

# Polipatologie e politrattamenti

I Convegno

**IGEA: dal progetto al sistema**

L'integrazione delle cure  
per le persone con malattie croniche

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22 – 23 aprile 2013



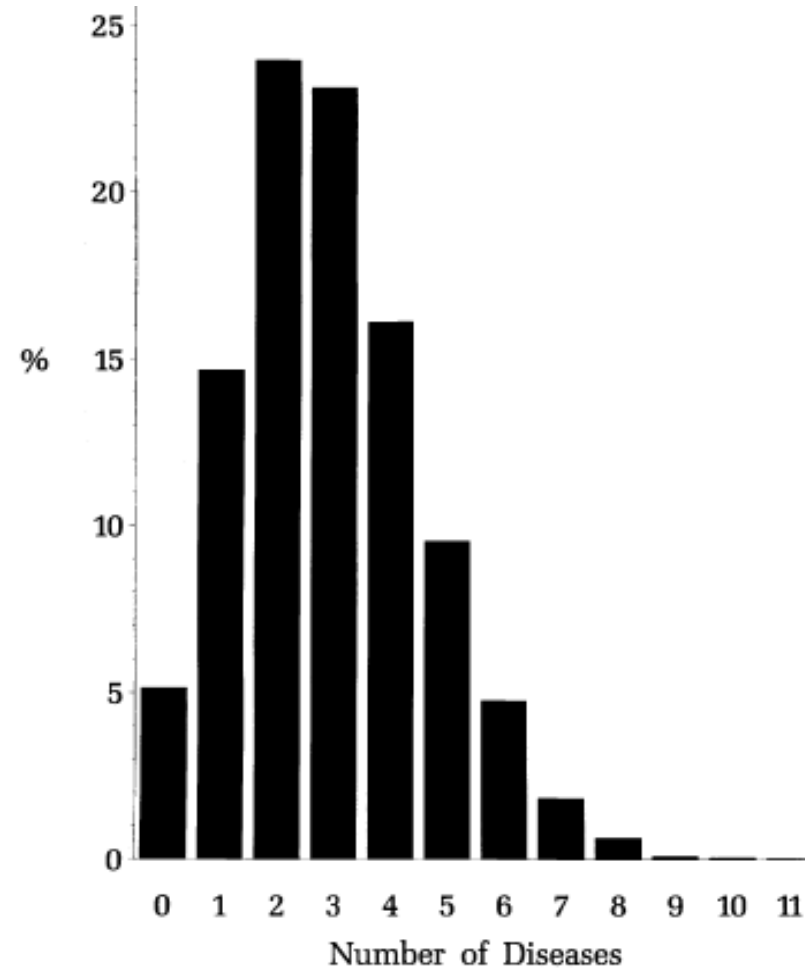
Graziano Onder  
Centro Medicina Invecchiamento  
Università Cattolica Sacro Cuore  
Roma



*ISTITUTO SUPERIORE DI SANITÀ*

# Comorbidity

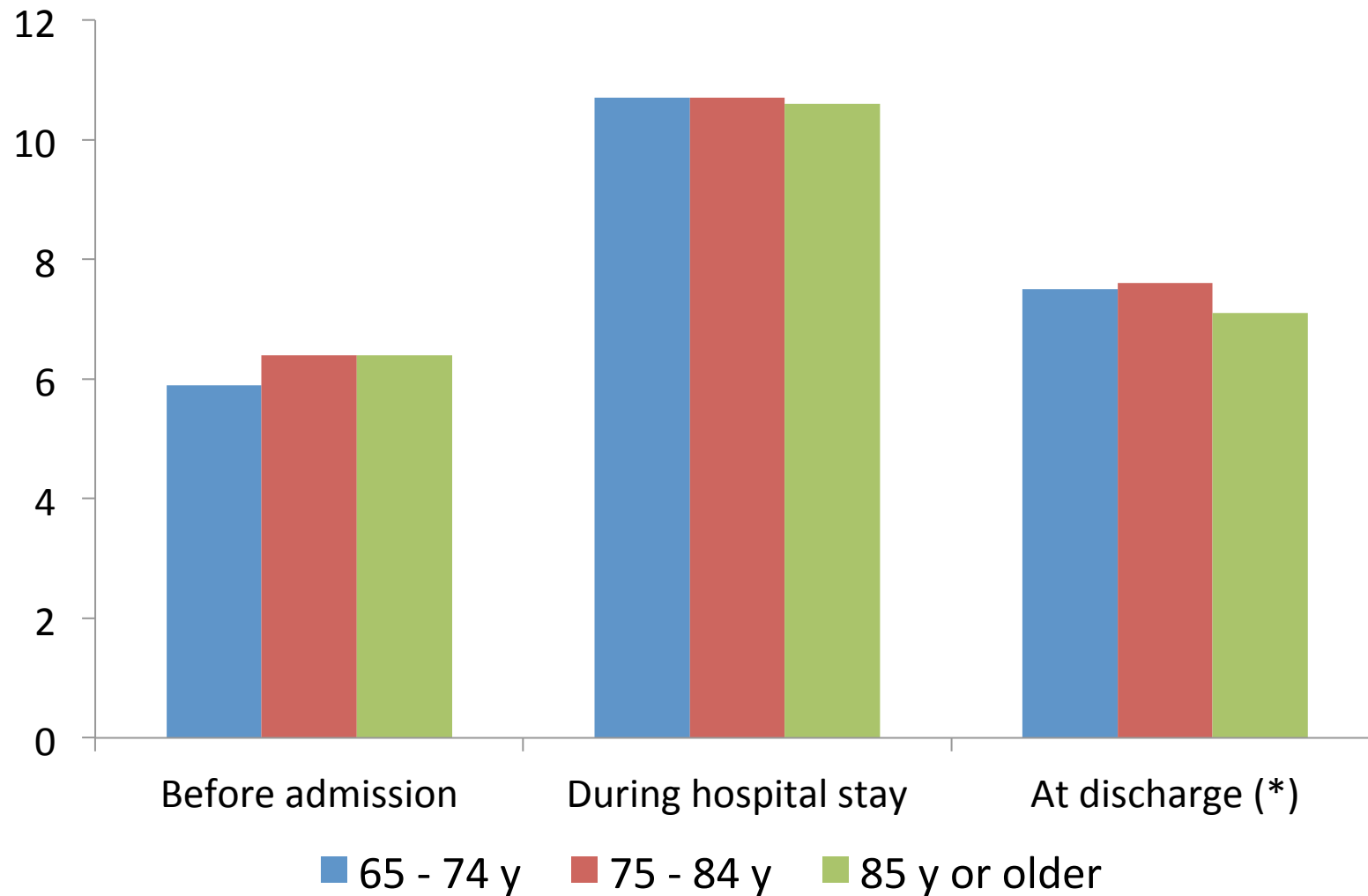
Age	Number of patients	Prevalent multi-morbidity (%)	Mean number of prevalent diseases
0-19	6994	10.7	0.51
20-39	9317	16.0	0.68
40-59	8243	33.6	1.27
60-79	4596	60.9	2.42
≥80	480	74.2	3.24
0-19	6723	9.2	0.46
20-39	9804	18.8	0.78
40-59	7821	35.9	1.35
60-79	5739	64.9	2.61
≥80	1140	79.9	3.57



Van den Akker M, et al. J Clin Epi 1998

Fried LP et al. J Clin Epi 1999

# Drug use in hospital patients



Dati CRIME unpublished

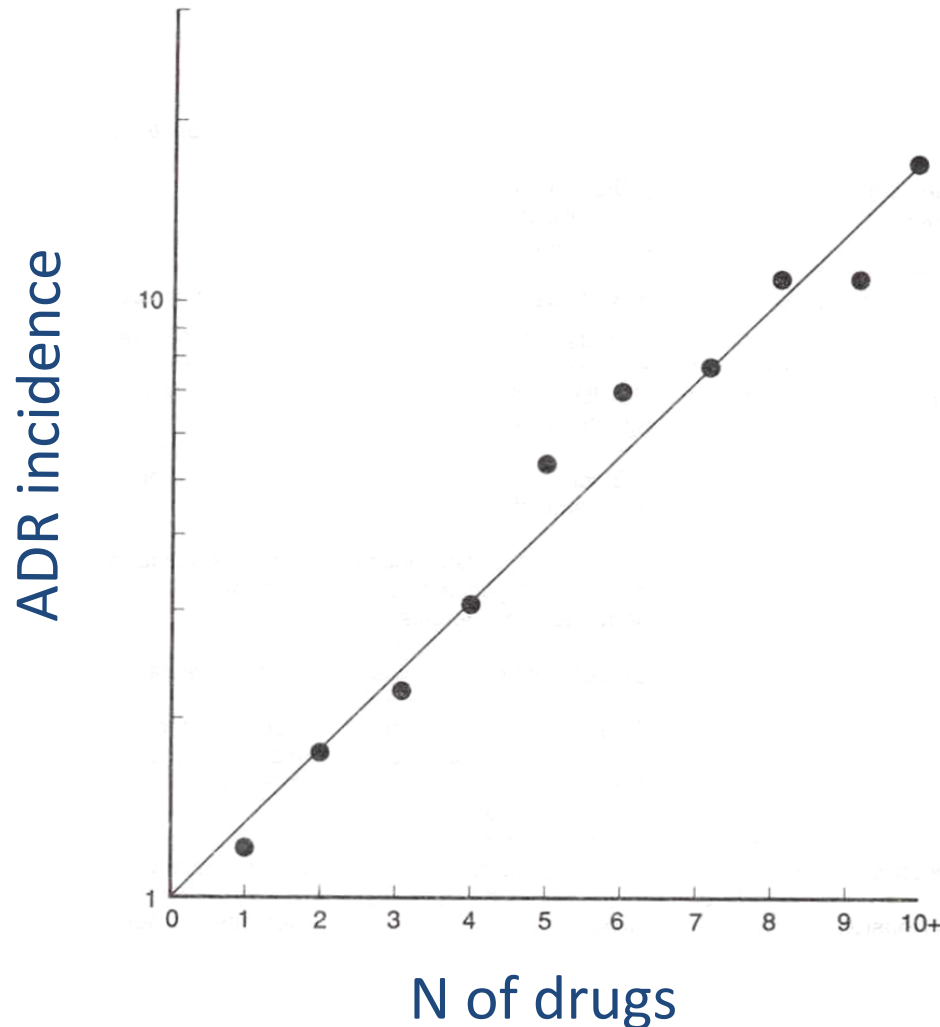
# Potentially Harmful Drug-Drug and Drug-Disease Combinations

	Drug-drug combination (%)	Drug-disease combination (%)
Total population	0.76	2.58
Age (years)		
65-79	0.64	2.25
70-74	0.63	2.62
75-79	0.95	2.79
80-84	0.95	2.44
≥85	0.52	3.03

# Major Predictors of Poor Adherence to Medication

Predictor	Study
<u>Presence of psychological problems, particularly depression</u>	van Servellen et al., <sup>51</sup> Ammassari et al., <sup>52</sup> Stilley et al. <sup>53</sup>
<u>Presence of cognitive impairment</u>	Stilley et al., <sup>53</sup> Okuno et al. <sup>54</sup>
<u>Treatment of asymptomatic disease</u>	Sewitch et al., <sup>55</sup>
Inadequate follow-up or discharge planning	Sewitch et al., <sup>55</sup> Lacro et al. <sup>56</sup>
Side effects of medication	van Servellen et al. <sup>51</sup>
Patient's lack of belief in benefit of treatment	Okuno et al., <sup>54</sup> Lacro et al. <sup>56</sup>
Patient's lack of insight into the illness	Lacro et al., <sup>56</sup> Perkins <sup>57</sup>
Poor provider-patient relationship	Okuno et al., <sup>54</sup> Lacro et al. <sup>56</sup>
Presence of barriers to care or medications	van Servellen et al., <sup>51</sup> Perkins <sup>57</sup>
Missed appointments	van Servellen et al., <sup>51</sup> Farley et al. <sup>58</sup>
<u>Complexity of treatment</u>	Ammassari et al. <sup>52</sup>
Cost of medication, copayment, or both	Balkrishnan, <sup>59</sup> Ellis et al. <sup>60</sup>

# N of drugs and ADR



N of drugs used increased the risk of experiencing an Adverse Drug Reaction

SOUNDING BOARD

**Potential Pitfalls of Disease-Specific Guidelines  
for Patients with Multiple Conditions**

Mary E. Tinetti, M.D., Sidney T. Bogardus, Jr., M.D., and Joseph V. Agostini, M.D.

 Comment

www.thelancet.com Vol 367 February 18, 2006

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Comorbidity and guidelines: conflicting interests

# 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.

**JAMA**





"Your numerous prescriptions really have improved my love life. I'm dating my pharmacist."

# Potential treatment interactions

Type of Disease	Medications With Potential Interactions	Type of Interaction		
		Medication and Other Disease	Medications for Different Diseases	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; aspirin 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

# Clinical Practice Guidelines and Quality of Care for Older Patients With Multiple Diseases

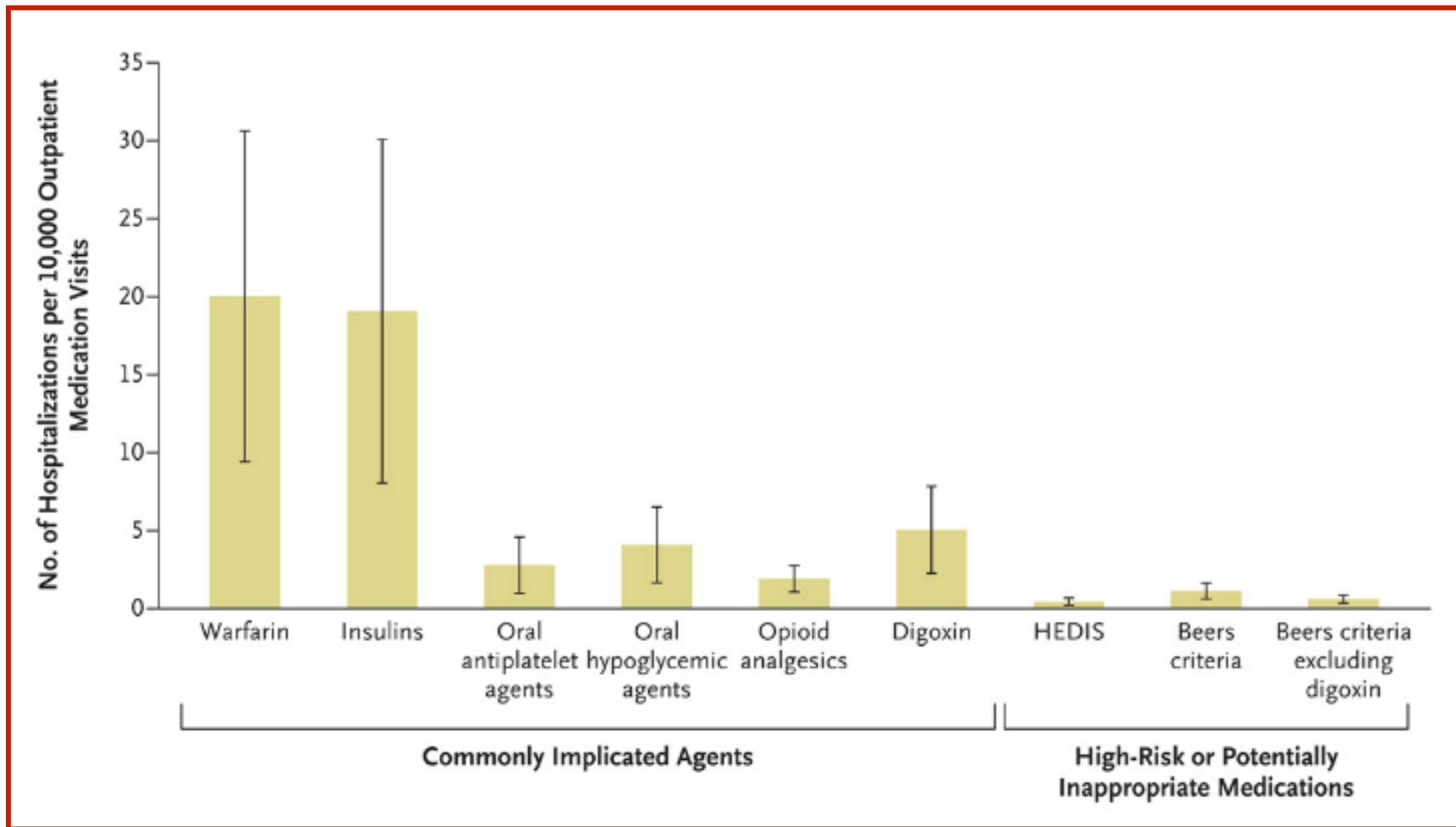
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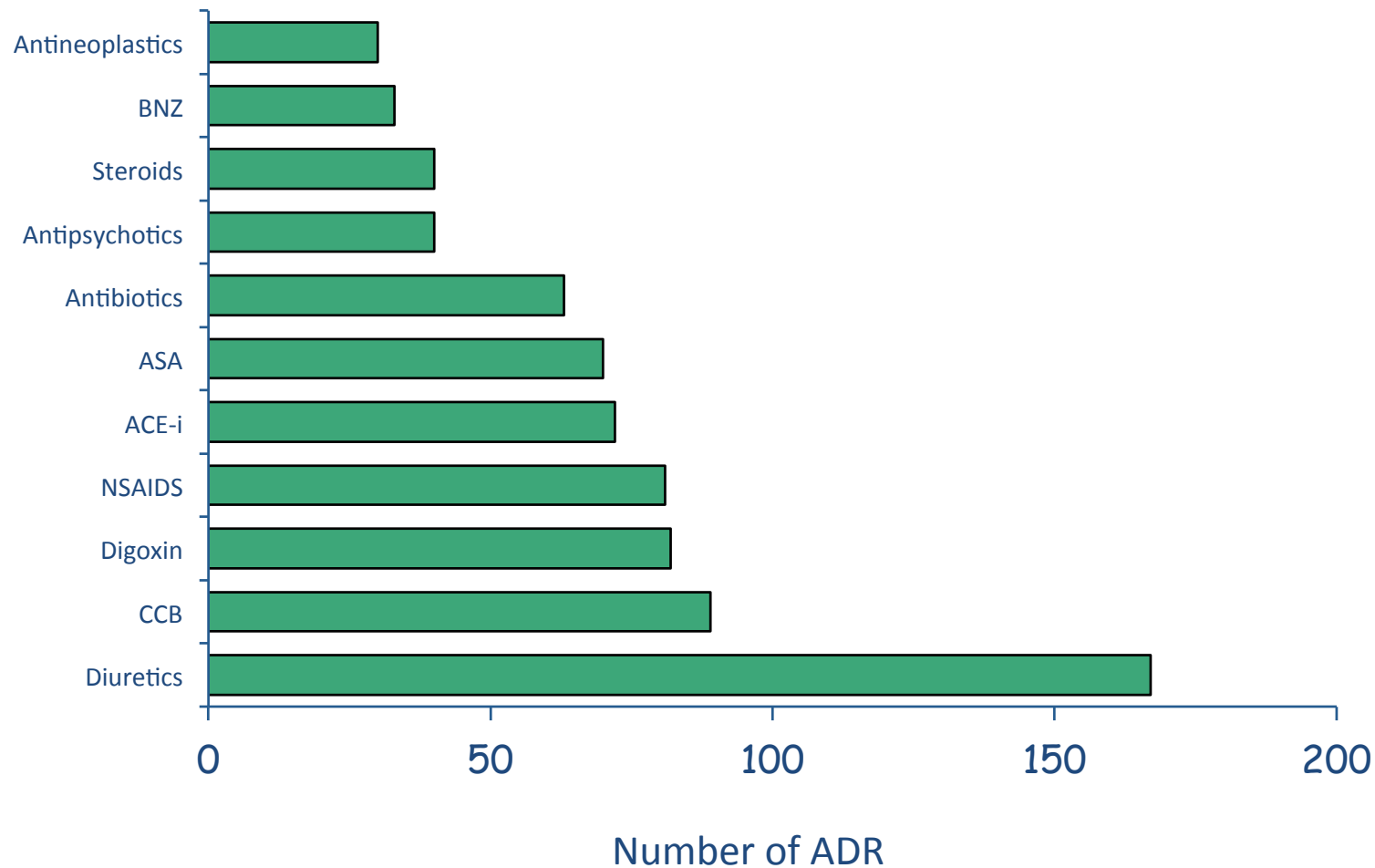
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# Rates of Emergency Hospitalizations for ADE in Older U.S. Adults.



# Drugs responsible for ADR: results from the GIFA study



Onder G et al. JAGS 2002



Several factors may limit the use of beneficial drugs in the elderly:

## 1. Comorbidity – Polipharmacy



Several factors may limit the use of beneficial drugs in the elderly:

1. Comorbidity – Polipharmacy
2. Limited life expectancy

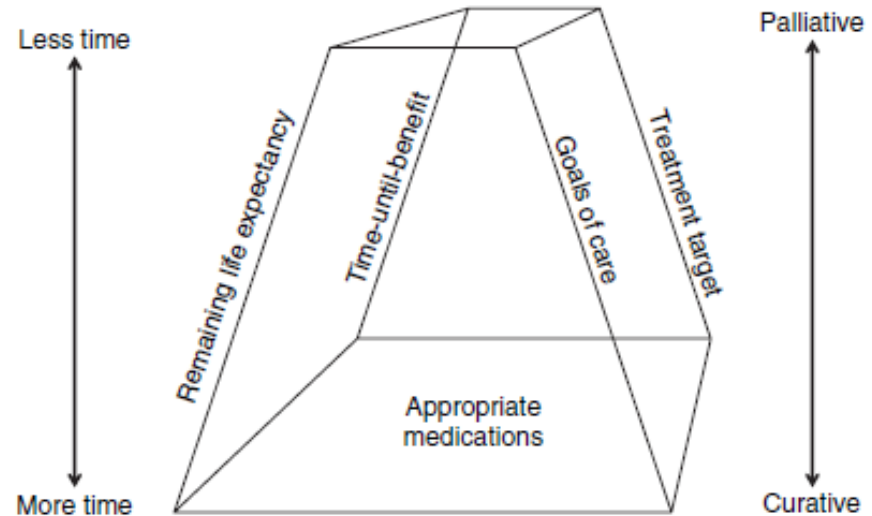
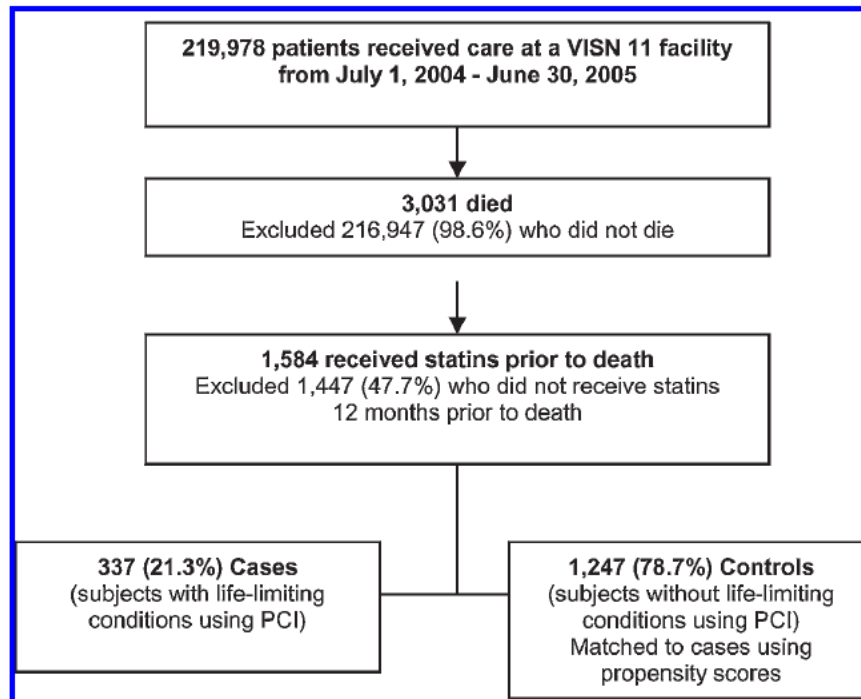


Brief Reports

Statins in the Last Six Months of Life: A Recognizable, Life-Limiting Condition Does Not Decrease their Use

MARIA J. SILVEIRA, M.D., M.A., M.P.H.,<sup>1,2</sup> ANAMARIA SEGNINI KAZANIS, M.A., M.A.,<sup>1</sup> and MATTHEW P. SHEVRIN, B.A.<sup>1</sup>

In conclusion, we find that statins are prescribed frequently in the last year of life for patients carrying recognizable, life-limiting conditions and that the patient's diagnosis does not appear to affect prescribing patterns. The small amount of discontinuation we did observe in the last 6 months of life occurs for reasons we have yet to understand. Still, our findings highlight an area for discussion as a specialty and potential intervention in the future.

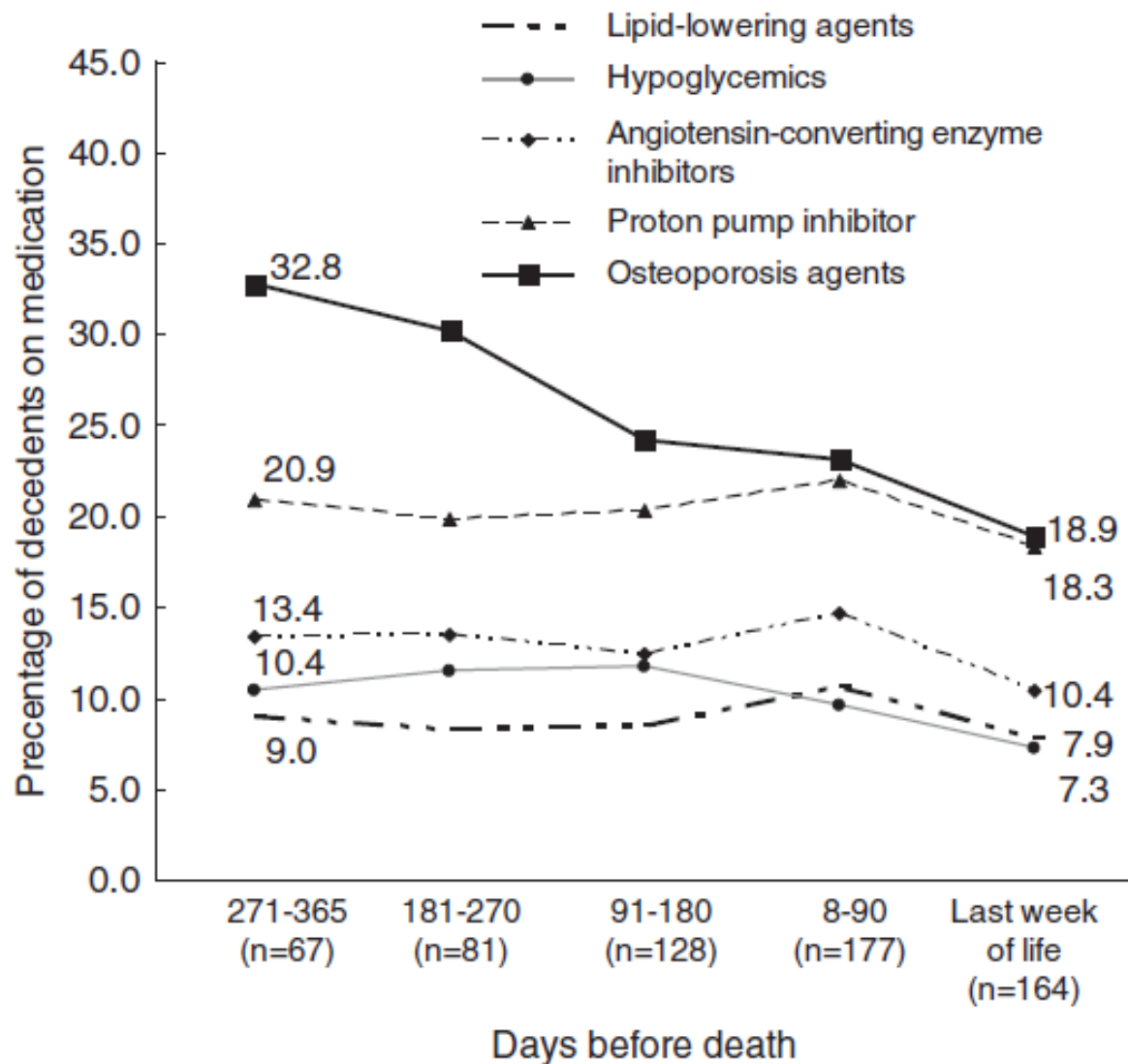


Holmes, Clin Pharmacol Ther 2009



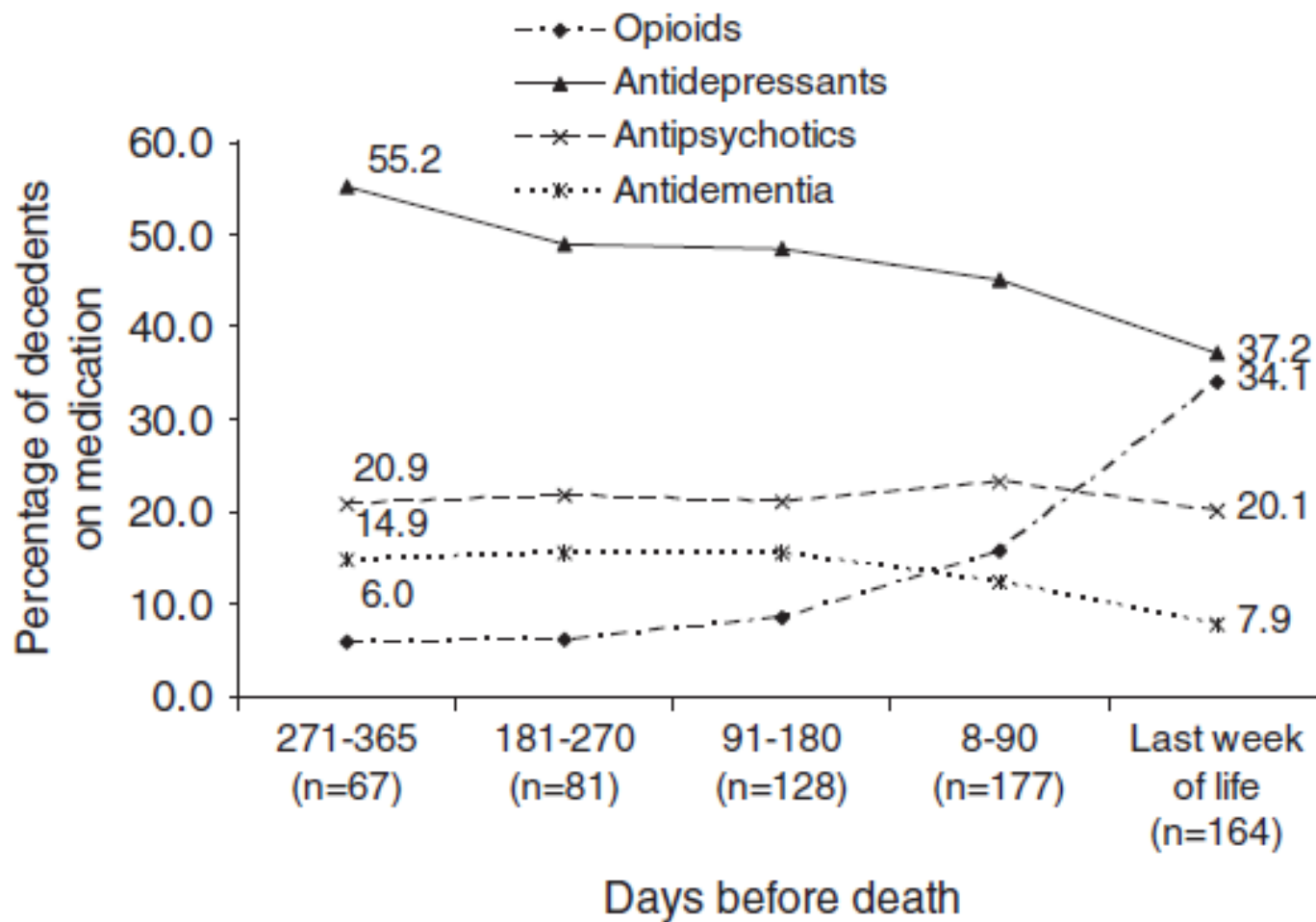


# Daily Medication Use in Nursing Home Residents with Advanced Dementia





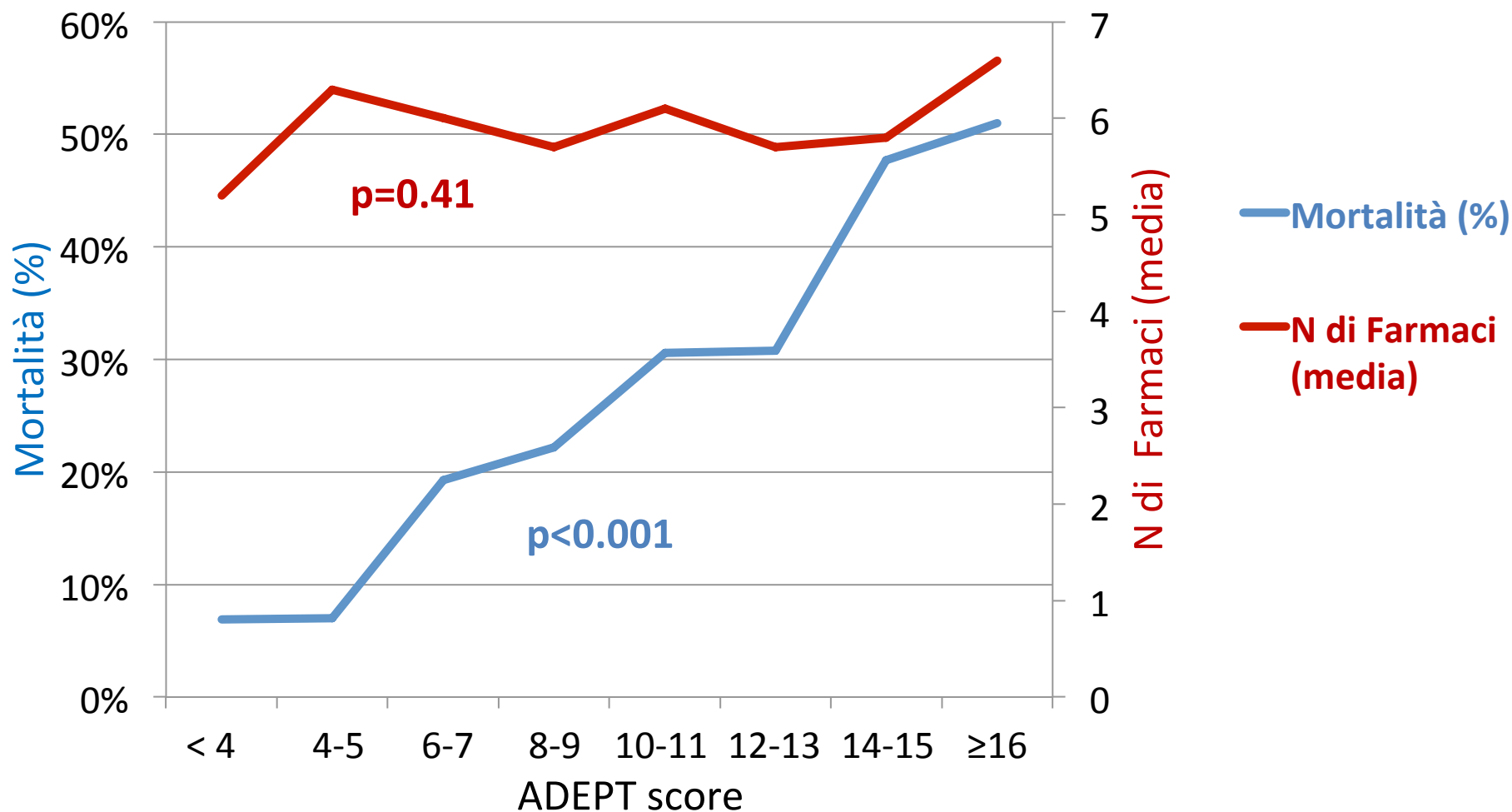
# Daily Medication Use in Nursing Home Residents with Advanced Dementia





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# RISULTATI – N di Farmaci e Aspettativa di Vita

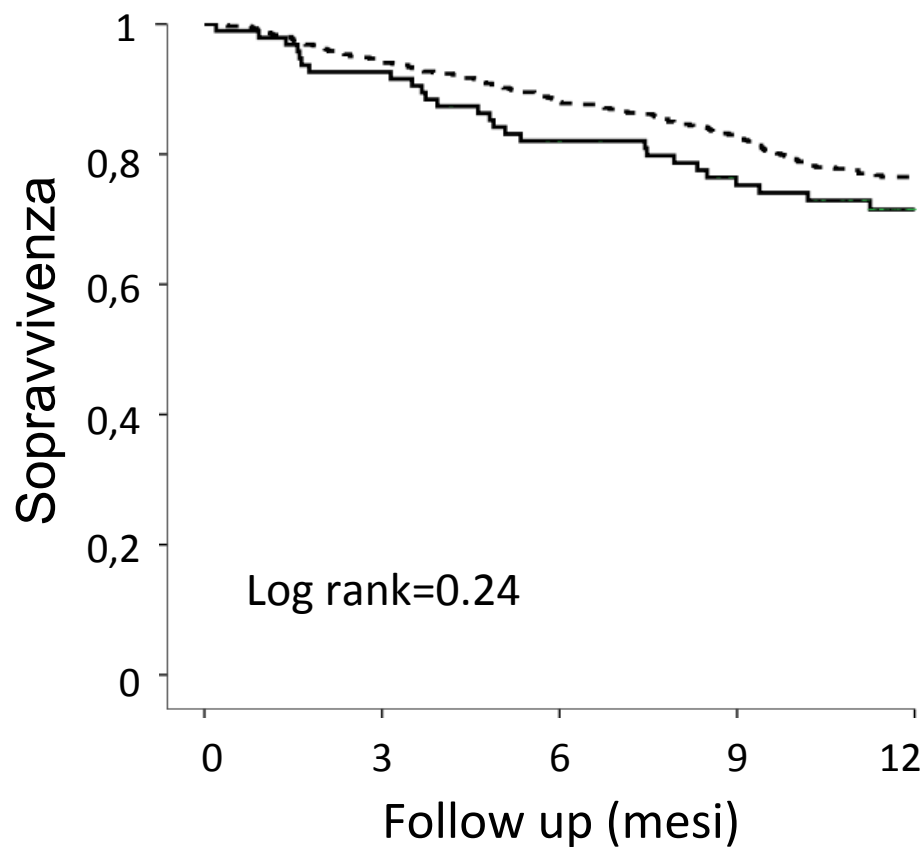




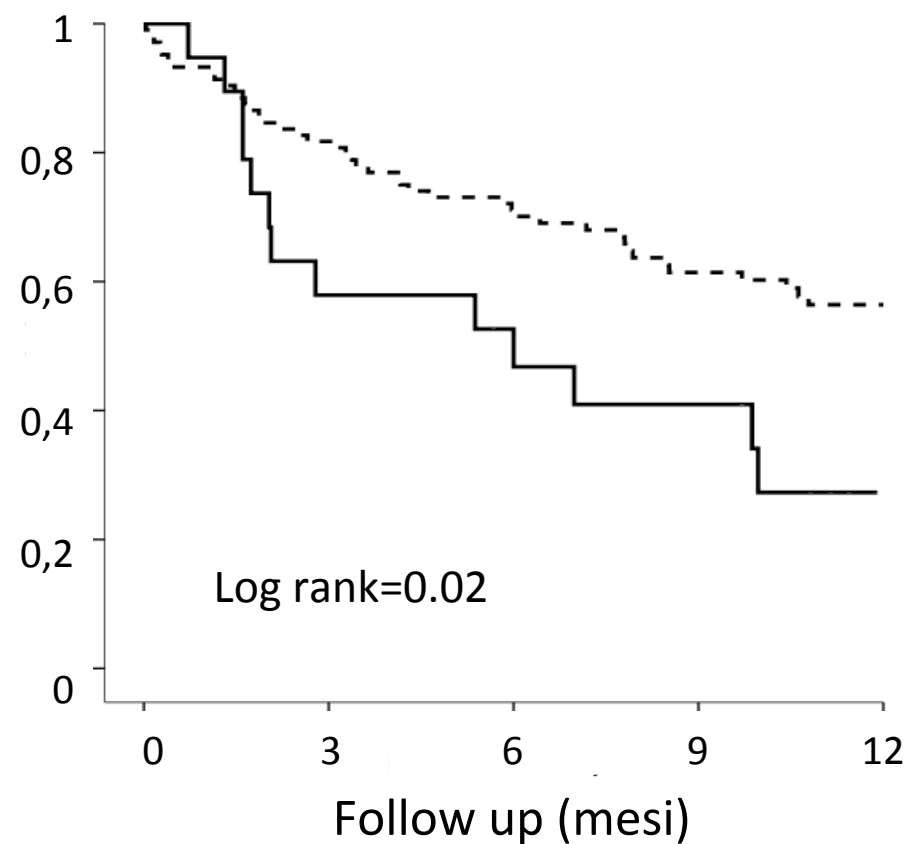
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del Sacro Cuore

# RISULTATI - Politerapia e sopravvivenza

**ADEPT score < 13.5**



**ADEPT score  $\geq 13.5$  (attesa di vita limitata)**



———— Politerapia      - - - - - Non politerapia

# Polypharmacy and mortality in dementia: the SHELTER study

	N of events	Crude Incident Rate per p-y	Crude Hazard Ratio (95% CI)	Adjusted* Hazard Ratio (95% CI)
<b>ADEPT &lt; 13.5 (n=718)</b>				
No polypharmacy	136/2,361 (21.9)	0.27	1 (Reference)	1 (Reference)
Polypharmacy	28/394 (28.6)	0.35	1.31 (0.87-1.97)	1.16 (0.76-1.77)
<b>ADEPT ≥ 13.5 (n=104)</b>				
No polypharmacy	37/88 (42.0)	0.63	1 (Reference)	1 (Reference)
Polypharmacy	11/16 (68.8)	1.50	2.15 (1.09-4.24)	2.17 (1.08-4.35)

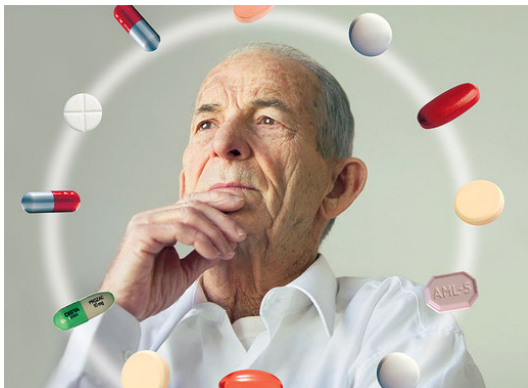
Several factors may limit the use of beneficial drugs in the elderly:

1. Comorbidity – Polipharmacy
2. Limited life expectancy
3. Functional and cognitive limitation

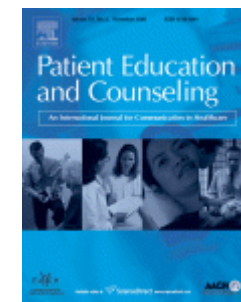


# Medication management by age

	Age groups		
	77-79	80-84	85+
<b>Tests</b>			
<u>Open bottle</u> ( $n = 487$ )	<u>8.3</u>	<u>10.9</u>	<u>24.8</u>
<u>Read instructions</u> ( $n = 489$ )	<u>0.8</u>	<u>6.9</u>	<u>20.1</u>
<u>Understand instructions</u> ( $n = 423$ )	<u>23.6</u>	<u>31.5</u>	<u>38.4</u>
Calculate number of days ( $n = 441$ )	43.0	44.5	56.6
Calculate change ( $n = 491$ )	13.6	26.2	39.4
Did not pass all tests	57.6	61.4	79.9



Beckmen A Patient Educ Couns. 2005



# Treatment of non dementia illness in patients with dementia

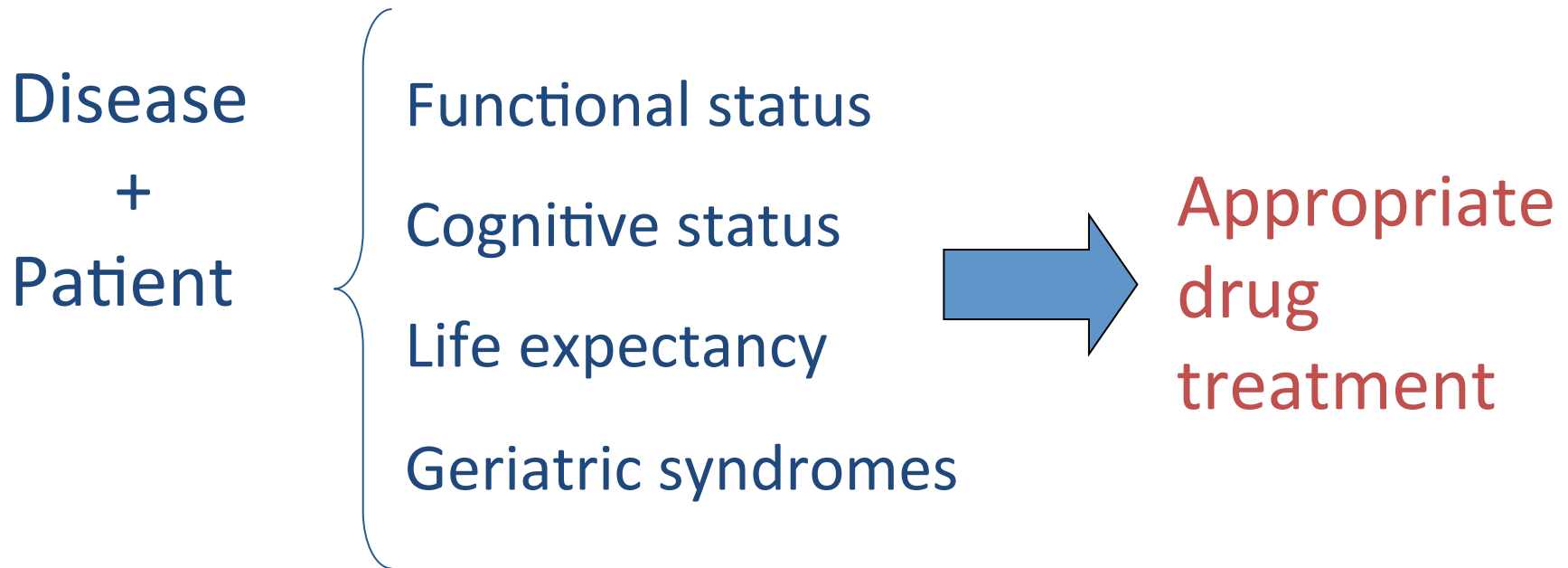
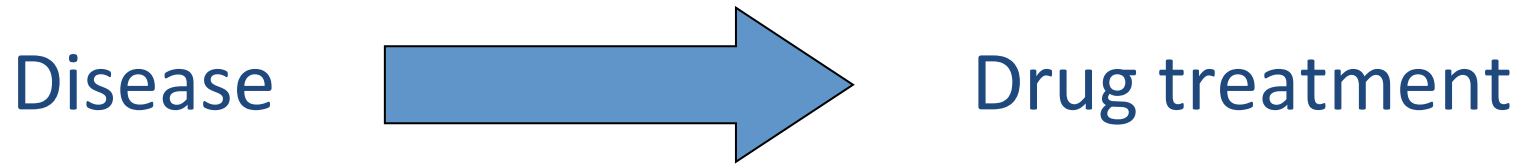
Problems	Consequences	Responses
Cognition and language	Decreased decision-making capacity Increased caregiver burden Increased risk of diagnostic procedures Adherence problems Difficulty reporting adverse effects Difficulty titrating medicines based on reporting by patient	Consider altered risk-benefit ratio balancing safety and autonomy Adjust communication strategies
Decreased life expectancy	Decreased potential benefit	Consider altered risk-benefit ratio Reserve therapy/screening for those with sufficient life expectancy to realize benefit
Exclusion from studies	Increased uncertainty about effects of therapy in this group	Policy changes to include patients with dementia in appropriate studies



# Concerns about older persons' ability to adhere to complex medication regimens

Concern	Representative Quotation
Historical evidence of inability to adhere	Also I factor in adherence to even a basic treatment. If they cannot manage a basic treatment, the one I am giving them, <u>I am not going to complicate it further by adding something to get to the goal range.</u>
Difficulty understanding medications	<u>Whenever [patients] are confused about what medications they are on that suggests a problem.</u> When they can not tell you what the medications either by name or description, and they are confused about when they are supposed to take them
Availability of social support	Often what you are doing is assessing someone's personality and their abilities to integrate complicated information and goals and <u>if you have a patient who is limited you are obviously not going to push the meds nearly as hard unless there is somebody else in the picture who can administer them.</u>  I look at their functioning as a whole and also whether or not they live alone, their support system, have help.

# Prescribing





## CRIME study

Scopo: fornire dei criteri per la valutazione  
l'appropriatezza della prescrizione  
farmacologica in pazienti anziani complessi, in  
rapporto a:

- attesa di vita;
- stato funzionale e cognitivo;
- sindromi geriatriche;

Inizio: Luglio 2009





# An example: diabetes

Guidelines recommendation	Appropriateness prescription criteria	Reference
<p>HbA1c &lt; 7%, less stringent goals for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, and those with longstanding diabetes in whom the general goal is difficult to attain (ADA)</p>	<ul style="list-style-type: none"> <li>• Not appropriate pursuing intensive glycemic control (HbA1c &lt; 7%) in patients with limited life expectancy (&lt;5 years) or cognitive impairment, or high level of comorbidities</li> <li>• Not appropriate pursuing intensive glycemic control or use complex drug regimens (including the use of insulin) in patients with history of falls or poor physical performance</li> <li>• Not appropriate pursuing intensive glycemic control in patients with known difficulties in managing therapy (i. e. cognitive impairment or mild cognitive impairment)</li> </ul>	<ul style="list-style-type: none"> <li>• Bremer JP. Diabetes Care, 2009.</li> <li>• Chelliah A. Drugs Aging, 2004.</li> <li>• Vijan S. Ann Intern Med, 1997.</li> <li>• Huang ES. Ann Intern Med, 2008.</li> <li>• Durso SC. JAMA, 2006.</li> <li>• Schwartz AV. Diabetes Care, 2008.</li> <li>• Monami M. Diabetes Care, 2008.</li> <li>• Volpato S. J Gerontol A Biol Sci Med Sci, 2005.</li> <li>• Nelson E J Am Geriatr Soc, 2007</li> </ul>

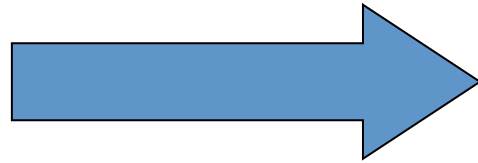


# An example: diabetes

Guidelines recommendation	Appropriateness prescription criteria	Reference
Systolic blood pressure < 130 mmHg Diastolic blood pressure < 80 mmHg	<ul style="list-style-type: none"> <li>• Not appropriate intensive blood pressure lowering (&lt; 130/80) in patients with a recent fall or high risk of falls, orthostatic hypertension or high number of comorbidities</li> </ul>	<ul style="list-style-type: none"> <li>• Wu JS. Diabetes Care, 2009.</li> <li>• Luukinen H. Arch Intern Med, 1999.</li> <li>• Hiitola P. J Hum Hypertens, 2009.</li> </ul>
Statins are indicated regardless or lipid profile for: patients with overt CVD, patients >40 y of age, with diabetes + 1 or more CV risk factor	<ul style="list-style-type: none"> <li>• Not appropriate to start statin therapy in older adults with life expectancy &lt; 5 years</li> </ul>	<ul style="list-style-type: none"> <li>• Mangoni AA. Br J Clin Pharmacol, 2006.</li> <li>• Brugts JJ. BMJ, 2008.</li> <li>• Cholesterol Treatment Trialists' (CTT) Collaborators. Lancet, 2008.</li> <li>• Cholesterol Treatment Trialists' (CTT) Collaborators. Lancet, 2005.</li> </ul>

# CRIME

Disease



Drug treatment

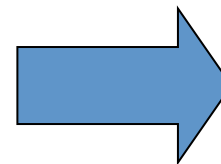
Disease  
+  
Patient

Functional status

Cognitive status

Life expectancy

Geriatric syndromes

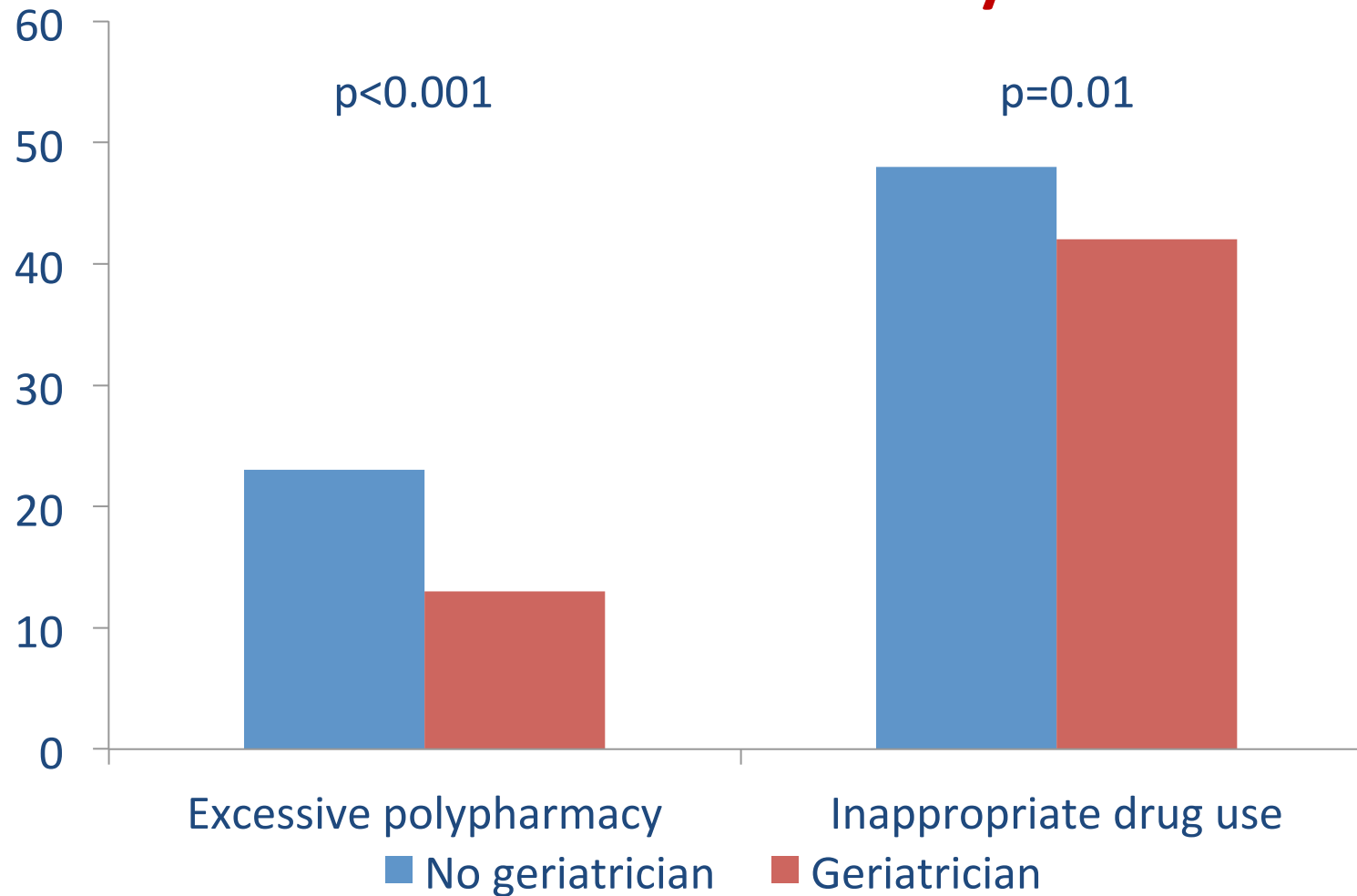


Appropriate  
drug  
treatment

# CGA and appropriate medication use

Author	Population	Intervention	Results
Owens (1990)	436 hospitalized older adults	Multidisciplinary team approach	Patients in the intervention group took fewer medications than controls (5.3 vs. 5.9) and fewer inappropriate medications (20% vs. 37%).
Schmader (2004)	834 frail hospitalized patients	CGA and management	35% reduction in the risk of a serious adverse drug reaction compared with usual care. Inpatient geriatric unit care reduced unnecessary and inappropriate drug use and underuse significantly.
Crotty (2004)	154 nursing home residents	Multidisciplinary case conferences	Medication appropriateness improved in the intervention group compared with the control group.
Saltvedt (2005)	254 hospitalized patients	Geriatric evaluation and management	Fewer intervention than control group patients had potential drug-drug interactions
Lampela (2010)	644 older adults living in the community	Comprehensive geriatric assessment and management	Reduction in the prescription of CNS active drugs and inappropriate drugs in the intervention group.

# Geriatric care and prescribing in NH: SHELTER study





# Conclusioni

- Le linee guida non sono adatte a guidare la prescrizione farmacologica negli anziani con polipatologia
- Una valutazione globale delle problematiche dell'anziano può condurre ad una riduzione della politerapia e miglioramento della qualità farmacologica



AGE 0-4  
AMOXICLIN

4-12  
RITALIN

12-18  
APPETITE  
SUPPRESSANTS

18-24  
NO-DOZ

24-38  
PROZAC

38-65  
ZANTAC

65 —  
EVERYTHING  
ELSE

GENE WILENSKI, Philadelphia Daily News