Gruppo di ricerca geriatrica

vent'anni per gli anziani
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Venerdì 2 maggio 2008

Il delirium: una conseguenza di eventi clinici avversi o entità clinica autonoma?

Giuseppe Bellelli

Outline della presentazione

- Il delirium impatta sugli outcomes di salute?
- Il rapporto tra delirium ed outcomes di salute è mediato da condizioni cliniche intercorrenti?
- Fisiopatologia del delirium
- I delirium sono tutti uguali?
  - Delirium e demenza
- Un tentativo di spiegazione: il concetto di "brain reserve"

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Delirium: a symptom of how hospital care is failing older persons and a window to improve quality of hospital care

Inouye SK et al., Am J Med 1999; 106:565-73

Delirium & institutionalization and re-hospitalization

Table 3. *Predictors of Institutionalization at 12-Month Follow-up*

	B	OR	95% Confidence Intervals	P
Age, y				
78 to 83	1.10	3.0	1.6–5.8	.001
≥84	1.56	4.8	2.6–8.9	.000
Mini Mental State Examination score ≤20/30	0.84	2.3	1.4–3.9	.001
Barthel Index at discharge				
69/100 to 85/100	1.56	4.8	2.2–10.5	.000
≤68/100	2.32	10.2	4.7–22.5	.000
Occurrence of delirium	0.82	2.3	1.3–3.9	.003
Living alone	−0.86	0.5	0.3–0.8	.012

Multiple stepwise logistic regression analysis adjusted for gender, albumin and cholesterol serum levels, Charlson Index, Body Mass Index, occurrence of adverse clinical events and intensity of the physiotherapic sessions.

B, regression coefficient; OR, odds ratio; *P*, significance.

Table 5. *Predictors of Rehospitalization at 12-Month Follow-up*

	B	OR	95% Confidence Intervals	P
Charlson Index score				
2 to 3	0.71	2.0	1.5–2.7	≤.0005
≥4	0.77	2.2	1.5–3.1	≤.0005
Occurrence of delirium	0.73	1.6	1.1–2.4	.01

Multiple stepwise regression analysis adjusted for age, gender, living alone, albumin and cholesterol serum levels, Body Mass Index, Mini Mental State Examination, Barthel Index at discharge, occurrence of adverse clinical events, and intensity of the physiotherapic sessions.

B, regression coefficient; OR, odds ratio; *P*, significance.

Bellelli G et al, JAMDA 2008

Prognosis after hospital discharge of older medical patients with delirium

- **Setting**: General medical wards of a teaching hospital.
- **Patients**: 229 consecutive patients (>70 years) who had been community-dwelling prior to admission. 50 patients met criteria for delirium (cases).
- 223 patients survived hospitalization (46 cases, 177 controls). Important exclusion criteria
- **Results**:
  - Up to discharge death was 12.1% vs control= 7.2
  - At 6 months death was 14.3% vs control = 10.1% (no independent effect when adjusted for cancer, ADL, and cognitive impairment, loss of independent community living)
  - At 24 months death was 39% vs controls = 23% (relative risk 1.82, 95% confidence interval 1.04-3.19).
    (no independent effect when adjusted for cancer, ADL, and cognitive impairment, loss of independent community living)

Francis et al., JAGS 1992

SYSTEMATIC REVIEW

Occurrence and outcome of delirium in medical in-patients: a systematic literature review

NAJMA SIDDIQI, ALLAN O. HOUSE, JOHN D. HOLMES

Age and Ageing 2006; **35**: 350–364

Abstract

Background: Despite the acknowledged clinical importance of delirium, research evidence for measures to improve its management is sparse. A necessary first step to devising appropriate strategies is to understand how common it is and what its outcomes are in any particular setting.

Objective: To determine the occurrence of delirium and its outcomes in medical in-patients, through a systematic review of the literature.

Method: We searched electronic medical databases, the Consultation-Liaison Literature Database and reference lists and bibliographies for potentially relevant studies. Studies were selected, quality assessed and data extracted according to preset protocols.

Results: Results for the occurrence of delirium in medical in-patients were available for 42 cohorts. Prevalence of delirium at admission ranged from 10 to 31%, incidence of new delirium per admission ranged from 3 to 29% and occurrence rate per admission varied between 11 and 42%. Results for outcomes were available for 19 study cohorts. Delirium was associated with increased mortality at discharge and at 12 months, increased length of hospital stay (LOS) and institutionalisation. A significant proportion of patients had persistent symptoms of delirium at discharge and at 6 and 12 months.

Conclusion: Delirium is common in medical in-patients and has serious adverse effects on mortality, functional outcomes, LOS and institutionalisation. The development of appropriate strategies to improve its management should be a clinical and research priority. As delirium prevalent at hospital admission is a significant problem, research is also needed into preventative measures that could be applied in community settings.

Does delirium contribute to poor hospital outcomes?

Delirium status	n/N(%) of in-hospital death	OR	Adj OR	95% CI (Adj OR)
Chicago				
delirious	0/20 (0)	NA	NA	NA
non delirious	6/179 (3)			
Cleveland				
delirious	3/33 (9)	2.8	0.9	(0.1-7.0)
non delirious	6/172 (3)			
Yale				
delirious	5/37 (14)	2.8	0.7	(0.1-5.9)
non delirious	15/286 (5)			
All sites				
delirious	8/90 (9)	2.2	0.7	(0.2-2.5)
non delirious	27/637 (4)			

* adj for age, gender, dementia, APACHE, ADL and IADL scores *Inouye, J Gen Intern Med 98*

Associations of delirium with in-hospital and in 6-months mortality in elderly medical inpatients

Dimitrios Adamis[1,2,3], Adrian Treloar[2,3], Fai-Zaza Darwiche[1], Norman Gregson[4], Alastair J. D. Macdonald[2], Finbarr C. Martin[1]

Age and Ageing 2007; **36:** 644–649

Background studies on the association between mortality and delirium in older hospital inpatients have produced conflicting results. This insconsistency might be explained by case-mix differences in terms of clinical or underlying patho-physiological processes. For example, both albumin and C-reactive protein (CRP) have been reported as predictors of in-hospital mortality and interleukin-6 of longer-term mortality.

Methods we used data from a longitudinal study of delirium to investigate the delirium–mortality relationship. A cohort of 164 patients, 70+ years were assessed within 3 days of acute hospital admission and hence twice weekly until hospital discharge, for the presence and severity of delirium and a range of clinical and laboratory measures, including initial albumin ($n = 149$), CRP ($n = 76$) and cytokine ($n = 60$) levels. In-hospital and 6-months mortality were determined from clinical records and telephone contact.

Results during hospitalisation 14 (8.5%) patients died, 6 with delirium: mortality was not associated with delirium. At 6 months, 119 of 150 (77.3%) discharged patients were still alive, 21 (14.0%) dead, and 13 (8.7%) uncontactable. In bivariate analysis, 6-months mortality was associated with older age ($P = 0.013$), lower albumin ($P = 0.001$), higher CRP ($P = 0.014$) and higher interleukin-6 levels ($P = 0.007$), but not with presence or severity of in-hospital delirium. After controlling for other variables significant predictors ($P < 0.05$) for six-month mortality were initial MMSE, albumin, interferon-λ and interleukin-6.

Conclusions the lack of demonstrable association between delirium and mortality may reflect inadequate statistical power in this study due to low numbers. These findings, however, highlight specific patho-physiological factors which may be important in the prognosis after delirium.

Summary of death rate in principal studies on delirium

	N° cases	Cases	Controls	Results
at discharge				
Inouye S, 98	33	9%	3%	Difference NS after adj for confounders
O' Keefe ST, 97	94	16%	5%	Difference NS after adj for confounders
McCusker J, 01	220	19%		Independent increase in mortality
Zanocchi M 98	130	25%	10%	Significant difference, not adj for confounders
at 6 months				
Francis J, 90	50	14.3%	10%	Difference NS after adj for confounders
O'Keefe ST 97	94	31%	15%	Difference NS after adj for confounders
at 12 months				
McCusker J, 01	220	42%	14%	2-fold increase in mortality after adjustement
Rahnoken T, 00	51	10%		
Ramsay R, 91	22	77%		
at 3-5 years				
Rockwood K, 99	38	21%	57%	Survival at 3 years, adj HR for death =1.71
Villapando-Berumen J, 03	80	55%	70%	Survival at 5 years

Considerazioni

- L’associazione tra delirium e rischio di mortalità alla dimissione, a 6, 12 e 36 mesi non è consistente in tutti gli studi e mostra ampie variazioni
- Vi sono significative differenze nei tassi di mortalità delle popolazioni reclutate e nei metodi di analisi dei dati

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Prognosis of delirium in elderly hospital patients

Martin G. Cole, MD, FRCPC; François J. Primeau, MD, FRCPC
CAN MED ASSOC J 1993; 149 (1)

Objective: To determine the prognosis of delirium in elderly patients.
Data sources: MEDLINE was searched for relevant articles published from January 1980 to March 1992. The bibliographies of identified articles were searched for additional references.
Study selection: Eight reports (involving 573 patients with delirium) met the following inclusion criteria: original research, published in English or French, prospective study design, diagnosis based on acute deterioration in mental state, sample of at least 20 patients, patients aged 60 years or over and follow-up of at least 1 week. The validity of the studies was independently assessed according to the criteria for prognostic studies established by McMaster University, Hamilton, Ont. No study met all the criteria.
Data extraction: Information about the patient sample, length of follow-up and results was systematically abstracted from each report and tabulated.
Data synthesis: A meta-analysis of the outcomes indicated that elderly patients with delirium had a mean length of stay of 20.7 days. One month after admission 46.5% were in institutions, and 14.2% had died; only 54.9% had improved mentally. Six months after admission 43.2% were in institutions. Compared with unmatched control subjects they had longer hospital stays, higher mortality rates at 1 month and higher rates of institutional care at 1 and 6 months. The presence of severe physical illness or dementia may have been related to some outcomes.
Conclusions: Delirium in the elderly appears to have a poor prognosis. However, this finding may have been confounded by the presence of concomitant dementia or severe physical illness. Future studies must pay attention to methods and design, particularly the composition of study populations and the control of extraneous prognostic factors.

Outcomes at 12 Months in a Population of Elderly Patients Discharged From a Rehabilitation Unit

Giuseppe Bellelli, MD, Francesca Magnifico, PsyD, and Marco Trabucchi, MD

Table 7. *Predictors of Death at 12-Month Follow-up*

	B	OR	95% Confidence Intervals	*P*
Age >83 years	0.80	2.2	1.3–3.9	.004
Barthel Index at discharge ≤60/100	1.07	2.9	1.7–5.1	≤.0005
Charlson Index score				
3 to 4	0.89	2.4	1.2–12.0	.015
≥5	1.78	6.0	3.0–11.8	≤.0005
Albumin serum levels (g/dL)				
3.2 to 2.9	1.48	4.4	1.8–15.2	.001
≥2.9	1.87	6.8	2.8–15.3	≤.0005
Geriatric Depression scale ≤2/15	−1.12	0.3	0.1–0.8	.02

Multiple stepwise regression analysis adjusted for gender, living alone, cholesterol serum levels, Mini Mental State Examination, occurrence of adverse clinical events, and intensity of the physiotherapic sessions.

B, regression coefficient; OR, odds ratio; *P*, significance.

Bellelli G et al., J Am Med Dir Assoc 2008; 9: 55–64

C-reactive protein levels predict the incidence of delirium and recovery from it

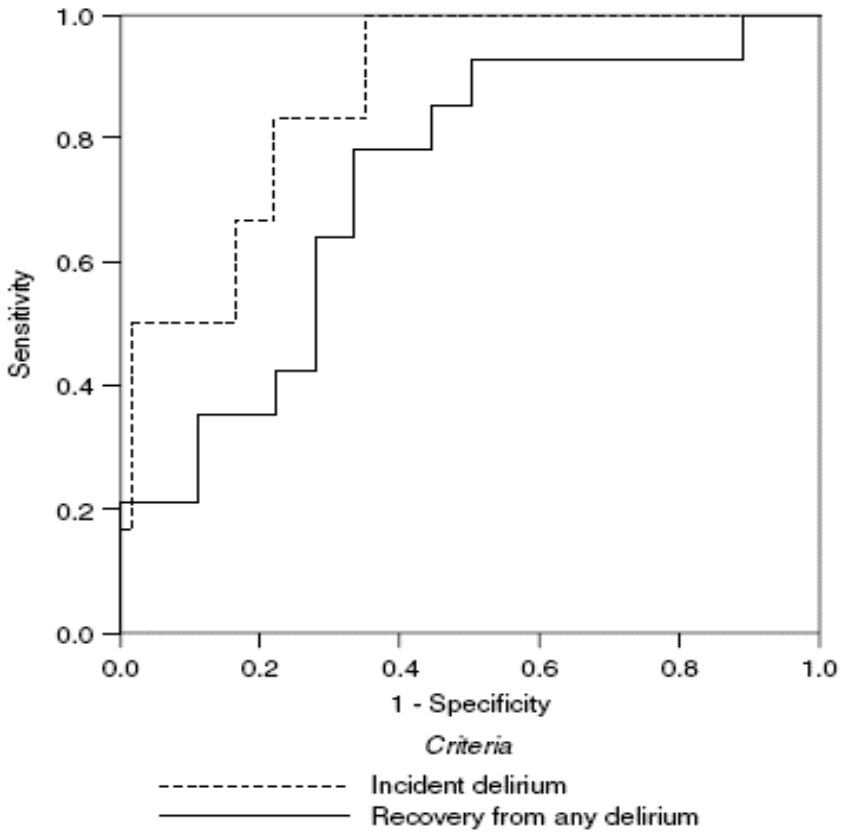

Figure 1. Receiver operator characteristics curves of C-RP with incident delirium (higher C-RP = more incidence) and recovery from incident or prevalent delirium (lower C-RP = more recovery).

Key points

- High levels of CRP independently predicted incidence of delirium
- A higher initial MMSE and low CRP predicted the recovery from delirium at any time during hospitalization
- Elevated CRP should alert clinicians to the possibility of incident delirium
- CRP in acute illness merits further investigation as a marker for potential precipitating or perpetuating mechanisms for delirium

MacDonald et al, Age Ageing 2007

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Fisiopatologia del delirium

- The pathophysiology of delirium remains poorly understood. Electroencephalographic studies have demonstrated diffuse slowing of cortical background activity, which does not correlate with underlying causes. Neuropsychological and neuroimaging studies reveal generalized disruption in higher cortical function, with dysfunction in the prefrontal cortex, subcortical structures, thalamus, basal ganglia, frontal and temporoparietal cortex, fusiform cortex, and lingual gyri, particularly on the nondominant side.

Inouye S, N Engl J Med 2006;354:1157-65.

Possible mechanisms in the development of delirium

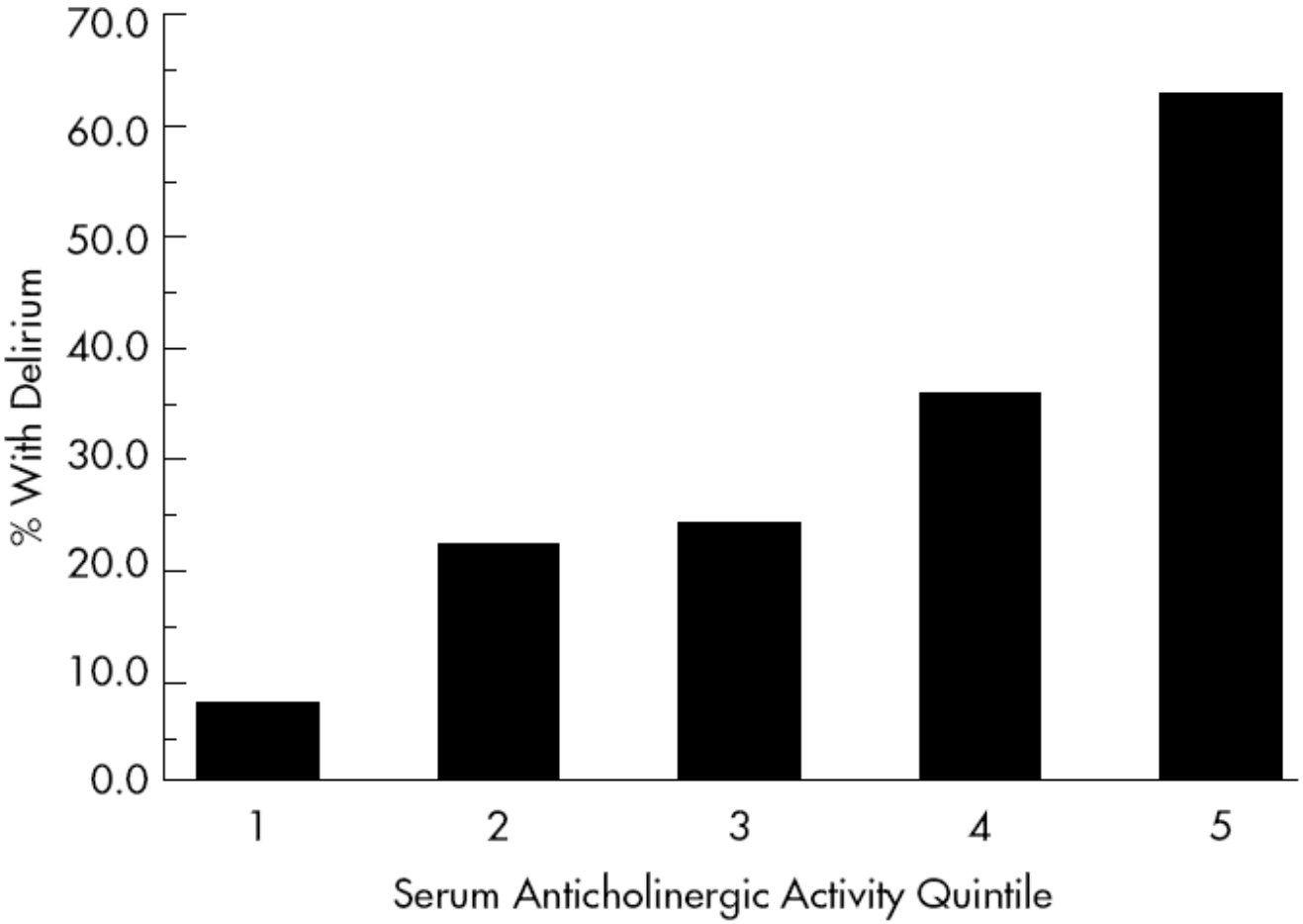
Mechanisms	Example
Altered neurotransmitters	Acetylcholine
	Dopamine
	Noradrenaline, GABA, glutammate
Altered hypothalamic-pituitary-adrenal axis	Hypercortisolims
Other mechanisms	Cytokine production, e.g. interleukin-1
	Alterations to the blood-brain barrier
	Oxidative stress

From McManus J et al., Age Ageing 2007

Elementi a supporto di un coinvolgimento di acetilcolina

- ACh is involved in several functions that are affected in delirium: arousal, attention, delusions, visual hallucinations, motor activity and memory; moreover anticholinergic drugs can cause delirium in susceptible patients *[Lindesay, 2002]*
- Cholinesterase inhibition can improve anticholinergic drug–induced delirium *[Han, 2001]*
- Patients with Lewy body dementia have several features common to delirious patients: severe cognitive impairment, fluctuating symptom severity, visual hallucinations and EEG slowing, with symptoms responding to cholinesterase inhibitors *[Kaufer, 1998]*

An essay to measure SAA in delirium



Flacker et al, Am J Ger Psych 98

Other mechanisms

- Dopamine and ACh neurotransmitter systems interact closely and often reciprocally and an imbalance between the two could underlie delirium syndromes. There is evidence that dopamine excess can cause delirium and that dopamine antagonists, particularly neuroleptics, modify the symptoms of delirium *[Caeiro, 2004]*
- Finally, chronic stress brought on by illness or trauma activates the sympathetic nervous system and hypothalamic–pituitary–adrenocortical axis, resulting in increased cytokine levels and chronic hypercortisolism *[Inouye, 2006]*
- Cytokines, including interleukin-1, interleukin-2, interleukin-6, tumor necrosis factor α (TNF-α), and interferon, may contribute to delirium1, by increasing the permeability of the blood–brain barrier and altering neurotransmission *[Inouye, 2006]*

Delirium and inflammation

- Some inflammatory molecules are involved in the modulation of neuronal functions, such as neurotransmission. Interestingly, delirium is a frequent presentation in patients with senile dementia of the tangle type, characterised by an abundance of neurofibrillary tangles, in the absence of significant numbers of senile (amyloid) plaques

[Ikeda, Dement Geriatr Cog Disord, 1999]

[George , Age Ageing, 2007]

Considerazioni

- I neurotrasmettitori implicati nella fisiopatogenesi del delirium sono gli stessi implicati in altre malattie neurodegenerative (Alzheimer, PD)

- È possibile pensare ad una substrato patologico comune?

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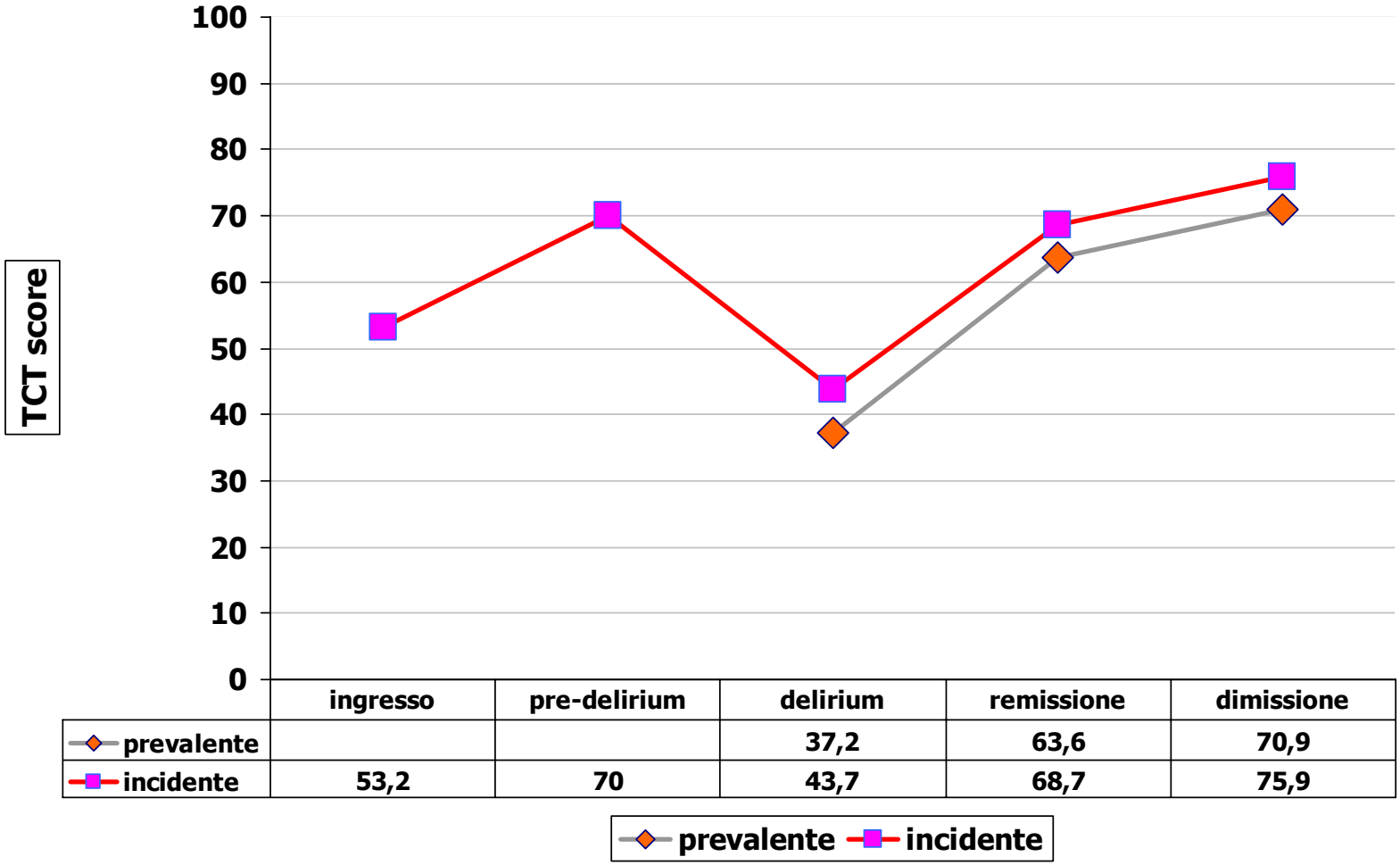
Criteria for Delirium (DSM IV)

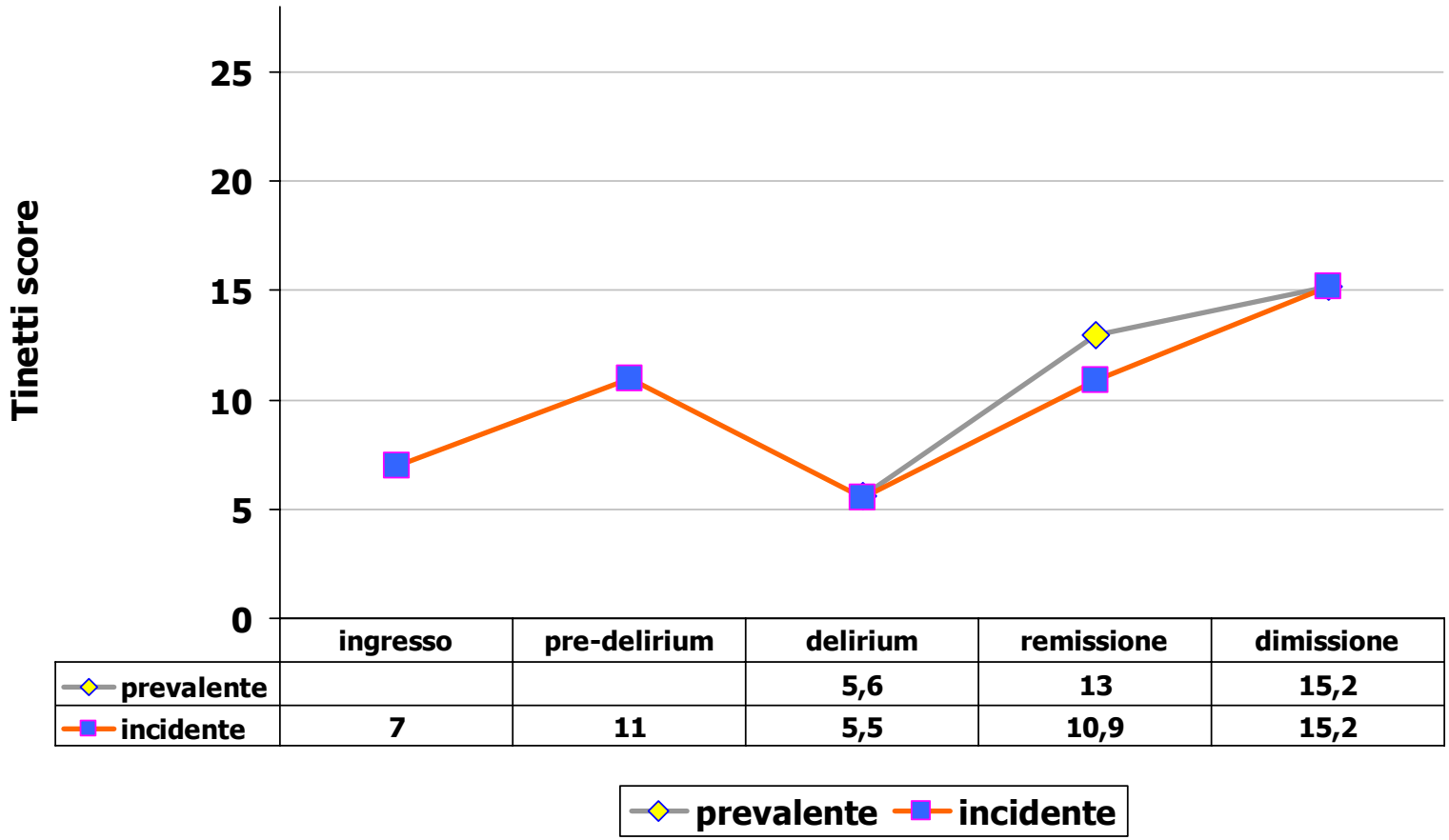
- A) Disturbance of consciousness with reduced ability to focus, sustain, or shift attention.
- B) A change in cognition or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established, or evolving dementia.
- C) The disturbance develops over a short period of time and tends to fluctuate during the course of the day.
- D) There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition, or substance intoxication or withdrawal, use of medication, toxin exposure, or a combination of these factors.

Modificazioni dello score di TCT in 116 pazienti (100 delirium prevalente e 16 delirium incidente) durante le fasi di delirium



P < .005 per tutti i valori al t-test per misure ripetute

Modificazioni dello score di Tinetti in 116 pazienti (100 delirium prevalente e 16 delirium incidente) durante le fasi di delirium



	ingresso	pre-delirium	delirium	remissione	dimissione
prevalente			5,6	13	15,2
incidente	7	11	5,5	10,9	15,2

Delirium & functional recovery in elderly patients

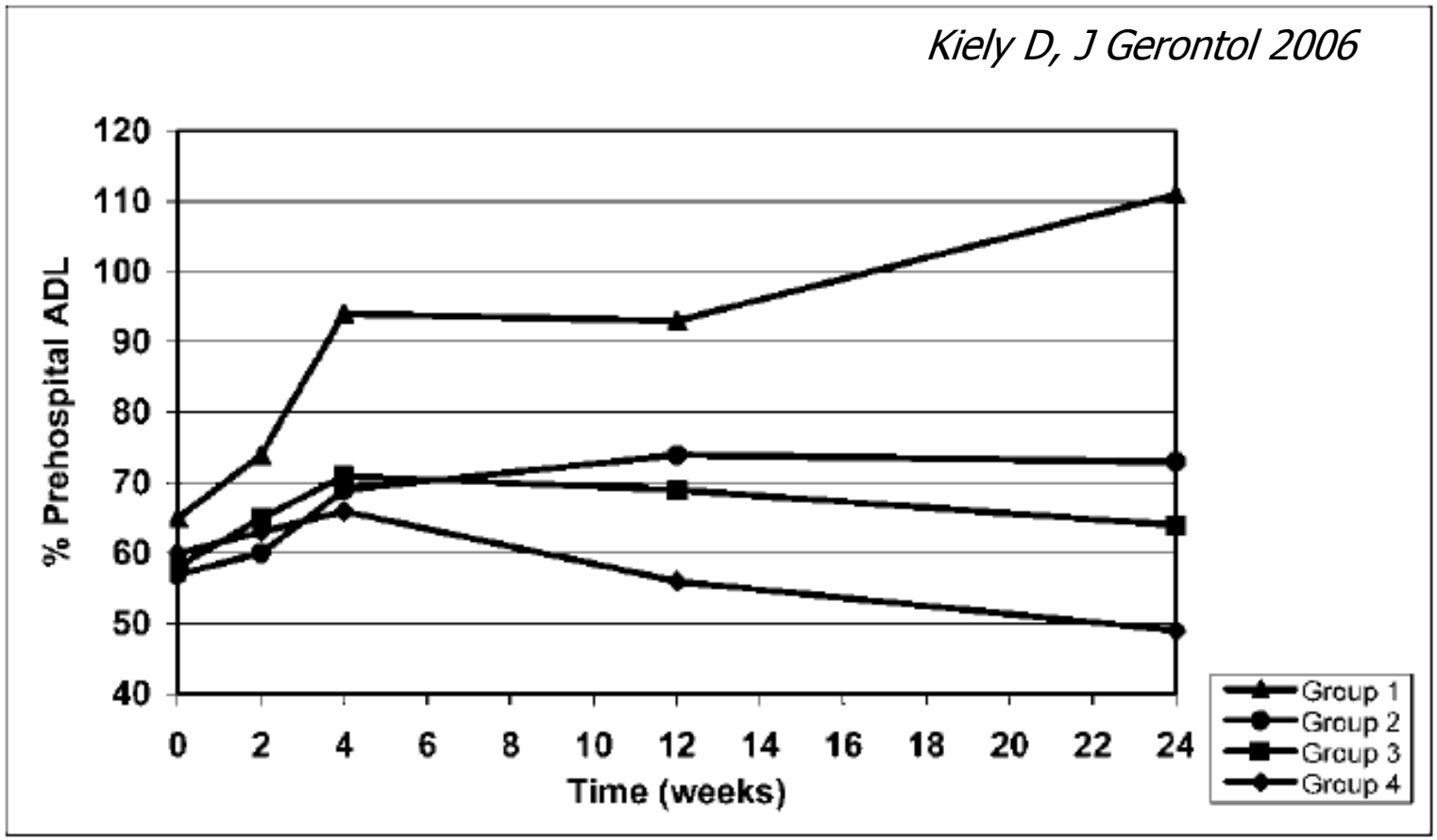
Table 1. Characteristics of 58 Patients With Delirium (Stratified by Duration of Delirium) on Admission to a Rehabilitation and Aged Care Unit

Characteristics	Delirium Resolution ≤ 1 Week (N = 15)	Delirium Resolution 1–2 Weeks (N = 25)	Delirium Resolution ≥2 Weeks (N = 18)	p
Age, y	81.7 ± 5.3	83.2 ± 5.1	82.8 ± 8.1	.78
Women, n (%)	9 (60.0)	18 (72.0)	13 (72.2)	.68
Charlson comorbidity index	2.7 ± 2.7	3.0 ± 2.0	3.5 ± 2.5	.56
Albumin serum level, g/dL	2.9 ± 0.6	2.9 ± 0.4	2.8 ± 0.3	.86
C-reactive protein	5.2 ± 5.4	5.7 ± 5.6	5.9 ± 6.1	.93
Mini-Mental State Examination (0–30)	21.1 ± 6.4	16.6 ± 6.8	14.9 ± 6.2	.03
Barthel Index on admission (0–100)	41.9 ± 26.0	33.9 ± 22.8	28.6 ± 24.4	.30
Trunk Control Test on admission (0–100)	46.7 ± 32.0	41.4 ± 27.5	38.5 ± 37.0	.76
Trunk Control Test at resolution of delirium (0–100)	66.7 ± 25.3	64.3 ± 30.1	68.2 ± 27.6	.89
Trunk Control Test at discharge (0–100)	83.7 ± 21.5	71.8 ± 25.9	68.9 ± 27.0	.22
Tinetti Score on admission (0–28)	9.0 ± 6.3	7.1 ± 7.6	5.7 ± 6.5	.42
Tinetti Score at resolution of delirium (0–28)	14.5 ± 4.4	14.0 ± 7.7	12.1 ± 7.1	.53
Tinetti Score at discharge (0–28)	18.7 ± 4.5	16.0 ± 6.7	13.3 ± 6.5	.05
Delirium duration, d	4.3 ± 1.4	9.1 ± 2.0	18.5 ± 4.6	.000
Length of stay without delirium, d	19.2 ± 6.7	15.3 ± 9.0	11.0 ± 6.8	.016
Total length of stay, d	24.3 ± 6.8	24.7 ± 8.6	30.4 ± 6.9	.03
IFRAD Trunk Control Test	0.9 ± 0.9	0.3 ± 0.6	0.03 ± 0.1	.003
IFRAD Tinetti score	0.22 ± 0.1	0.15 ± 0.2	0.09 ± 0.1	.22

Note: IFRAD = Index of Functional Recovery After Delirium (calculated as the difference in Trunk Control Test or Tinetti score from resolution of delirium to discharge divided by the length of stay [days] without delirium).

Speciale, Bellelli, Lucchi, Trabucchi J Gerontol 2007

Association between delirium resolution & functional recovery



Group 1 resolved their delirium by 2 weeks, and delirium did not recur during the follow-up (FU).
Group 2 resolved their delirium after 2 weeks, and delirium did not recur during the FU.
Group 3 resolved their delirium (any time), and delirium recurred during the FU.
Group 4 never resolved their delirium during the FU

Caratteristiche di 107 pazienti con delirium ricoverati e dimessi da una RACU

	Vivi a 12 mesi dalla dimissione *n=56* Media ± DS (%)	**Deceduti entro 12 mesi dalla dimissione** *n=25* Media ± DS (%)	**Deceduti durante la degenza in reparto** *n=26* Media ± DS (%)	**p**
Età	82.3 ± 6.6	83.7 ± 6.9	86.2 ± 5.9	.04
Sesso femminile	(75)	(72)	(62,2)	.85
CIRS Severità	1.7 ± 0.3	2.0 ± 0.3	2.2 ± 0.3	.000
CIRS Comorbilità	3.8 ± 1.8	5.2 ± 1.6	6.4 ± 2.0	.000
Albumina	2.9 ± 0.4	2.9 ± 0.4	2.7 ± 0.5	.21
Barthel pre-ingr	76.6 ± 24.0	72.9 ± 21.9	69.7 ± 29.6	.49
Barthel ingr	29.0 ± 19.1	21.6 ± 21.0	16.5 ± 17.9	.02
Barthel dimissione	61.4 ± 25,8	27.0 ± 27.7	--	.000
Incontin/catetere	42 (75.0)	20 (80)	22 (84.6)	.60
Non malnutr	10 (30.3)	--	3 (12.5)	
Rischio malnutr	16 (48.5)	5 (27.8)	6 (25.0)	.001
Malnutr	7 (21.2)	13 (72.2)	15 (62.5)	
Delirium dim	3 (5.4)	10 (40.0)	--	.000
Delirium dubbio dim	--	3 (12.0)	--	

L'interazione tra differenti condizioni sindromiche

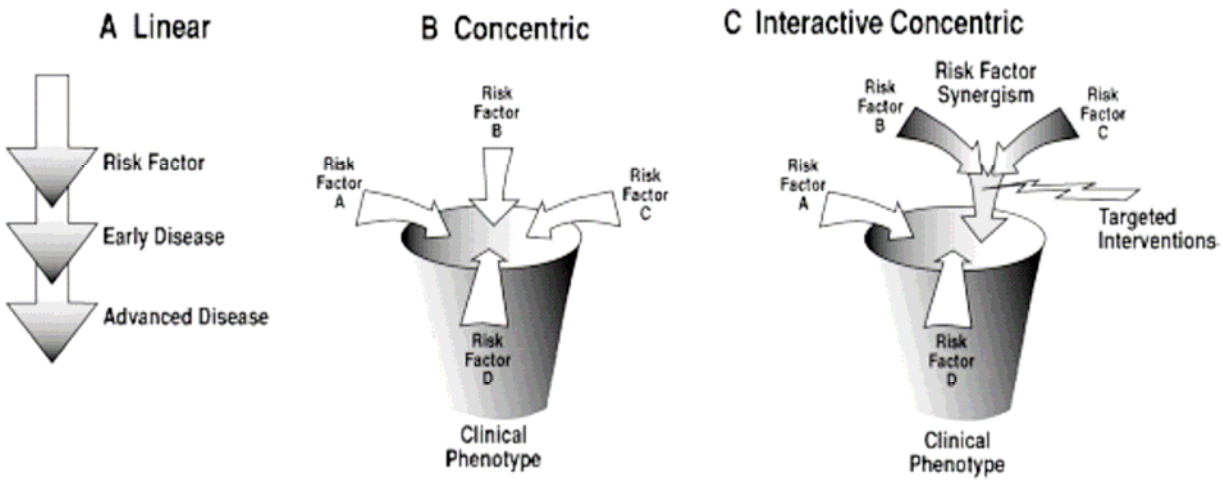


Figure 3. Mechanistic research addressing the pathophysiology of complex multifactorial geriatric syndromes will require the development of new conceptual models. The traditional linear model (A) has proven highly effective for the discovery of pathophysiologically relevant mechanisms in conditions such as inborn errors of metabolism, yet it does not adequately capture the multifactorial nature of geriatric syndromes. Cancer researchers developed the concentric model (B) as a means of designing more-effective cancer treatments by targeting multiple distinct oncogenic pathways.[97] This approach may also not be suitable for geriatric syndromes, because interventions targeting only one risk factor would address only a small portion of the overall risk for such conditions, whereas multicomponent pharmaceutical interventions risk being unfocussed and could lead to adverse effects typically associated with geriatric polypharmacy. An interactive concentric model (C) is proposed as a means of reconciling the need for mechanistic research with the conditions' multifactorial complexity by focusing on pathways associated with risk factor synergisms, thus offering a locus for the design of targeted interventions. Modified from Decker and Sausville.[97]

Inouye et al, JAGS 2007

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Do delirium and Alzheimer's dementia share specific pathogenetic mechanisms?

Eikelenboom P., Dement Geriatr Cogn Disord, 1999

Elucidating the Pathophysiology of Delirium and the Interrelationship of Delirium and Dementia

Sharon K. Inouye[1] and Luigi Ferrucci[2]

- Il delirium persistente è molto frequente [Marcantonio, 2005] ed è spesso difficilmente distinguibile da una condizione di demenza [McCusker, 2003]
- Studi epidemiologici hanno documentato che ad una condizione di delirium spesso consegue lo sviluppo di decadimento cognitivo [Clarfielf, 1998]
- La demenza è uno dei fattori di rischio principali per lo sviluppo di delirium [Inouye, 1998]

J Gerontol Bio Sci, 2006

Delirium Superimposed on Dementia: è una condizione diversa dal delirium?

DSD & mortality

Table 1. Characteristics of Patients in Four Matched Study Groups

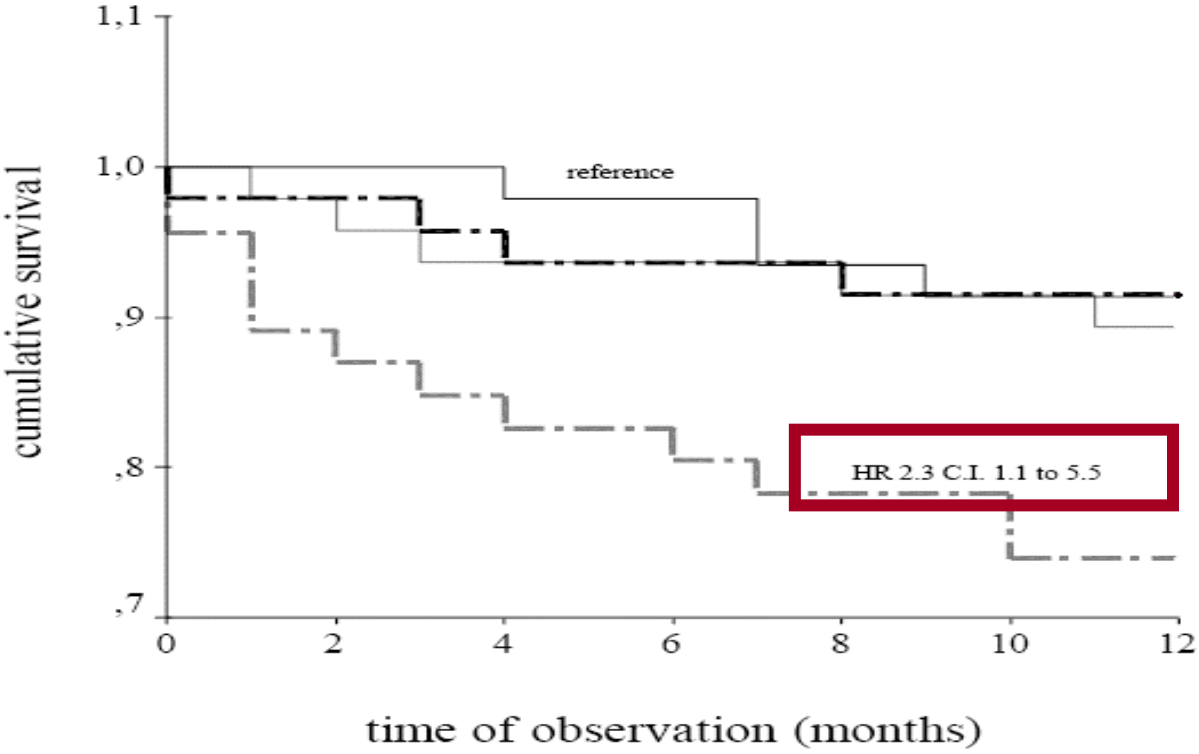
Characteristics	Neither Delirium Nor Dementia ($N = 47$)	Dementia Alone ($N = 47$)	Delirium Alone ($N = 47$)	Delirium and Dementia ($N = 47$)	p
Age, y	79.3 ± 6.4	79.6 ± 6.8	79.4 ± 6.8	80.1 ± 6.6	.94
Female sex	37 (78%)	37 (78%)	37 (78%)	37 (78%)	1.0
Postsurgical rehabilitation	22 (47%)	22 (47%)	22 (47%)	22 (47%)	1.0
Living alone before admission	27 (59%)	15 (32%)	16 (34%)	14 (30%)	.01
Barthel Index before admission (0–100)	89.0 ± 20.2	78.9 ± 26.0	83.0 ± 27.2	74.1 ± 24.5	.03
Charlson comorbidity score	1.6 ± 1.6	2.1 ± 1.5	2.6 ± 1.8	2.4 ± 2.0	.04
Medical conditions					
Cerebrovascular disease	10 (21%)	31 (66%)	23 (49%)	26 (55%)	< .0005
Congestive heart failure	5 (11%)	5 (11%)	8 (17%)	6 (13%)	.76
Respiratory diseases	4 (8%)	7 (15%)	11 (23%)	7 (15%)	.25
Uncomplicated diabetes	1 (1%)	—	1 (7%)	3 (2%)	.27
Peripheral vascular disease	3 (6%)	3 (6%)	2 (4%)	1 (2%)	.73
Cancer	—	—	1 (2%)	—	.39
Mini-Mental State Examination (0–30)*	26.2 ± 3.4	18.2 ± 6.2	22.5 ± 6.7	13.4 ± 6.0	< .0005
Drugs on admission, n	4.7 ± 2.6	5.1 ± 2.3	6.0 ± 3.0	5.7 ± 2.7	.12
Length of stay, d	22.8 ± 6.8	23.1 ± 6.8	27.8 ± 12.4	24.0 ± 10.6	.04

Notes: Values denote mean ± standard deviation (*SD*) or n (%); p denotes significance on analysis of variance (ANOVA) for continuous or Chi-square for categorical variables.

*Scores refer to the cognitive assessment at resolution of delirium; it was not available for four patients with delirium alone and for four patients with delirium superimposed on dementia, respectively, because they were still delirious at discharge.

Bellelli G et al J Gerontol 2007; Nov;62(11):1306-9

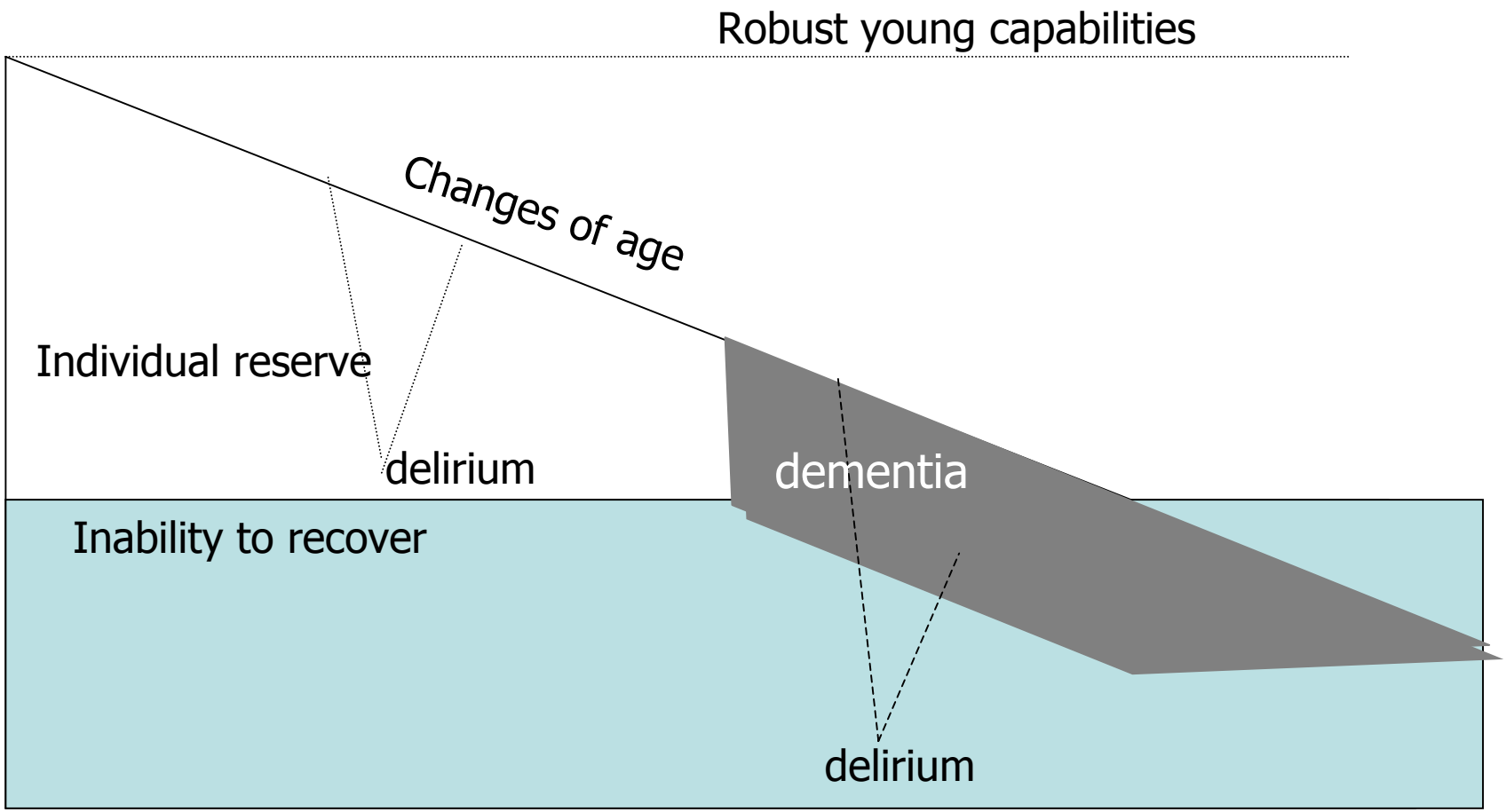
Il delirium associato a demenza (DSD) ha un impatto significativo ed indipendente sulla mortalità



black solid line=no delirium no dementia; black dotted line=dementia

grey solid line= delirium; grey dotted line = DSD

Hypothetical processes leading to death in DSD



Does Educational Attainment Contribute to Risk for Delirium? A Potential Role for Cognitive Reserve

Richard N. Jones,[1,2,5] Frances M. Yang,[1,2,4,5] Ying Zhang,[1] Dan K. Kiely,[1] Edward R. Marcantonio,[1,3,5] and Sharon K. Inouye[1,2,5]

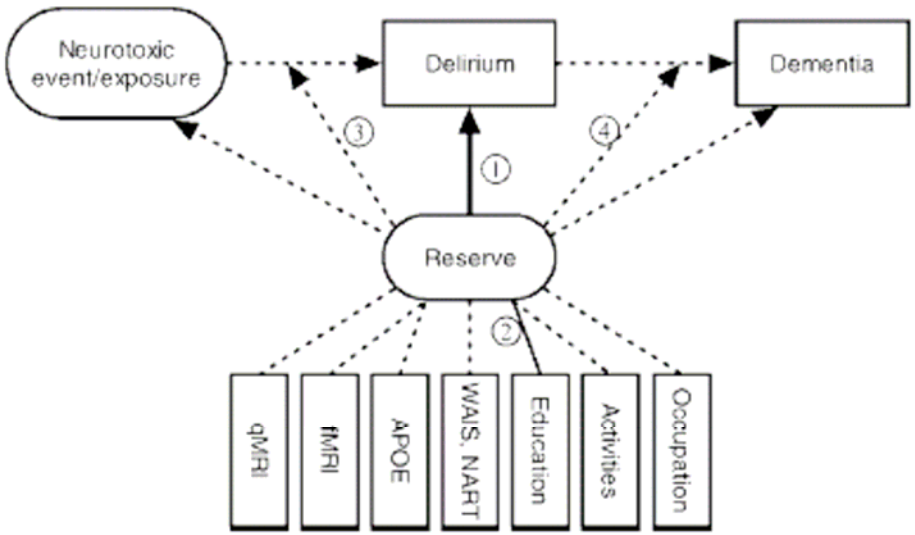
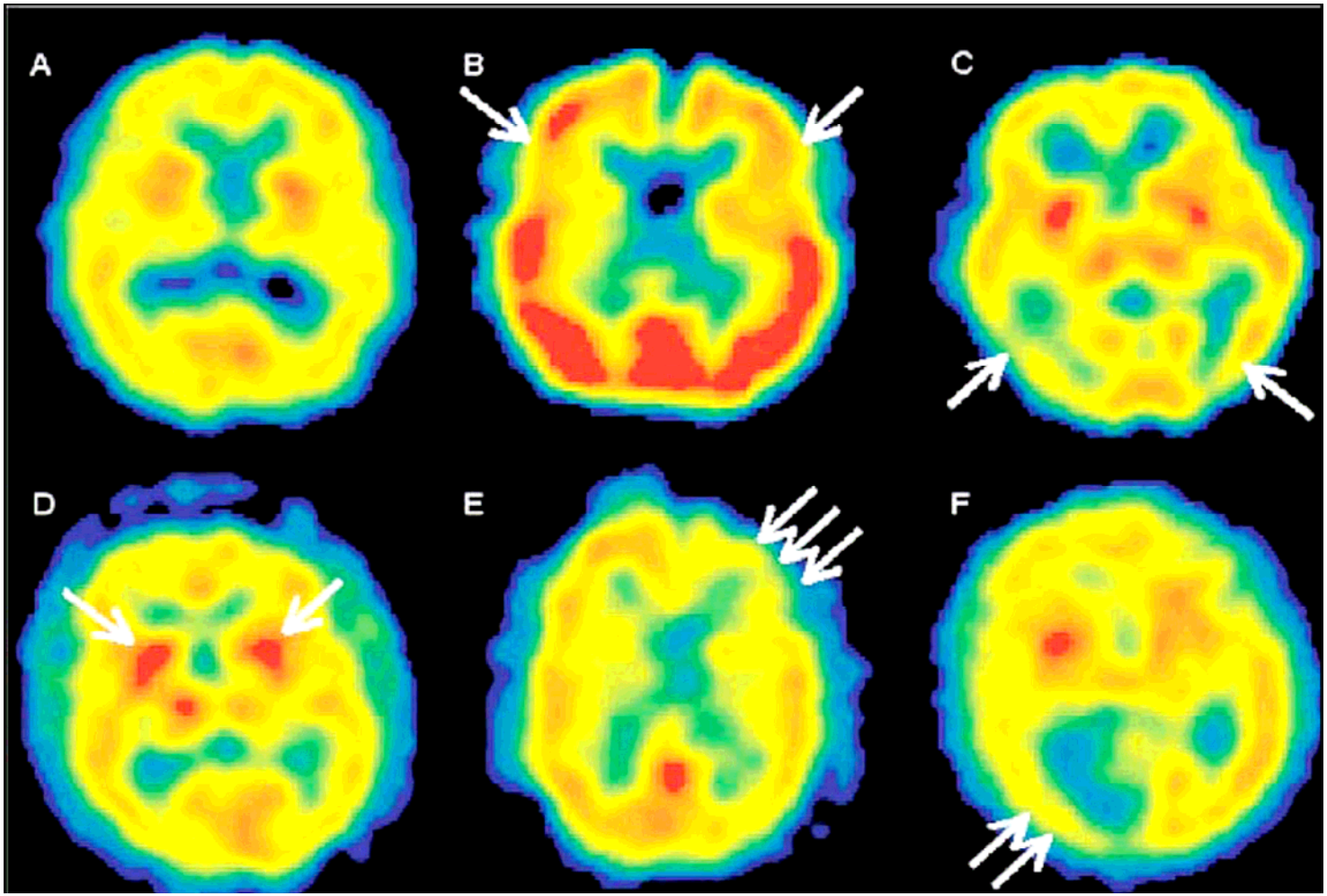


Figure 2. A generalized reserve theory experimental design linking neurotoxic event or exposure, delirium, and dementia, and expanding the reserve concept. [See text for full description of annotations.] qMRI = quantitative magnetic resonance imaging; fMRI = functional magnetic resonance imaging; APOE = apolipoprotein E genotype; WAIS = Wechsler Adult Intelligence Scale; NART = National Adult Reading Test.

- Controlling for age, sex, dementia, comorbidity, and severity of illness, each year of completed education was associated with a 0.91 lower odds of delirium (95% confidence interval: 0.87, 0.95); compared to persons with 12 years of education, persons with 7 years of education had 1.6-fold increased odds of delirium (95% confidence interval: 1.4, 2.0).

J Gerontol Biol Sci, 2006

Delirium may incite a derangement in brain vascular function



Fong J Gerontol 2006

SPECT cerebral blood flow in delirium and related conditions

Reference (Ref. No.)	No. of Patients/Controls	Cause of Onset	Location
Bogousslavshy et al. (10)	1/0	Right thalamic infarction	Right frontal hypoperfusion
Shih et al. (46)	1/0	Drug withdrawal	Left frontotemporal hypoperfusion
Kohira et al. (47)	1/0	Hepatic encephalopathy	Cerebellum, basal ganglia, cortical hyperperfusion
Doyle and Warden (48)	1/0	Cardiotomy	Right temporal-occipital hypoperfusion
Ohta et al. (49)	1/0	Portal-systemic encephalopathy	Bilateral parietal hypoperfusion Basal ganglia hyperperfusion
Kamijo et al. (50)	1/0	Barbiturate withdrawal	Diffuse bilateral decrease
Pittock et al. (51)	1/0	Transplant immunosuppression	Bilateral frontal, parietal, temporal hypoperfusion
Ikeda et al. (52)	6/0	Hepatic encephalopathy	Diffusely decreased cortical perfusion; in 4 participants recovery after liver transplant
Jalan et al. (53)	8/0	Oral amino acid loading in cirrhosis	Bilateral temporal lobe, left superior frontal gyrus, and right parietal and cingulate gyrus decrease
Trzepacz et al. (54)	6/6	Cirrhosis	Right basal ganglia and bilateral frontotemproal hypoperfusion
Strauss et al. (55)	10/9	Hepatic encephalopathy	Frontal and basal ganglia hypoperfusion
O'Carroll et al. (56)	10/10	Cirrhosis	Basal ganglia and occipital increase Anterior cingulate decrease
Yazgan et al. (57)	12/8	Hepatic encephalopathy	Bilateral thalamic hypoperfusion
Catafau et al. (58)	13/13	Hepatic encephalopathy	Prefrontal hypoperfusion. Striatal and medial temporal perfusion was higher in more impaired participants
Fong et al. (59)	22/6	Multiple etiologies in hospitalized medical patients	Parietal hypoperfusion in 6 Frontal hypoperfusion in 5 Reversible parietal hypoperfusion in 3 of 6
Ogasawara et al. (60)	5/36	Subdural hematoma	Hyperperfusion under surgical site
Gokgoz et al. (61)	6/44	Cardiac surgery	Reduced perfusion in bilateral temporoparietal and frontal and right occipital
Gunaydin et al. (62)	7/43	Cardiac surgery	Bilateral temporoparietal, frontal, and occipital

Alsop D et al, J Gerontol 2006

È sostenibile l'idea che il delirium sia una conseguenza di eventi clinici avversi ma diventi un'entità clinica autonoma quando sovraimposto a demenza?

Delirium in older people: an epiphenomenon of incipient death or a separate biological process?

Table 1. Characteristics of patients in three groups (delirium superimposed on dementia, delirium alone and no delirium)

	Delirium and dementia ($n = 168$)	Delirium alone ($n = 71$)	No delirium ($n = 1,572$)	P
Age (years)	82.8 ± 7.7	78.8 ± 6.1	77.1 ± 7.9	0.00
Female gender	122 (72.2)	49 (70.0)	1160 (73.8)	0.72
Living alone before RACU admission	50 (29.6)	21 (30.0)	552 (35.5)	0.31
Charlson Index	3.8 ± 2.1	2.9 ± 2.1	2.6 ± 2.2	0.00
C-reactive protein serum levels (mg/dl)	5.0 ± 5.5	4.9 ± 4.9	2.8 ± 4.8	0.00
Albumin serum levels (g/dl)	2.8 ± 0.4	2.9 ± 0.4	3.2 ± 0.6	0.00
Mini Mental State Examination[a]	15.5 ± 6.2	22.7 ± 6.5	23.8 ± 5.3	0.00
IADL 1 month before admission	3.5 ± 1.5	2.9 ± 1.9	2.9 ± 1.8	0.00
Length of RACU stay	26.2 ± 9.5	27.5 ± 12.3	22.4 ± 9.2	0.00
Died at 12 months	47 (27.8)	8 (8.6)	137 (8.5)	0.00

Bellelli et al., Age Ageing 2008

Multiple logistic regression to test the effect of delirium on 1-year mortality

	O.R.	C.I.	p
Age	**1.07**	**1.04-1.10**	**<.0005**
Gender	n.s.		
Charlson	**1.33**	**1.20-1.40**	**<.0005**
C-RP	n.s.		
Albumin	n.s.		
MMSE	**1.06**	**1.02-1.09**	**<.0005**
IADL	n.s.		
Delirium	n.s.		
DSD	--		

Multiple logistic regression to test the effect of delirium on 1-year mortality

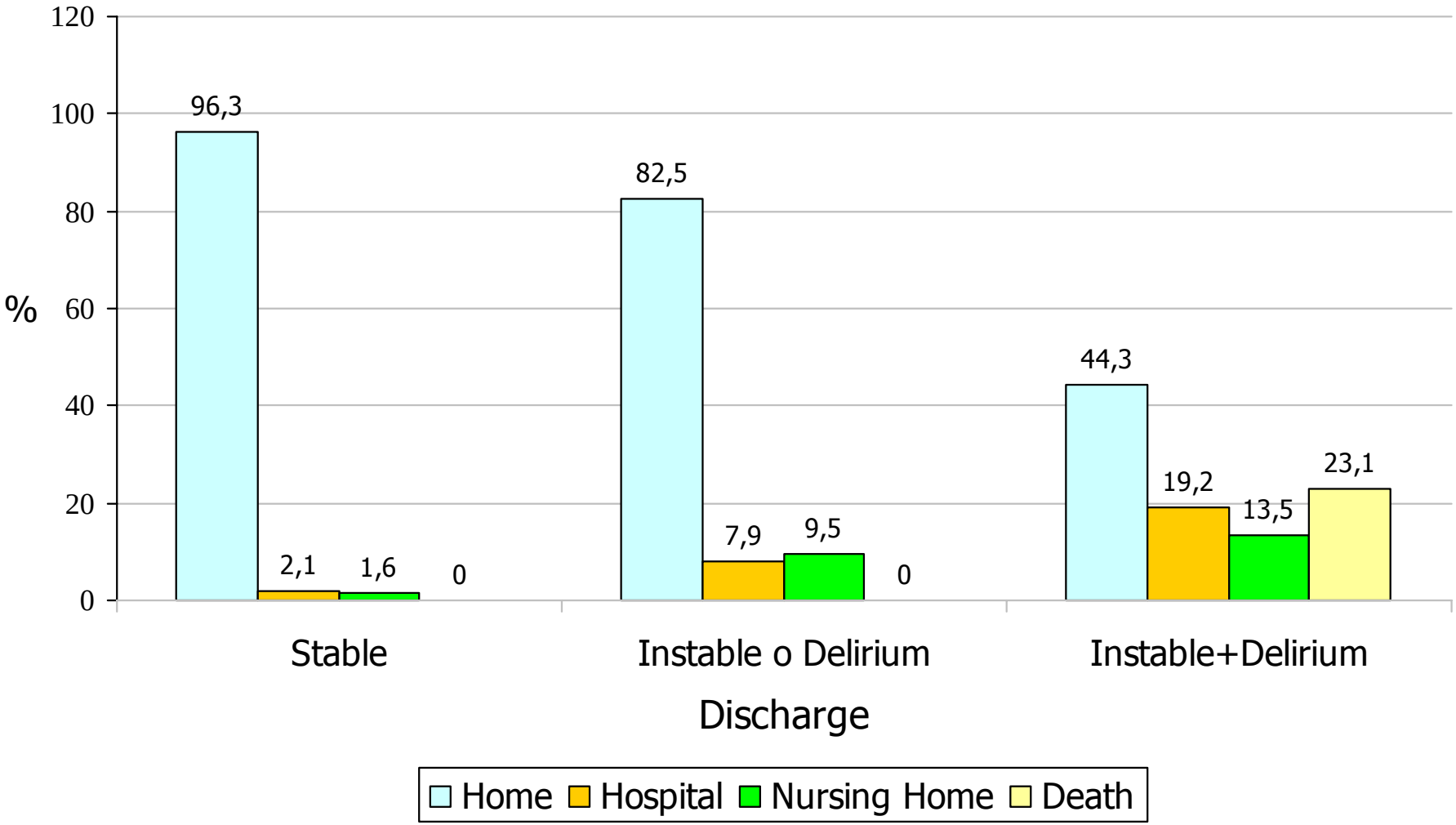
	O.R.	C.I.	p
Age	**1.07**	**1.04-1.10**	**<.0005**
Gender	n.s.		
Charlson	**1.33**	**1.23-1.44**	**<.0005**
C-RP	n.s.		
Albumin	n.s.		
MMSE	**1.06**	**1.03-1.09**	**<.0005**
IADL	n.s.		
Delirium	--		
DSD	**1.69**	**1.14-2.76**	**<.003**

Instabilità clinica: i criteri di Halm

	NO	SI
A. Temperatura Corporea >37.8 °C	0	1
B. Frequenza respiratoria >24/min	0	1
C. Frequenza cardiaca >100/min	0	1
D. Pressione arteriosa sistolica ≤90	0	1
E. Saturazione di ossigeno <90%	0	1
F. Alterato livello di vigilanza §	0	1
G. Incapacità ad alimentarsi autonomamente §§	0	1
Score totale (per il punteggio considerare F e G solo se presente almeno 1 da A ad E)		

§ Fare riferimento a sezione IV. della CAM
§§ Barthel Index subscore alimentazione ≤ 2

Adverse outcome at discharge in a population of 496 patients consecutively admitted to our Rehabilitation Unit, stratified by clinical instability.



Conclusioni

- Il delirium è una condizione di frequente riscontro in ambito geriatrico ed è associata ad outcomes negativi
- Non vi sono attualmente dati che supportino, in modo definitivo, l'ipotesi che il delirium sia un'entità clinica autonoma
- Nel soggetto demente una ridotta "brain reserve" potrebbe determinare l'incapacità del paziente a recuperare lo status quo ante, e portare a morte attraverso meccanismi complessi e non ancora noti
- I progressi in ambito di biologia e di neuroimaging potrebbero permettere di comprendere meglio nei prossimi anni la fisiopatologia del delirium