Villaggio Amico
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Convegno annuale
APPROCCI NON CONVENZIONALI
NELLA CURA DELLA PERSONA CON DEMENZA:
SUPERARE GLI STEREOTIPI NEGATIVI

VENERDÌ 21 SETTEMBRE 2018
ore 14.00 - 18.30
presso StarHotels Gran Milan via Varese 23 - Saronno

La terapia farmacologica è sempre l'unica soluzione per la persona con disturbi del comportamento? Un approccio di cura ragionato

Giuseppe Bellelli

Dipartimento di Medicina e Chirurgia, Università Milano-Bicocca
SCC Geriatria, AO S Gerardo Monza

UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

Obiettivi

- Rivedere i comportamenti prescrittivi nei pazienti con demenza e disturbi del comportamento
- Valutare rischi/benefici degli approcci farmacologici e non farmacologici
- Fornire un razionale scientifico per i differenti approcci differenziati

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Frequenza dei disturbi comportamentali nelle demenze

Aggressività verbale e fisica	43%
Allucinazioni	7%
Paranoie/ False idee	5%
Disturbi del sonno	17%
Attività disturbanti	25%
Vagabondaggio	24%
Ansia /fobie	20%
Disturbi del tono dell'umore	16%

Sampson E, BJP 2014

Disturbi del comportamento: impatto sulla salute

- Causa più frequente di istituzionalizzazione
- Causa più frequente di prescrizione farmacologica
- Causa più frequente di intervento medico
- Aumento della disabilità
- Causa di stress grave dei *caregiver*
- Ridotta qualità di vita del paziente e del *caregiver*
- Aumento dei costi economici della malattia

Disturbi del comportamento: management

- Gli studi dimostrano che all'incirca 80% dei pazienti con demenza nelle RSA ricevono farmaci antipsicotici. Negli ospedali il 12-20%
- Molti antipsicotici sono usati in prima battuta per disturbi comportamentali di varia natura (insonnia, agitazione, psicosi) osservati o anche solo "riferiti"
- Antipsicotici con profili d'azione notevolmente differenti sono usati in modo sovente interscambiabile e a dosaggi inadatti

Dove vengono prescritti gli antipsicotici?

- Di 7,496 anziani residenti in RSA con antipsicotici, 4,794 (64.0%) lo iniziano in RSA, 1,392 (18.6%) in ospedale, e 1,310 (17.5%) ricevono antipsicotici dispensati come outpatients.
- Gli antipsicotici sono comunemente prescritti nei primi giorni di degenza in RSA, e 3,026 (40.4%) ricevono gli antipsicotici nei primi 7 giorni dall'ammissione.
- Solo il 58% (n = 4,348) dei residenti iniziano un antipsicotico con indicazioni appropriate in base a quanto riportato nella documentazione sanitaria.

Zhang Y et al., J Am Geriatr Soc 66:1082–1088, 2018.

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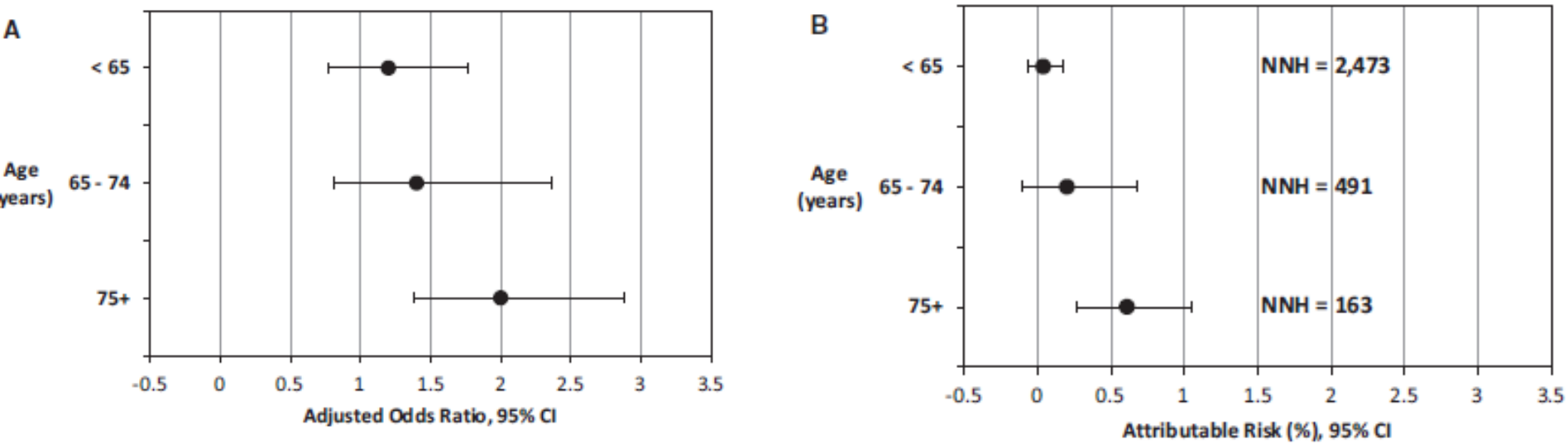
Antipsychotics and the Risk of Aspiration Pneumonia in Individuals Hospitalized for Nonpsychiatric Conditions: A Cohort Study

CLINICAL INVESTIGATION



(A) Adjusted association between antipsychotic exposure and aspiration pneumonia according to age. (B) Adjusted absolute incidence of aspiration pneumonia attributable to antipsychotic exposure (attributable risk), calculated as the difference between the adjusted incidence of aspiration pneumonia in exposed and unexposed individuals, derived using Bayes theorem.

Herzig SJ J Am Geriatr Soc 2018

Original Investigation

Antipsychotics, Other Psychotropics, and the Risk of Death in Patients With Dementia

Number Needed to Harm

Donovan T. Maust, MD, MS; Hyungjin Myra Kim, ScD; Lisa S. Seyfried, MD, MS; Claire Chiang, PhD; Janet Kavanagh, MS; Lon S. Schneider, MD, MS; Helen C. Kales, MD

Table 2. Crude Death Rates During a 180-Day Observation Period Among Patients With Dementia Starting Therapy With a New Medication

Medication	No. of Pair[a]	Death, No. (%)		Risk Difference, % (95% CI)[b]	NNH (95% CI)[b]
		Users	Nonusers		
Haloperidol	1921	398 (20.7)	162 (8.4)	3.8 (1.0 to 6.6)[c]	26 (15 to 99)
Olanzapine	1908	265 (13.9)	187 (9.8)	2.5 (0.3 to 4.7)[d]	40 (21 to 312)
Quetiapine	4621	545 (11.8)	378 (8.2)	2.0 (0.7 to 3.3)[c]	50 (30 to 150)
Risperidone	6338	883 (13.9)	538 (8.5)	3.7 (2.2 to 5.3)[c]	27 (19 to 46)
Valproic acid	901	110 (12.2)	65 (7.2)	4.1 (−1.0 to 9.2)	NA[e]
Antidepressant	29 704	2472 (8.3)	2367 (8.0)	0.6 (0.3 to 0.9)[c]	166 (107 to 362)

JAMA Psychiatry 2015

Choosing Wisely®

An initiative of the ABIM Foundation

American Geriatrics Society

AGS Geriatrics Healthcare Professionals

Leading Change. Improving Care for Older Adults.

Five Things Physicians and Patients Should Question

2 Don't use antipsychotics as the first choice to treat behavioral and psychological symptoms of dementia.

People with dementia often exhibit aggression, resistance to care and other challenging or disruptive behaviors. In such instances, antipsychotic medicines are often prescribed, but they provide limited and inconsistent benefits, while posing risks, including over sedation, cognitive worsening and increased likelihood of falls, strokes and mortality. Use of these drugs in patients with dementia should be limited to cases where non-pharmacologic measures have failed and patients pose an imminent threat to themselves or others. Identifying and addressing causes of behavior change can make drug treatment unnecessary.

3 Avoid using medications to achieve hemoglobin A1c <7.5% in most adults age 65 and older; moderate control is generally better.

There is no evidence that using medications to achieve tight glycemic control in older adults with type 2 diabetes is beneficial. Among non-older adults, except for long-term reductions in myocardial infarction and mortality with metformin, using medications to achieve glycated hemoglobin

Measurement (QPMC) committees. AGS members were invited to submit feedback and recommendations as to what they thought should be included in the list

4 Don't use benzodiazepines or other sedative-hypnotics in older adults as first choice for insomnia, agitation or delirium.

Large-scale studies consistently show that the risk of motor vehicle accidents, falls and hip fractures leading to hospitalization and death can more than double in older adults taking benzodiazepines and other sedative-hypnotics. Older patients, their caregivers and their providers should recognize these potential harms when considering treatment strategies for insomnia, agitation or delirium. Use of benzodiazepines should be reserved for alcohol withdrawal symptoms/delirium tremens or severe generalized anxiety disorder unresponsive to other therapies.

5 Don't use antimicrobials to treat bacteriuria in older adults unless specific urinary tract symptoms are present.

Cohort studies have found no adverse outcomes for older men or women associated with asymptomatic bacteriuria. Antimicrobial treatment studies for asymptomatic bacteriuria in older adults demonstrate no benefits and show increased adverse antimicrobial effects. Consensus criteria has been developed to characterize the specific clinical symptoms that, when associated with bacteriuria, define urinary tract infection. Screening for and treatment of asymptomatic bacteriuria is recommended before urologic procedures for which mucosal bleeding is anticipated.

Caso clinico

- Donna di 66 anni, coniugata, 2 figlie, ricoverata da PS con diagnosi di "sepsi". Residente in RSA da marzo 2017. Dipendente in tutte ADL (mangia in autonomia, con supervisione), posizionata in carrozzina durante il giorno. Effettua qualche passo sorretta.
- APR:
  - Emiplegia dx, complicata da afasia fluente in esiti di evacuazione voluminoso ematoma intra-assiale parieto-occipitale sx. Dimessa a 01/2017 ricoverata per "infarcimento emorragico parieto-occipitale sx in paziente in TAO per Fibrillazione atriale parossistica”
  - Sindrome mielodisplastica (leucemia mielomonocitica cronica) associata a delezione cromosoma 5
  - Pregressi interventi di parziale tiroidectomia (20 anni fa), asportazione di polipo peduncolato del sigma (adenoma tubulo-villoso con displasia a basso grado dell'epitelio), colecistectomia (2002), artroprotesi anca dx (2010)
- Portatrice di PEG dal gennaio 2017, in corso tentativo di introduzione di dieta per disfagici.

Caso clinico

- Recente comparsa di disturbi del comportamento, per i quali sostiene visita psichiatrica (atteggiamenti talora aggressivi).
- Terapia in atto: acido folico, ferro, amlodipina 10 mg, citalopram 20 mg, lansoprazolo 30 mg, paracetamolo 1 g, propafenone 325 mg x2, fondaparinux 1 fl, ramipril 5 mg, metoprololo 100 mg x 2 , levetiracetam 500 mg x2, gabapentin 100 mg x2, lacosamide 1 x 2, quetiapina 50 mg + 100 mg
- Accesso in PS il 12/06 per anemia: trasfonde 2 sacche EC per Hb 6.1 (creatinina 1.4, K 4.6)
- Condotta in PS il 02/07 per episodio di dispnea.
- In RSA somministrate: metilprednisolone 40 mg ev, adrenalina 1 fl ev.

Caso clinico

- In PS esegue:
  - EE: GB 17.83, Hb 7.6, PLT 74, K 8.7, crea 3.6, Ca 8.2, glc 165, Tropo 40, pro BNP 3172, digossina 0.2, CKMB 0.45, D-Dimero 3603

→ "Delirium ipercinetico secondario a pielonefrite sx, disidratazione e squilibrio idroelettrolitico, bradiaritmia iatrogena e inappropriato uso di farmaci"

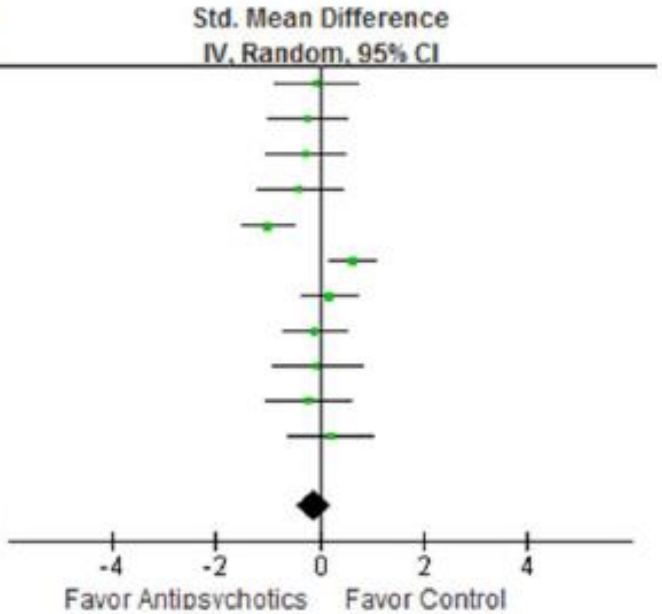
Antipsychotic Medication for Prevention and Treatment of Delirium in Hospitalized Adults: A Systematic Review and Meta-Analysis

Karin J. Neufeld, MD, MPH,[a] Jirong Yue, MD,[§a] Thomas N. Robinson, MD, MPH,[||] Sharon K. Inouye, MD, MPH,**[††b] and Dale M. Needham, MD, PhD[†‡b]*

C Delirium Severity in Hospitalized Patiens

Study or Subgroup	Antipsychotics Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Breitbart 1996	11.6	6.1	11	11.9	6.7	13	8.0%	-0.05 [-0.85, 0.76]
Grover 2011	10.1	6.4	10	11.7	7.2	21	8.4%	-0.22 [-0.98, 0.53]
Grover 2011	10.1	6.4	10	12	6.8	23	8.5%	-0.28 [-1.02, 0.47]
Han 2004	21.8	4.4	12	23.5	4.2	12	7.9%	-0.38 [-1.19, 0.43]
Kalisvaart 2005	14.4	3.4	32	18.4	4.3	36	11.3%	-1.01 [-1.52, -0.51]
Larsen 2010	16.4	3.7	28	14.5	2.7	82	12.1%	0.63 [0.20, 1.07]
Maneeton 2013	-21.7	6.7	28	-22.9	6.9	24	10.8%	0.17 [-0.37, 0.72]
Tahir 2010	7.1	3.3	21	7.4	3.3	21	10.1%	-0.09 [-0.69, 0.52]
Yoon 2013	8.5	4.6	7	8.8	6	18	7.3%	-0.05 [-0.92, 0.82]
Yoon 2013	8.5	4.6	8	9.8	6.7	21	7.8%	-0.20 [-1.02, 0.61]
Yoon 2013	8.5	4.6	8	7.6	3.7	18	7.7%	0.22 [-0.62, 1.05]
Total (95% CI)			**175**			**289**	**100.0%**	**-0.11 [-0.43, 0.22]**

Heterogeneity: Tau² = 0.18; Chi² = 25.55, df = 10 (P = 0.004); I² = 61%
Test for overall effect: Z = 0.65 (P = 0.52)



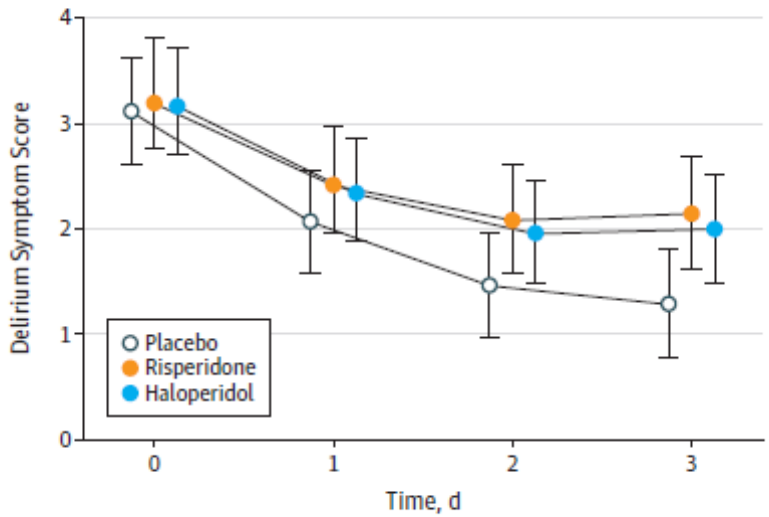
JAGS 2016: DOI: 10.1111/jgs.14076

JAMA Internal Medicine | Original Investigation

Efficacy of Oral Risperidone, Haloperidol, or Placebo for Symptoms of Delirium Among Patients in Palliative Care

A Randomized Clinical Trial

Figure 2. Secondary Multivariable Mixed-Model Analysis of Delirium



No. at risk				
Placebo	84	63	59	55
Risperidone	82	58	49	39
Haloperidol	81	64	55	51

The dependent variable was delirium score at each day. The independent variables comprise the covariates in Table 2, group, time, and 2 interaction terms, time × risperidone and time × haloperidol. The relative difference in improvement between groups at 72 hours was determined using the *lincom* function in Stata. Placebo vs risperidone: $P < .001$; placebo vs haloperidol: $P = .002$. Error bars indicate 95% CIs.

Agar M et al , 2016

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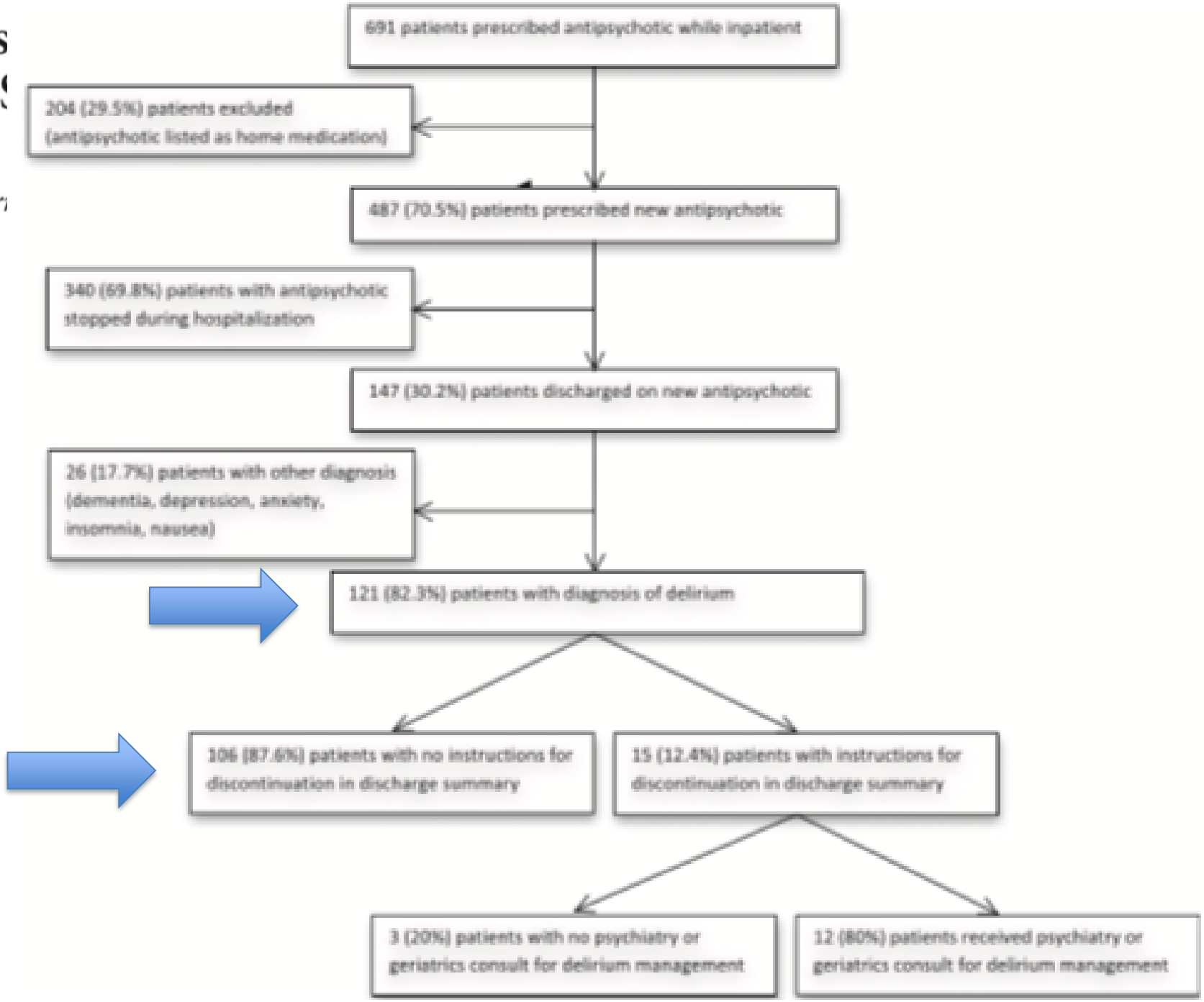


E’ possibile (ed efficace) l’approccio non farmacologico ai disturbi del comportamento?

Effectiveness of Nonpharmacological Interventions in Delaying the Institutionalization of Patients with Dementia: A Meta-Analysis

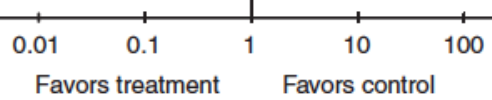
Anouk Spijker, MA,† Myrra Vernooij-Dassen, PhD,*† Emmelyne Vasse, MSc,*† Eddy Adang, PhD,‡ Hub Wollersheim, MD, PhD,* Richard Grol, PhD,* and Frans Verhey, MD, PhD§*

J Am Geriatr Soc 56:1116–1128, 2008.

Review: Effectiveness of non-pharmacological interventions in delaying the institutionalization of people with dementia (OR)
Comparison: 01 Institutionalization (Number)
Outcome: 01 Odds of Institutionalization

Study or subcategory	Treatment n/N	Control n/N	OR (random) 95% CI	Weight %	OR (random) 95% CI
Brodaty 1991	14/33	25/31		8.00	0.18 [0.06–0.55]
Droës 2004	3/40	10/33		6.10	0.19 [0.05–0.75]
Eloniemi-Sulk 2001	17/53	14/47		10.75	1.11 [0.48–2.61]
Miller 1999	1,831/4,151	1,692/3,944		19.56	1.05 [0.96–1.15]
Mittelman 1993	11/103	24/103		11.66	0.39 [0.18–0.85]
Mohide 1990	11/30	11/30		8.68	1.00 [0.35–2.86]
Nobili 2004	4/35	4/34		5.62	0.97 [0.22–4.23]
Teri 2003	21/76	22/77		12.54	0.95 [0.47–1.93]
Vernooij-Dassen 1993	8/58	17/61		9.84	0.41 [0.16–1.05]
Woods 2003	5/43	7/61		7.26	1.02 [0.30–3.44]
Total (95% CI)	4,622	4,421		100.00	0.66 [0.43–0.99]

Total events: 1,925 (Treatment), 1,826 (Control)
Test for heterogeneity: $Chi^2 = 24.90$, df = 9 (P = 0.003), $I^2 = 63.9\%$
Test for overall effect: Z = 2.00 (P = 0.05)



Special care units for BPSD management

	Mean ± SD at baseline	Mean ± SD at 3 months	Mean ± SD at 6 months	*P**	*P***
MMSE	6.1 ±5.0	6.8 ±6.1	6.2 ±6.8	n.s.	n.s.
Barthel Index	36.2 ±26.3	39.7 ±27.0	41.6 ±28.2	n.s.	n.s.
NPI	38.2 ±16.5	29.2 ±15.7	25.6 ±16.7	.001	<.0005
Psychotropic drugs	1.5 ±.9	1.1 ±.8	.8 ±.8	<.0005	<.0005
Physical restraints	20 (36.4 %)	--	16 (29.0 %)	--	.002

Bellelli G et al, Gerontologist, 1998

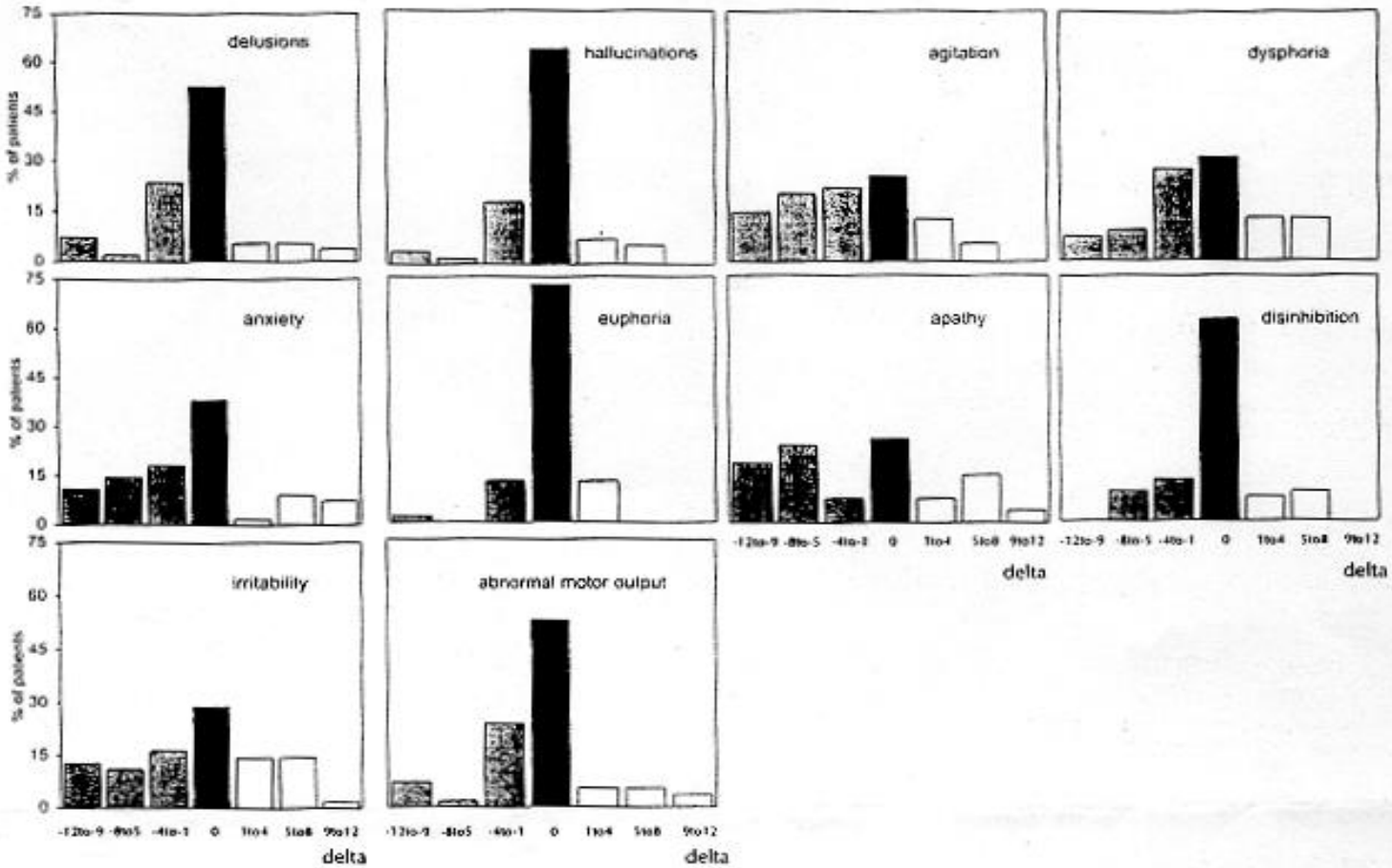


Figure 1. Changes of behavioral disturbances in 55 demented patients between admission to SCUs and 6-month follow-up. Delta denotes the difference of behavioral disturbance score between admission and 6 months later. Negative values of delta indicate improvement (▒), zero indicates no change (■), and positive values indicate worsening (□). Columns indicate percentages of patients.

Bellelli G. et al., Gerontologist 1998

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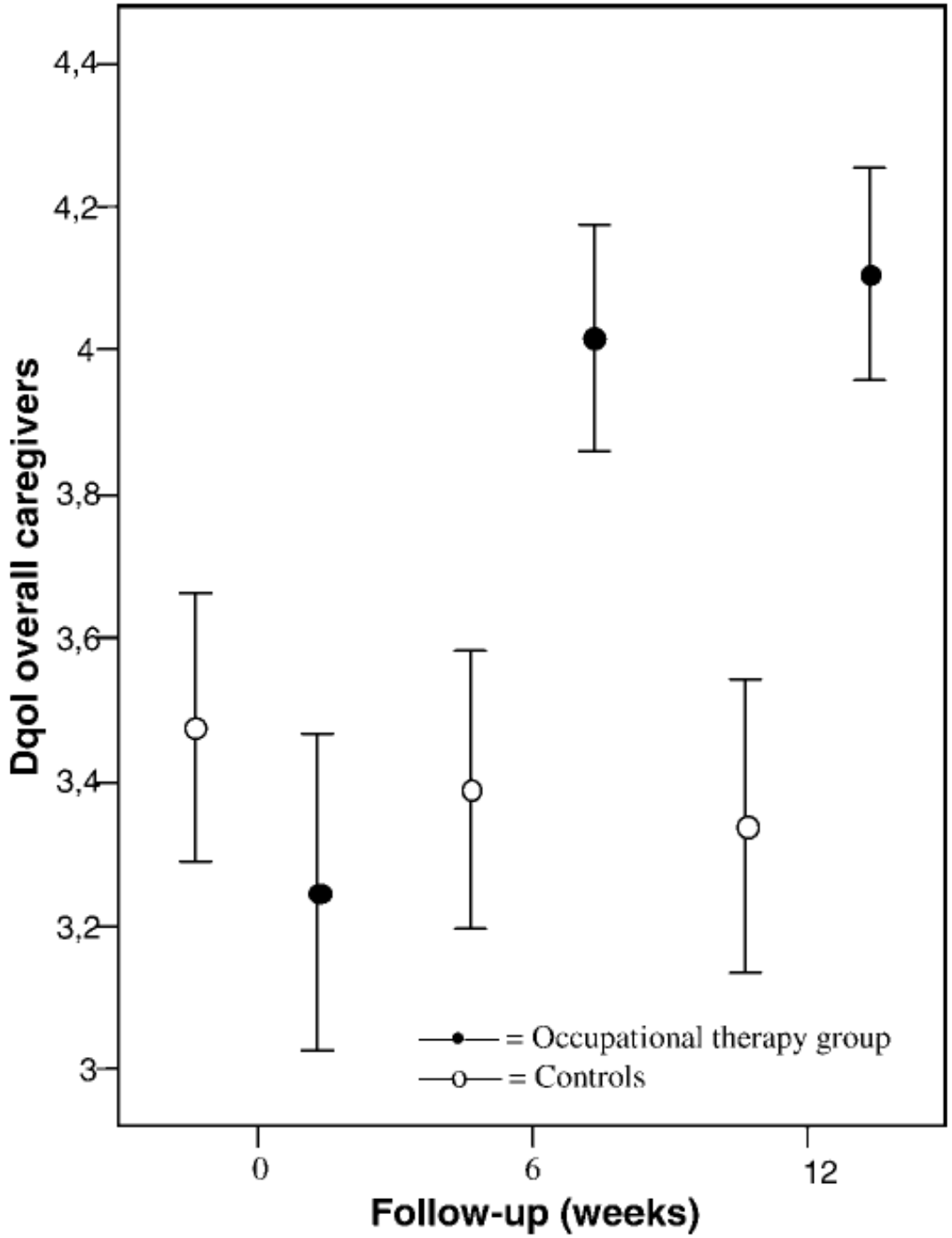

l Biol Med Sci, 2007

Targeting Behavioral Symptoms and Functional Decline in Dementia: A Randomized Clinical Trial

*Laura N. Gitlin, PhD,[*] Paul Arthur, PhD, OTR/L,[†‡] Catherine Piersol, PhD, OTR/L,[§] Virginia Hessels, BA,[‡] Samuel S. Wu, PhD,[¶] Yunfeng Dai, MS,[¶] and William C. Mann, PhD, OTR[‡**]*

- Single-blind (interviewer), parallel, RCT
- Veterans with dementia and their family caregivers (N = 160 dyads)
- Dyads in Tailored Activity Program-VA underwent 8 sessions with occupational therapists to customize activities to the interests and abilities of the veterans and educate their caregivers about dementia and use of customized activity.
- At 4 months, compared to controls, the TAP-VA group showed reductions in number (difference in mean change from baseline = −0.68 and frequency by severity (−24.3) of behavioral symptoms, number of activities needing assistance, functional dependence level, and pain. Caregivers of veterans in TAP-VA reported less behavior-related distress.

J Am Geriatr Soc 66:339–345, 2018.

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Primo: escludere la presenza di delirium

- “Il delirium è un messaggero molto più comune di malattia acuta in una persona anziana di quanto non lo siano, ad esempio, febbre, dolore, o tachiacrdia”
- “L’incapacità di diagnosticare il delirium e di identificare e trattare le cause sottostanti può avere conseguenze letali per il paziente, dato che spesso è il “sintomo” di presentazione di infarto del miocardio, polmonite, o altre malattia che pongono il paziente a rischio della vita”.

Lipowski ZJ, Am J Psychiatry 1983
Lipowski ZJ, NEJM 1989

A Model for Managing Delirious Older Inpatients

***D**rugs*	*Farmaci*
***E**lecrolyte disturbances*	*Disturbi elettrolitici*
***L**ack of drugs*	*Mancanza analgesici-sedativi*
***I**schemia/Intracranial disorders*	*Ictus ischemico/emorragico, tumori*
***R**etention/poor sensory input*	*Ritenzione urinaria/ assenza protesi*
***I**nfections*	*Infezioni*
***U**nderhydration*	*Disidratazione*
***M**etabolic/Myocardial*	*Disordini metabolici/IMA*
***S**ubdural*	*Ematoma subdurale*

Mod da Flaherty, JAGS 2003 e Marcantonio NEJM 2017

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Secondo: escludere che il farmaco sia richiesto dal caregiver senza un reale bisogno!

Table 3 Logistic regression on determinants of antipsychotics prescription

Covariates	OR (95% CI)	*P*
Age	1.00 (0.96–1.03)	0.846
Female (ref. male)	1.18 (0.74–1.86)	0.485
Living condition (ref. alone)	–	–
Only with care worker	2.64 (1.21–5.75)	0.015
With care worker and family members	1.01 (0.23–4.41)	0.986
Only with family members	1.31 (0.71–2.40)	0.385
Adjusted MMSE (ref. >24)	–	–
18–24	1.00 (0.55–1.11)	0.991
<18	1.49 (0.88–2.53)	0.135
Delirium (ref. no)	3.87 (2.01–7.47)	0.000
Depression (ref. no)	0.59 (0.34–1.02)	0.061
Stroke (ref. no)	0.93 (0.51–1.68)	0.800
Dementia (ref. no)	2.73 (1.65–4.51)	0.000
No. pathologies	0.91 (0.82–1.00)	0.055
ADL limitations	1.02 (0.89–1.16)	0.811
IADL limitations	1.12 (1.05–1.21)	0.001
No. medicines beside antipsychotics at discharge	0.96 (0.89–1.05)	0.403

928 pazienti ricoverati in unità per acuti; età 80.8 ± 7.2 anni, 54.9% femminile

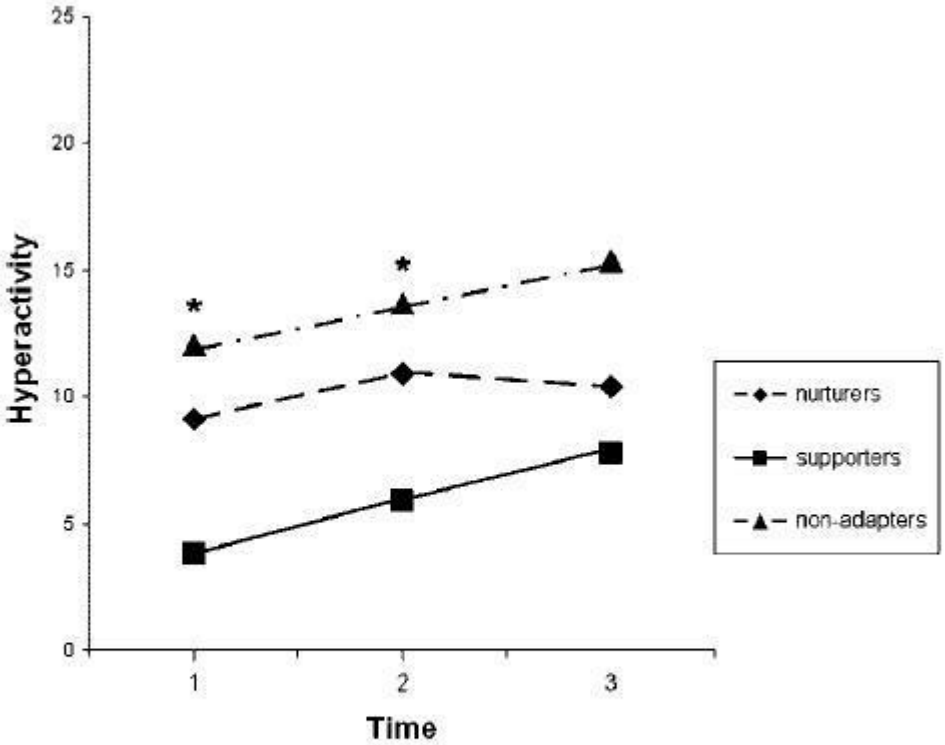
Variabili indipendentemente associate alla prescrizione di AP alla dimissione:

- Storia di demenza (OR 2.73, 95% CI 1.65–4.51),
- IADL impairment (OR 1.12, 95% CI 1.05–1.21)
- Delirium intercorrente (OR 3.87, 95% CI 2.01–7.47)

Di Rosa M et al., Geriatr Gerontol Int 2016

Do caregivers management strategies influence patient behavior in dementia?

99 pazienti con demenza e caregiver informali seguiti per un anno
Senso di competenza misurato con SSCQ e BPSD con NPI



$* \, p < 0.05$

Figure 2. Hyperactivity in patients of nurterers ($n = 23$), supporters ($n = 44$), and non-adapters ($n = 14$)

De Vugt ME, Int J Geriatr Psych 2004

In sintesi: The DICE Approach

Management of Neuropsychiatric Symptoms of Dementia in Clinical Settings: Recommendations from a Multidisciplinary Expert Panel

Helen C. Kales, MD,[a,b,c] Laura N. Gitlin, PhD,[d,e,f,g] and Constantine G. Lyketsos, MD,[g,h] for the Detroit Expert Panel on the Assessment and Management of the Neuropsychiatric Symptoms of Dementia

J Am Geriatr Soc 2014.

- **D**escribe
  - Contesto (chi, cosa, quando e dove)
- **I**nvestigate
  - Paziente (effetti collaterali farmaci, dolore, limitazione funzionale, condizioni mediche, comorbilità psichiatrica, severità deficit cognitivo, scarsa igiene, paura, isolamento)
  - Aspettative caregiver
  - Ambiente
  - Fattori culturali
- **C**reate
  - Risolvi problemi clinici
  - Migliora comunicazione con paziente
  - Proponi attività significative per il paziente
  - Crea ambiente idoneo
- **E**valute

Terapia non farmacologica

1. Stimolazione cognitiva/riorientamento
2. Comunicazione adeguata: rassicurare, parlare chiaramente, guardare negli occhi, evitare movimenti bruschi
3. Coinvolgimento dei familiari
4. Favorire la mobilizzazione e attività salient (OT/FT)
5. Ridurre al minimo mezzi di contenzione e utilizzo di presidi invasivi (catetere vescicale, linee venose)
6. Ridurre i deficit sensoriali: illuminazione adeguata, occhiali, protesi acustica
7. Facilitare il ritmo sonno-veglia (evitare rumori non necessari, illuminazione di bassa intensità)
8. Stanza adeguata: quieta, no spostamenti se possibile, vicino a postazione infermieristica

Conclusioni

- I disturbi del comportamento sono una condizione di frequente riscontro in ambito assistenziale
- Di fronte a un nuovo disturbo del comportamento va sempre e prioritariamente esclusa la presenza di delirium
- L'approccio farmacologico è più rischioso in termini di complicanze e mortalità
- L'approccio non farmacologico è sempre da preferire ed è eventualmente complementare al trattamento farmacologico