DEMENZA E MALATTIE SOMATICHE

Alessandra Marengoni, MD, PhD

BRESCIA UNIVERSITY - HEALTH & WEALTH
Università degli Studi di Brescia

History

Oslerian formalism: disease is defined on the basis of the organ system in which symptoms are manifest, and in which pathology is correlated.

This approach to **disease by disease** diagnosis, prognosis, and treatment has served the medical establishment and society well for many years but vastly overgeneralizes pathophenotypes.
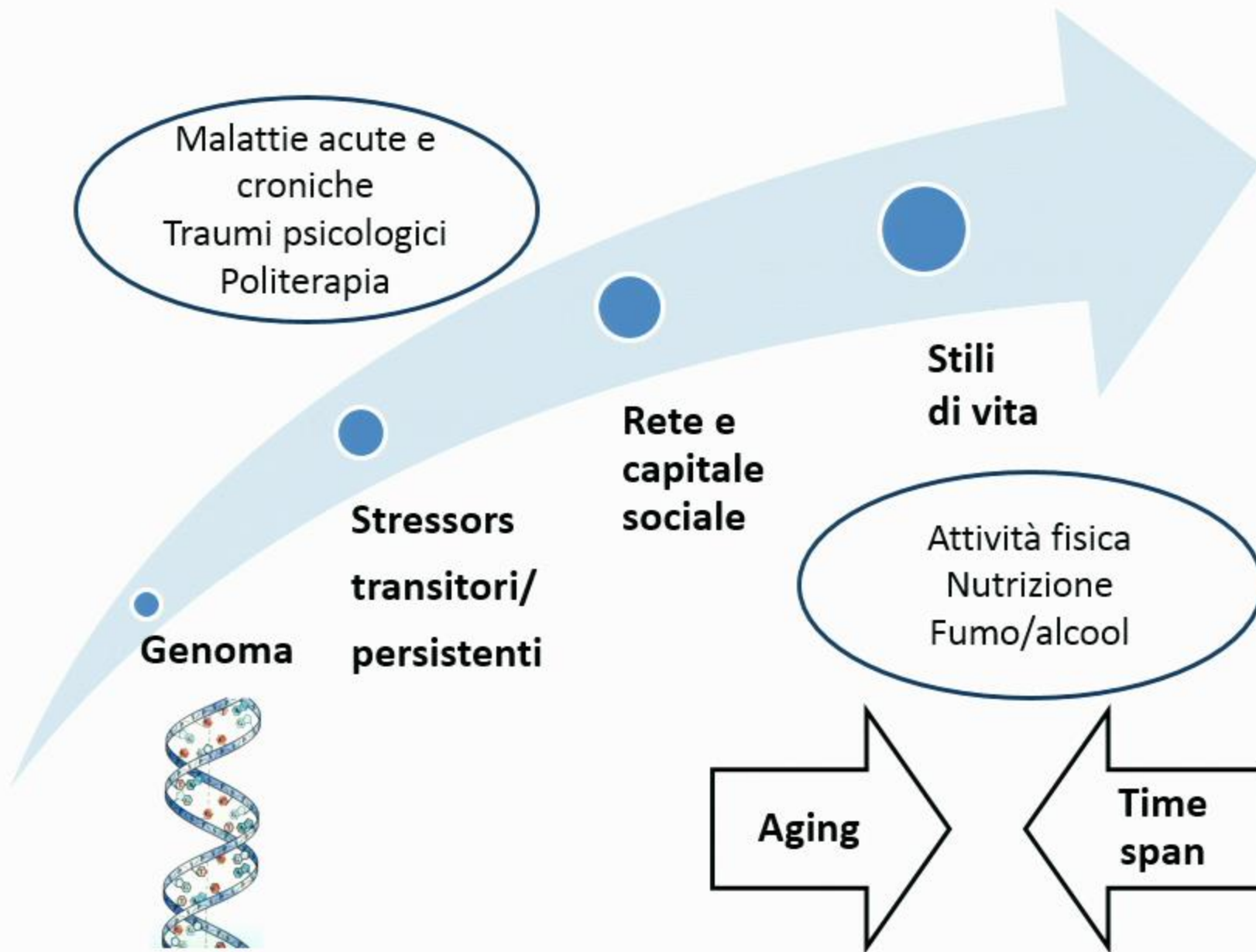
"the effective, moving, vitalizing work of the world is done between the ages of twenty-five and forty"
Sir William Osler, "The Fixed Period", farewell address at Johns Hopkins Medical School, 1905
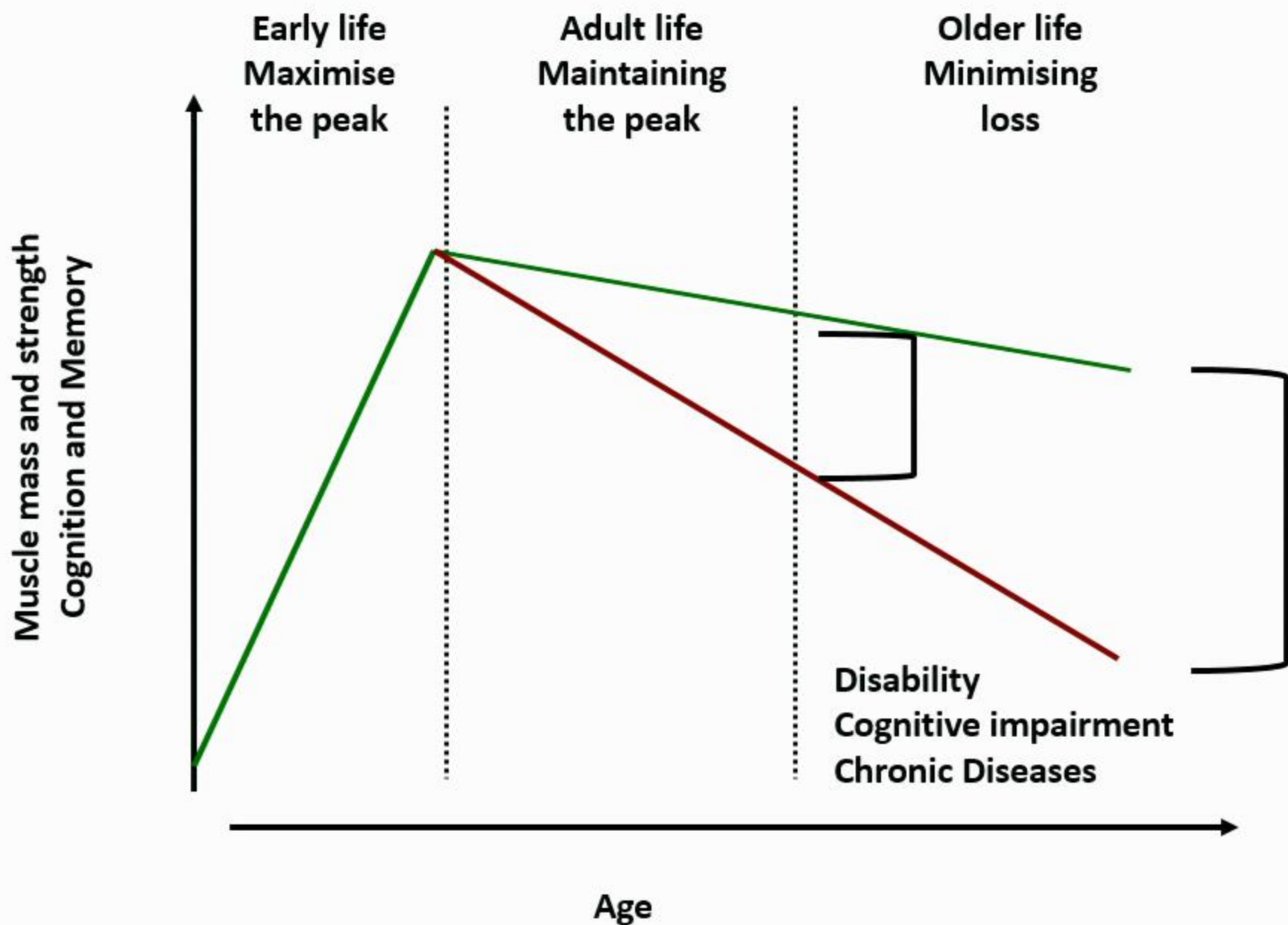

William Osler (1849-1919)

"Father of Modern Medicine"

Un complesso di fattori protettivi (o di rischio) durante l'arco della vita agisce come determinante di un invecchiamento di successo (o di fragilità)

Malattie acute e croniche
Traumi psicologici
Politerapia

Stili
di vita

Rete e
capitale
sociale

Stressors
transitori/
persistenti

Attività fisica
Nutrizione
Fumo/alcool

Genoma

Aging

Time
span

Early life
Maximise
the peak

Adult life
Maintaining
the peak

Older life
Minimising
loss

Muscle mass and strength
Cognition and Memory

Age

Disability
Cognitive impairment
Chronic Diseases

Modified WHO/HPS, Geneva 2000

Matthias Brandes   'Acqua Alta' 2010

- **Cluster di malattie somatiche e demenza**

- **Malattie somatiche e rischio di demenza**

- **Malattie somatiche e progressione di demenza**

- **Farmaci per malattie somatiche e demenza**

- **Malattie somatiche/demenza e eventi avversi**

BMC
Psychiatry

RESEARCH ARTICLE   **Open Access**

Comorbidity of dementia: a cross-sectional study of primary care older patients

Beatriz Poblador-Plou[1,2,3], Amaia Calderón-Larrañaga[1,2,3,4*], Javier Marta-Moreno[1,5], Jorge Hancco-Saavedra[3], Antoni Sicras-Mainar[6], Michael Soljak[7] and Alexandra Prados-Torres[1,2,3,4]

Table 1 Study population

	Patients ≥65 without dementia			Patients ≥65 with dementia			p value
	Total	Men	Women	Total	Men	Women	
n (%)	68,844 (94.55)	28,176 (40.93)	40,668 (59.07)	3,971 (5.45)	1,185 (29.84)	2,786 (70.16)	0.000
Mean age (SD)	75.53 (7.28)	74.62 (6.85)	76.16 (7.51)	80.22 (7.09)	79.10 (6.94)	80.70 (7.10)	0.000
Number of diseases n (%)							
1	15,052 (21.86)	6,718 (23.84)	8,334 (20.49)	490 (12.34)*	137 (11.56)*	353 (12.67)*	0.000
2	15,934 (23.15)	6,730 (23.89)	9,204 (22.63)	717 (18.06)	218 (18.40)	499 (17.91)	0.000
3	12,795 (18.59)	5,085 (18.05)	7,710 (18.96)	856 (21.56)	260 (21.94)	596 (21.39)	0.000
4	8,500 (12.35)	3,203 (11.37)	5,297 (13.02)	700 (17.63)	222 (18.73)	478 (17.16)	0.000
5	4,604 (6.69)	1,634 (5.80)	2,970 (7.30)	555 (13.98)	151 (12.74)	404 (14.50)	0.000
≥6	3,831 (5.55)	1,320 (4.68)	2,511 (6.17)	653 (16.44)	197 (16.62)	456 (16.38)	0.000
Mean number of diseases (SD)	2.44 (1.75)	2.32 (1.69)	2.52 (1.79)	3.69 (1.95)	3.69 (1.94)	3.68 (1.96)	0.000

SD, standard deviation.
*Patients with dementia only.

BMC
Geriatrics

RESEARCH ARTICLE   **Open Access**

A claims data-based comparison of comorbidity in individuals with and without dementia

Kathrin Bauer[1], Larissa Schwarzkopf[1*], Elmar Graessel[2] and Rolf Holle[1]

In più
Anemia
Diabete
Disturbi elettrolitici
Depressione
Psicosi
Parkinson
Scompenso cardiaco
CVD
IRC
Fratture
Polmonite

In meno
Neoplasie
Dislipidemie
Ipovisus
Ipertensione
Artrosi
Gotta
Dolore

Malattia di Parkinson, CVD, diabete, e forse depressione sono anche fattori di rischio per demenza

Disturbi idroelettrolitici da inadeguato apporto di liquidi, polmonite, incontinenza, disturbi pscichiatrici, cadute e fratture sono sequele della demenza
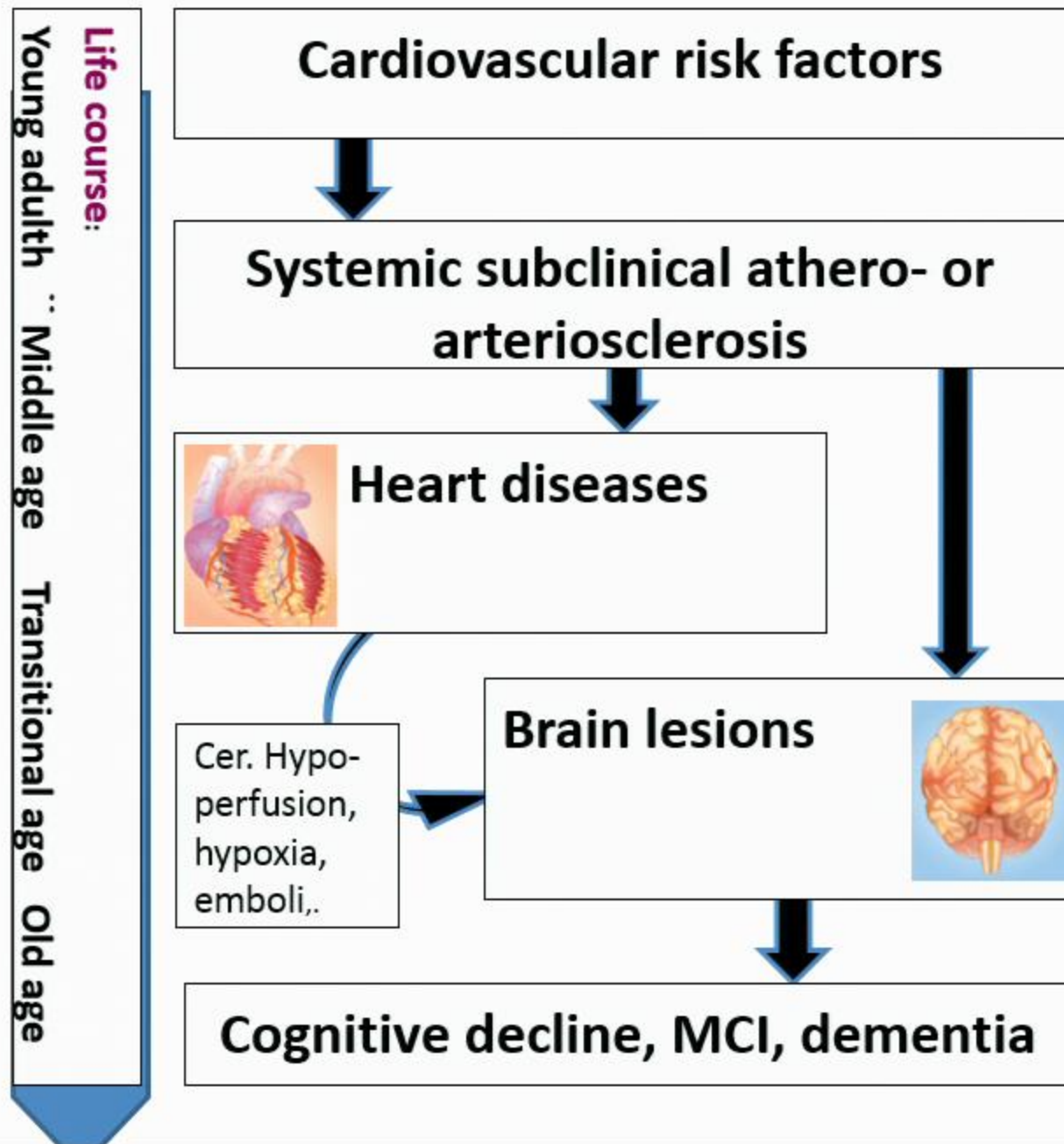
Ipovisus per deficit di comunicazione

In presenza di demenza il medico può non considerare malattie meno gravi e decidere di non trattarle per non ridurre la qualità della vita in proporzione a quello che sarebbe il beneficio del farmaco
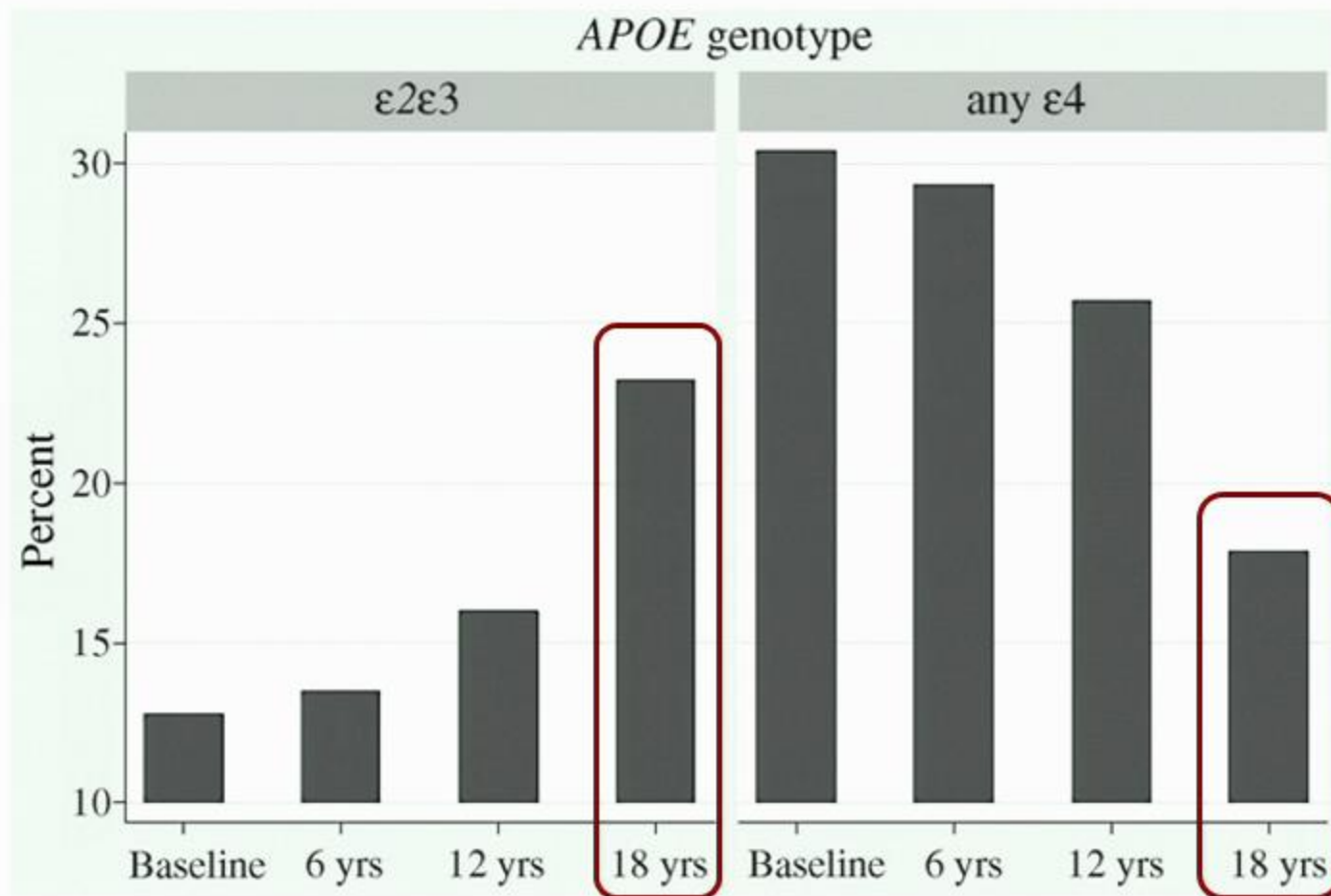
Heart-brain connection in aging

Qiu & Fratiglioni. Nat Rev Cardiol 2014 (in press)

APOLIPOPROTEIN E, APOE

Associato alla longevità forse per le associazioni con la Malattia di Alzheimer e le malattie cardiovascolari

Rosvall et al. Neurob Aging 2009;30:1545-1551

Preventive strategies against CVD and Dementia

➤ **Promoting healthy lifestyles**
  - non-smoking
  - moderate alcohol intake
  - physical activity
  - (diet)

➤ **Decreasing vascular burden**
  - hypertension   - heart disease
  - diabetes   - stroke

➤ **Increasing brain reserve**

© The Sports Museum of Finland

Association between potential predictors and the incidence of multimorbidity

| Predictors of interest	No chronic disease at baseline (n=140)	One chronic disease at baseline (n=250)
	OR (95% CI)*	OR (95% CI)*
Age (years, continuous)	0.99 (0.89-1.11)	1.09 (1.01-1.17)**
Sex (female vs male)	0.87 (0.30-2.52)	0.88 (0.42-1.87)
Education (low vs high education)	1.36 (0.56-3.32)	0.94 (0.51-1.75)
Katz ADL(number of disabilities, continuous)	0.80 (0.25-2.60)	1.01 (0.64-1.60)
Hemoglobin (g/l, continuous)	0.98 (0.93-1.03)	1.01 (0.99-1.04)
ESR (mm/hour, continuous)	1.02 (0.99-1.06)	1.02 (0.99-1.04)
WBC (*10^9 leucocytes/l, continuous)	1.19 (0.89-1.58)	1.06 (0.92-1.22)
Diastolic blood pressure (increase of 10 mmHg)	0.98 (0.94-1.01)	0.99 (0.96-1.02)
Physical activity (yes vs no)	0.44 (0.15-1.28)	1.55 (0.61-3.92)
Depressive symptoms (CPRS , continuous)	1.18 (0.99-1.40)***	1.03 (0.93-1.14)
Worse cognitive abilities (MMSE, continuous)	1.22 (1.00-1.48)**	1.04 (0.96-1.12)
Smoking (3 categories: never, former, current, continuous)	0.86 (0.49-1.52)	1.29 (0.80-2.07)
Alcohol drinking		
< 1 unit/week vs 1-6 units/week	0.90 (0.36-2.22)	1.87 (0.98-3.58)***
≥ 7 units/week vs 1-6 units/week	11.43 (0.37-348.43)	2.89 (0.36-22.97)
BMI		
<18.5 kg/m^2 vs 18.5-25 kg/m^2	1.30 (0.11-7.98)	0.95 (0.30-3.03)
>25 kg/m^2 vs 18.5-25 kg/m^2	1.48(0.47-4.71)	1.33 (0.68-2.60)

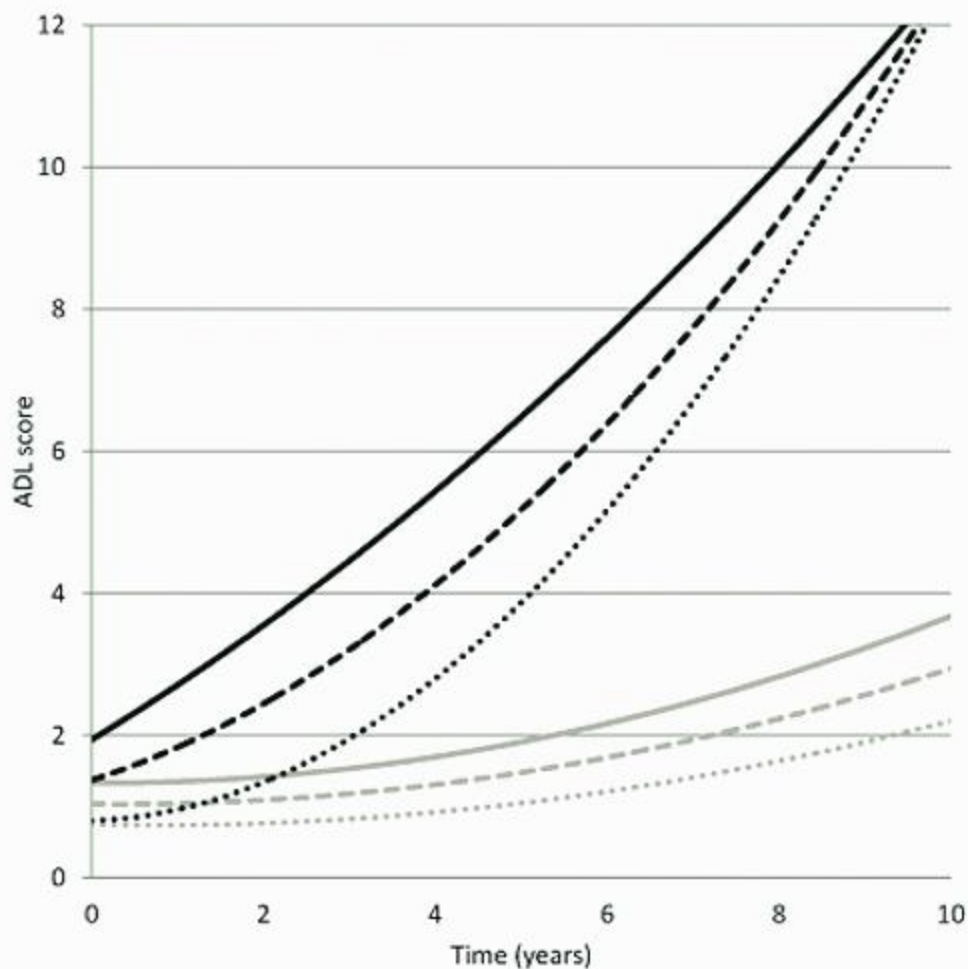PREVALENCE OF DISABILITY IN DIFFERENT DISEASE CLUSTERS

PLOS | ONE
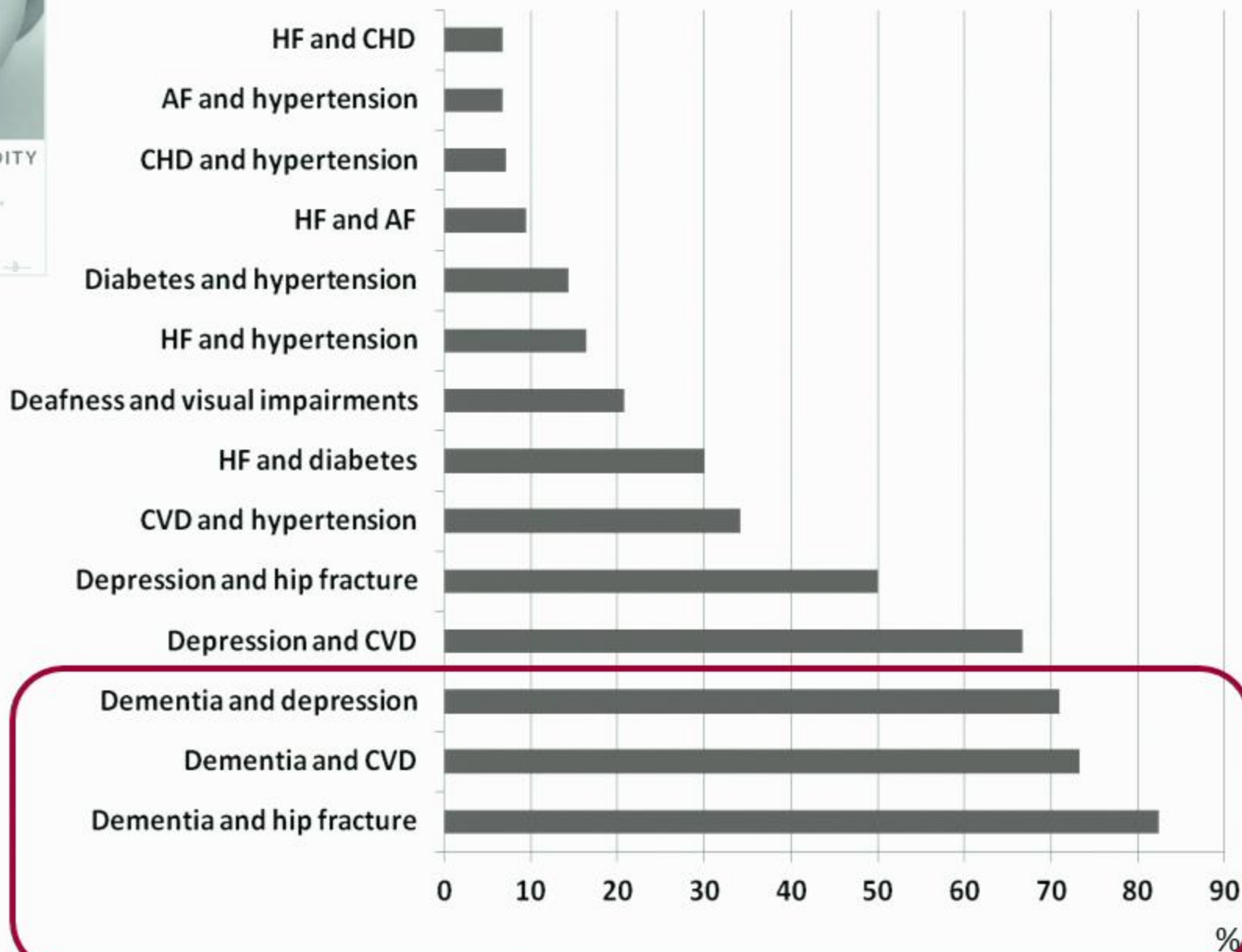
The Influence of Multimorbidity on Clinical Progression of Dementia in a Population-Based Cohort

René J. F. Melis[1]*, Alessandra Marengoni[2], Debora Rizzuto[3], Steven Teerenstra[4], Miia Kivipelto[3], Sara B. Angleman[3], Laura Fratiglioni[3]
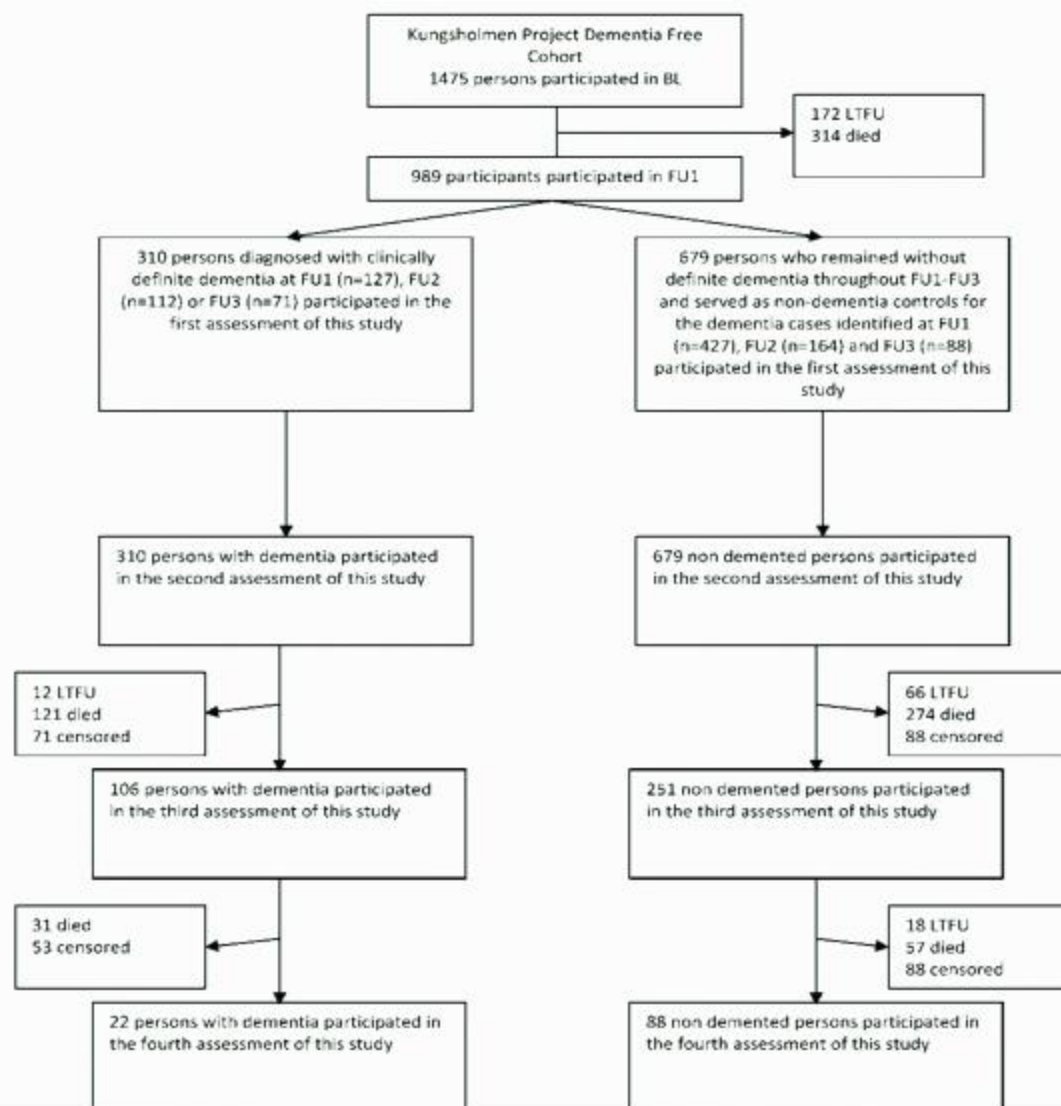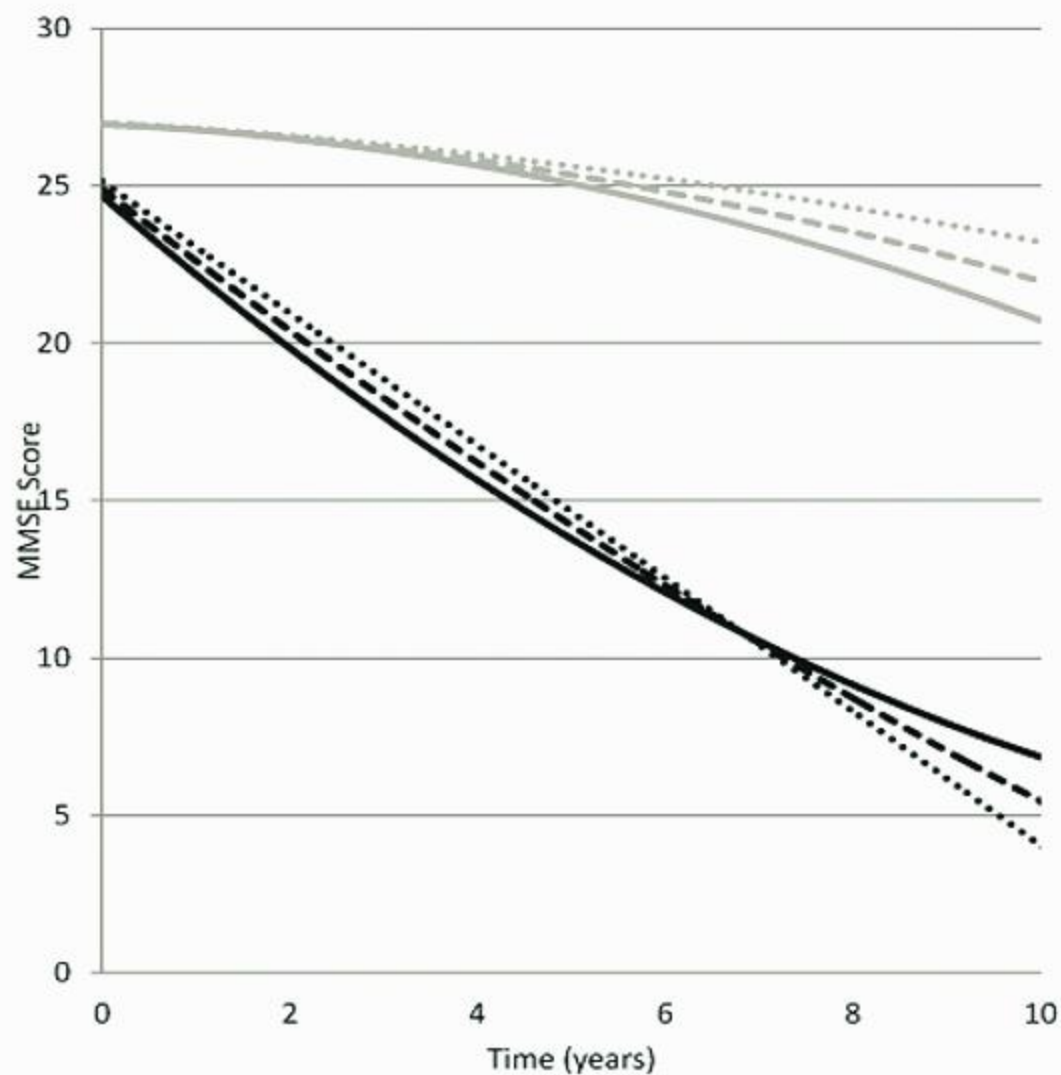
Figure 2. Mean Growth Curves for ADL Functioning. Mean Growth Curves for ADL Functioning* (Higher Score Indicates Worse Functioning) for Persons with Incident Dementia with 0 (black, dotted), 1 (black, dashed) or 2+ (black, solid) Diseases and Persons without Dementia with 0 (grey, dotted), 1 (grey, dashed) or 2+ (grey, solid) Diseases as Predicted by a Model 3 in Table 3. * Functioning in Activities of Daily Living (ADL) was assessed with the six Katz ADL items scored on a three point scale (0=no help needed, 1=some help needed, 2=much help needed), resulting in a score ranging 0–12, where higher scores indicate more help needed.

Figure 3. Mean Growth Curves for Cognitive Functioning. Mean Growth Curves for Cognitive Functioning* (Higher Score Indicates Better Functioning) for Persons with Incident Dementia with 0 (black, dotted), 1 (black, dashed) or 2+ (black, solid) Diseases and Persons without Dementia with 0 (grey, dotted), 1 (grey, dashed) or 2+ (grey, solid) Diseases as Predicted by a Model 6 in Table 4. *Cognitive functioning was assessed with MiniMental State Examination (MMSE), score ranging 0–30, where lower scores indicate worse functioning.
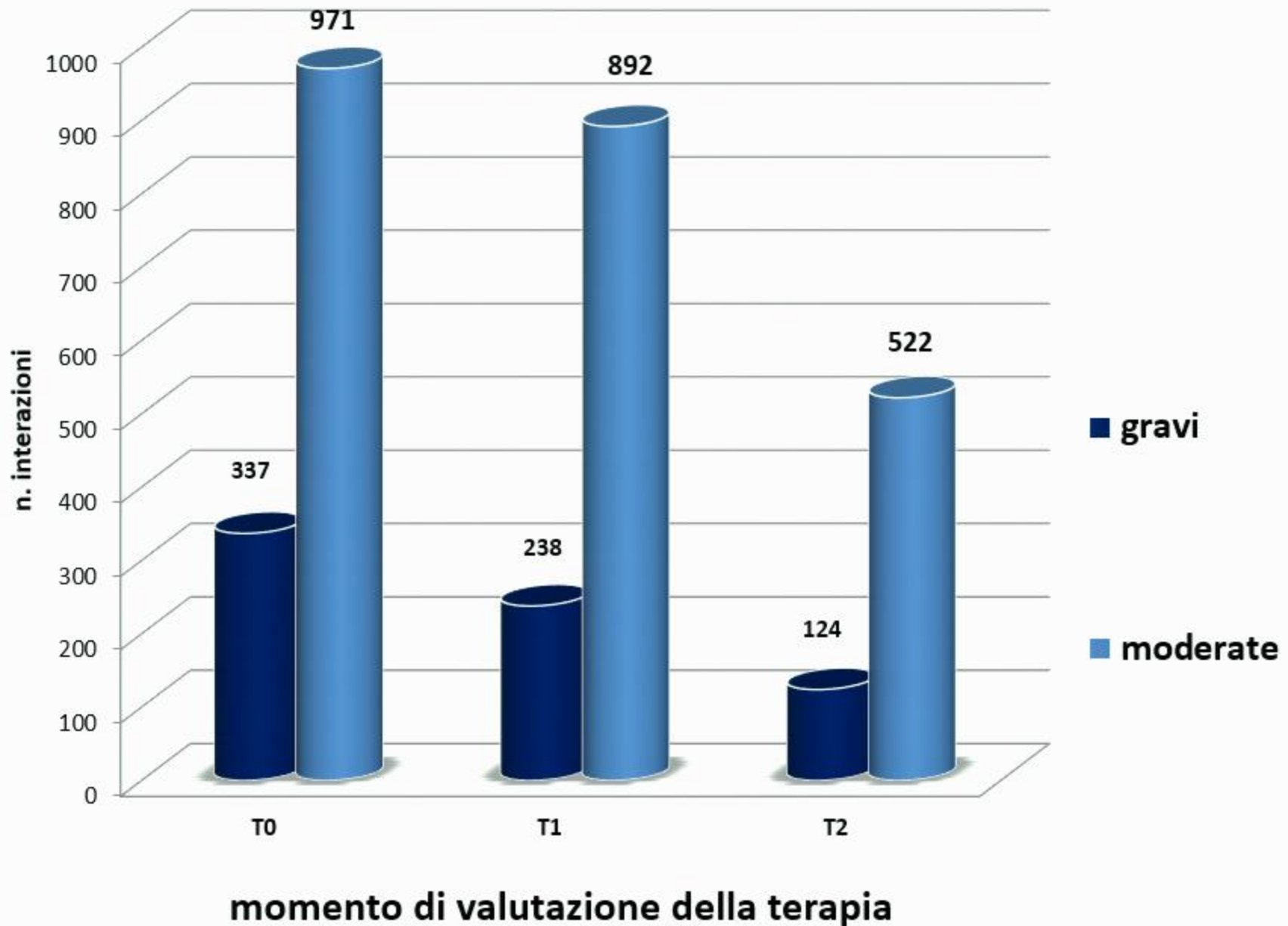
Medication Use in Nursing Home Residents with Advanced Dementia

Tija et al, J Am Geriatr Soc 2010
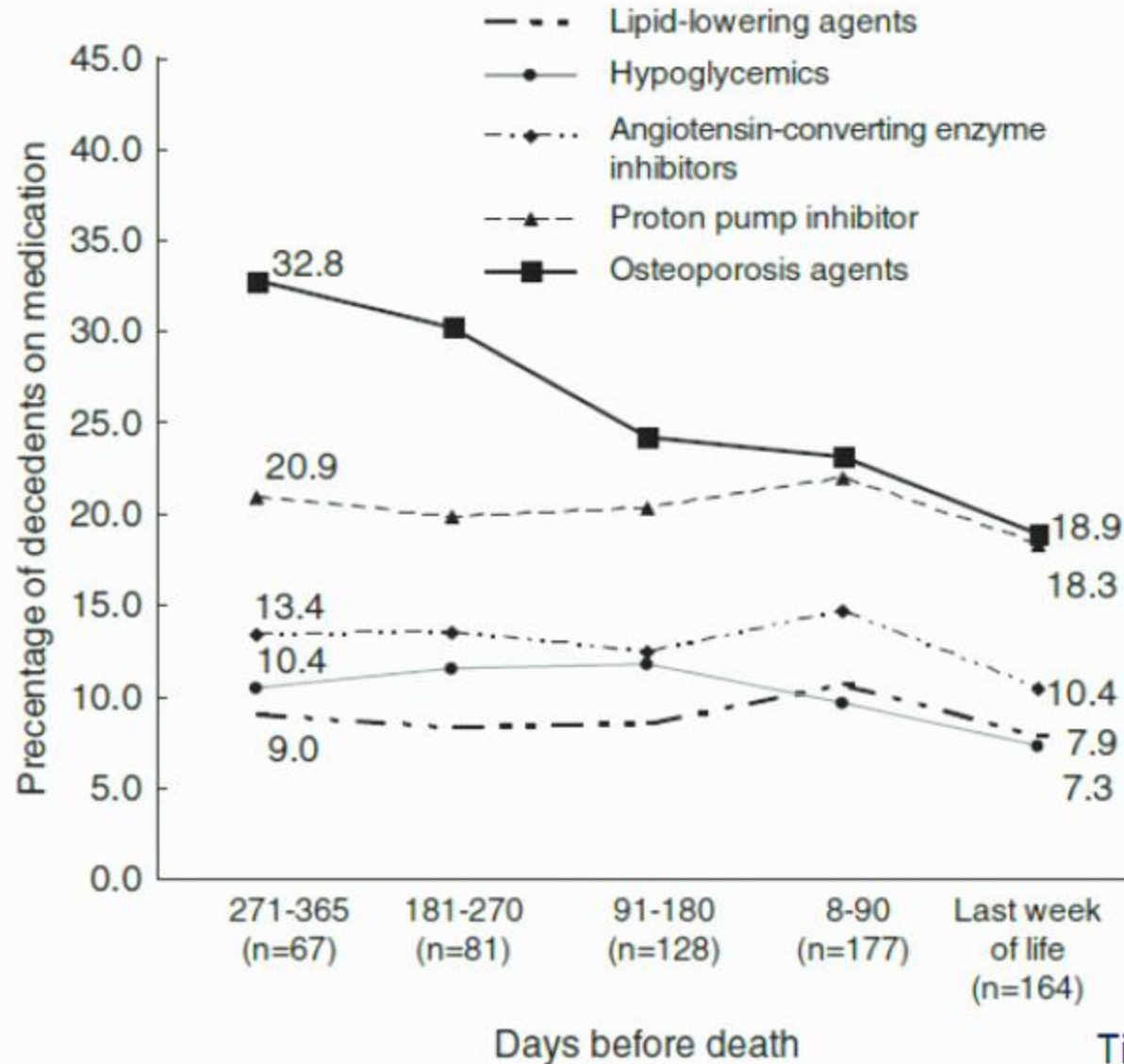
STUDIO OPEN
Optimizing prescription in Elderly patients in Nursing home
Interazioni gravi e moderate

Original Study

Impact of Polypharmacy on Occurrence of Delirium in Elderly Emergency Patients

Christophe Hein MD [a,*], Adrien Forgues MD [a], Antoine Piau MD [a], Agnès Sommet MD, PhD [b,c], Bruno Vellas MD, PhD [a,c], Fati Nourhashémi MD, PhD [a,c]
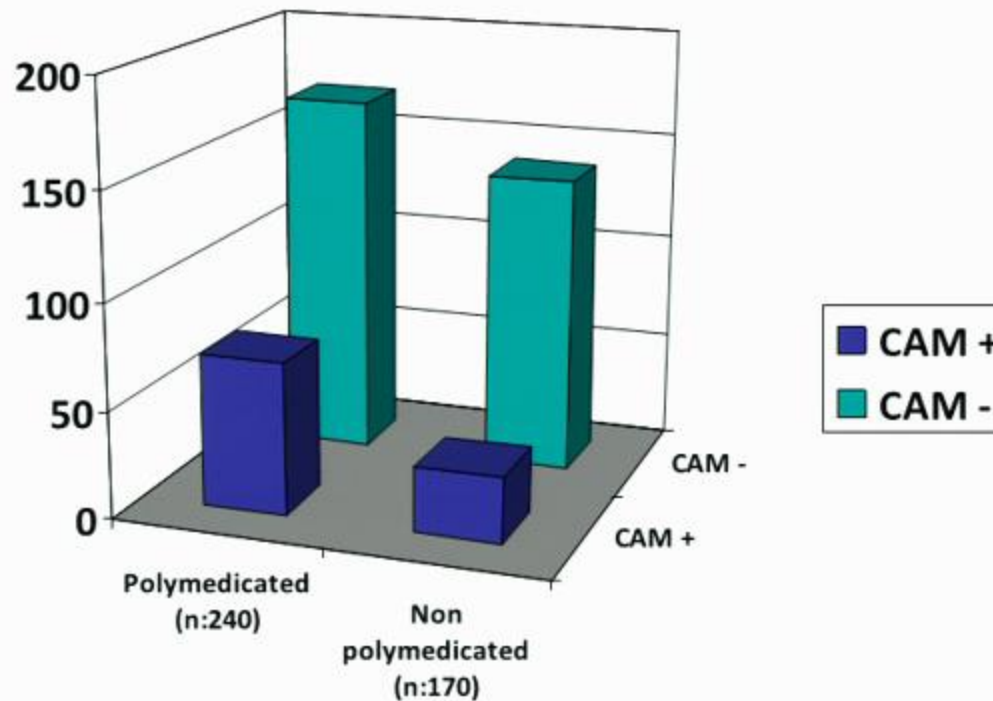

Fig. 1. Proportion of delirium and polypharmacy.

Multivariate Analysis of Risk Factors for Delirium (CAM+)

CAM+	OR	P	95% CI
Age	2.15	.016	(1.15–3.99)
Dementia	3.16	.001	(1.74–5.72)
Renal insufficiency	1.08	.798	(0.59–1.96)
Delirium-inducing drugs	0.74	.335	(0.40–1.35)
Polypharmacy	2.33	.010	(1.23–4.41)

CAM, Confusion Assessment Method.

IM - ORIGINAL

The stigma of low opioid prescription in the hospitalized multimorbid elderly in Italy

Table 4 Univariate associations with opioid prescription at hospital discharge in the three samples of REPOSI

	Sample 2008		Sample 2010		Sample 2012	
	Opioids		Opioids		Opioids	
	No	Yes	No	Yes	No	Yes
Age, yrs, mean (SD)	79.2 (7.5)	77.7 (8.0)	78.9 (7.4)	78.6 (7.9)	79.3 (7.5)	78.7 (6.9)
Male, number (%)	506 (46.5)	29 (43.3)	540 (48.4)	25 (39.7)	523 (48.1)	40 (51.9)
Total drugs at discharge, mean (SD)	5.9 (2.8)	6.4 (3.3)	6.2 (2.8)	6.9 (3.0)*	6.3 (3.1)	7.1 (2.8)†
SBT, mean (SD)	–	–	9.6 (8.0)	8.4 (8.8)	9.1 (7.8)	8.6 (7.1)
Barthel Index, mean (SD)	–	–	78.4 (29.6)	72.9 (31.6)	74.9 (31.1)	68.1 (32.8)
Dementia diagnosis, number (%)	102 (9.4)	4 (6.0)	84 (7.5)	6 (9.5)	113 (10.4)	3 (3.9)
Severe constipation, number (%)	23 (2.1)	3 (4.5)	19 (1.7)	1 (1.6)	7 (0.6)	2 (2.6)*

* $p = 0.05$

† $p < 0.01$

	Dementia diagnosis		
	No	Yes	p.
	(N=324)	(N=230)	
Hypertension			
At least one procedure (%)	35.0	28.6	.184
Echocardiograpy	13.4	9.1	.191
Abdominal ultrasounds	19.9	18.8	.789
24-hours Blood Pressure	1.6	0.6	.392
Heart failure			
Echocardiograpy	18.9	18.2	.921
Arrythmias			
Echocardiograpy	33.8	11.9	<0.003
Holter-ECG	36.4	18.6	<0.02
Coronary heart diseases			
Echocardiograpy	16.2	5.6	.266

Sampson E et al. Dementia in the acute hospital: Prospective cohort study of prevalence and mortality. *Br J Psych 2009 195, 61-6*

- 671 consecutive emergency admissions >70 to London DGH
- Assessed within 72 hours by old age psychiatrist and screened with CAM then MMSE and structured clinical assessment
- **42.4% had dementia**
- **Only half had been diagnosed before admission**
- In Men 70-79, prevalence 16%
- In Men over 90, 48%
- In Women 70-79, prevalence 29%
- In Women over 90, 75%
- "UTI" or "Pneumonia" were cause of admission in 41%
- **Associated with higher mortality. For those with severe cognitive impairment adjusted mortality risk 4.02 (2.24, 7.36)**

Characteristics and 3-months mortality rate of 3300 in patients affected by Low Respiratory Tract Infections (LRI) and dementia.

	Total (N=3300)	NoLRI-NoD (N=2566)	YLRI-NoD (N=265)	NoLRI-YD (N=345)	YLRI-YD (N=124)	p
	M±SD (%)	M±SD (%)	M±SD (%)	M±SD (%)	M±SD (%)	
Age (years)	79.2±8.0	78.4±7.7	80.0±8.2	83.2±7.7	83.4±8.4	0.001
Gender (males)(%)*	(38.3)	(24.5)	(24.5)	(24.5)	(19.3)	0.001
MMSE score	21.8±8.5	24.9±4.4	23.4±4.9	4.5±4.7	3.7±4.4	0.001
GDS score	4.6±3.5	4.6±3.5	4.2±3.1	---	---	0.155
Barthel Index (15 days bef)	78.7±27.9	86.5±19.8	76.2±26.6	45.7±34.5	30.2±28.7	0.001
Barthel Index (on adm)	60.1±38.1	71.8±32.2	48.6±37.1	22.0±29.2	5.5±14.2	0.001
IADL (functions lost)	3.3±2.9	2.6±2.6	3.4±2.9	6.3±2.4	7.0±1.6	0.001
Diseases (n)	5.1±2.0	5.1±1.9	5.3±2.0	5.2±2.2	5.4±2.3	0.142
Charlson Index	5.3±1.8	5.0±1.7	5.5±1.9	5.8±2.1	6.5±2.2	0.001
Drugs (n)	5.7±2.9	5.4±2.6	6.2±3.3	5.8±3.1	6.9±3.0	0.194
APACHE II score	10.6±5.9	9.1±4.9	13.7±4.9	13.0±6.8	18.3±6.6	0.001
APACHE II-APS subscore	4.4±5.2	3.1±3.9	6.1±5.1	6.5±6.4	10.9±6.9	0.001
Serum Albumin (g/dl)	3.7±0.7	3.8±0.6	3.4±0.6	3.3±0.7	3.1±0.6	0.001
Hemoglobin (g/dl)	12.5±2.3	12.6±2.3	12.2±2.2	12.0±2.5	11.9±2.5	0.000
Serum Cholesterol (mg/dl)	187.3±53.3	192.2±51.9	162.8±49.6	175.4±53.5	160.9±52.5	0.001
CPR (mg/dl)	4.4±7.4	2.9±5.7	9.1±10.4	7.3±9.6	11.1±9.1	0.001
Creatinine (mg/dl)	1.1±0.7	1.1±0.6	1.3±0.8	1.2±1.0	1.4±1.1	0.000
Length of stay (days)	6.5±3.7	6.5±3.6	7.8±4.1	5.8±4.0	5.4±3.9	0.001
3 mos mortality (%)*	(13.9)	(9.0)	(14.7)	(35.4)	(54.0)	0.001

In-hospital death according to dementia diagnosis in acutely ill elderly patients: the REPOSI study

A. Marengoni[1], S. Corrao[2], A. Nobili[3], M. Tettamanti[3], L. Pasina[3], F. Salerno[4], A. Iorio[5], M. Marcucci[5], F. Bonometti[1] and P.M. Mannucci[6] on behalf of SIMI Investigators

Table 3 Odds ratio (OR) and 95% confidence intervals (CI) for in-hospital death due to the combined effect of dementia and adverse clinical events. N = Number

	All	N of deaths	OR	95% CI
No dementia and no events	720	10	1	—
No dementia and at least one event	384	45	10.80	4.87–24.08
Dementia and no events	64	3	4.25	1.00–19.16
Dementia and at least one event	53	8	20.74	6.94–61.96

Model adjusted for age, gender, education, number of drugs, the Charlson Index, length of hospital stay and vital parameters.

Adverse Clinical Events and Mortality During Hospitalization and 3 Months After Discharge in Cognitively Impaired Elderly Patients

Alessandra Marengoni,[1] Alessandro Nobili,[2] Valentina Romano,[1] Mauro Tettamanti,[2] Luca Pasina,[2] Sylvestre Djade,[2] Salvatore Corrao,[3] Francesco Salerno,[4] Alfonso Iorio,[5] Maura Marcucci,[6] and Pier Mannuccio Mannucci[7] on behalf of SIMI* Investigators
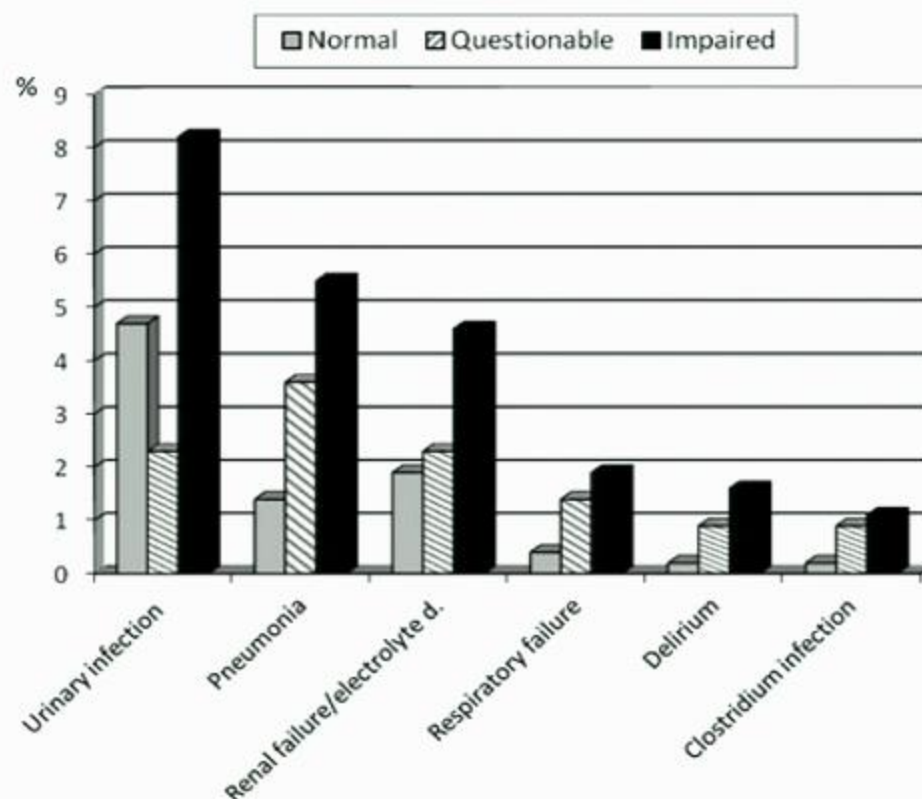
Figure 1. Prevalence of most frequent adverse clinical events according to cognitive status (normal = Short Blessed Test [SBT] 0–4, questionable = SBT 5–9, and impaired = SBT 10–28).

FONDAZIONE
CASSA DI RISPARMIO
DI PISTOIA E PESCIA

Centro Monteoliveto

"Casa dell'Anziano"

6° CONVEGNO NAZIONALE SUI CENTRI DIURNI ALZHEIMER

15-16 Maggio 2015

**Auditorium
Via Panconi, 14 - Pistoia**