rischio di eventi clinici: disabilità, ospedalizzazione, istituzionalizza-zione, morte
- Condizione complessa e dinamica, della quale si sono proposti numerosi modelli