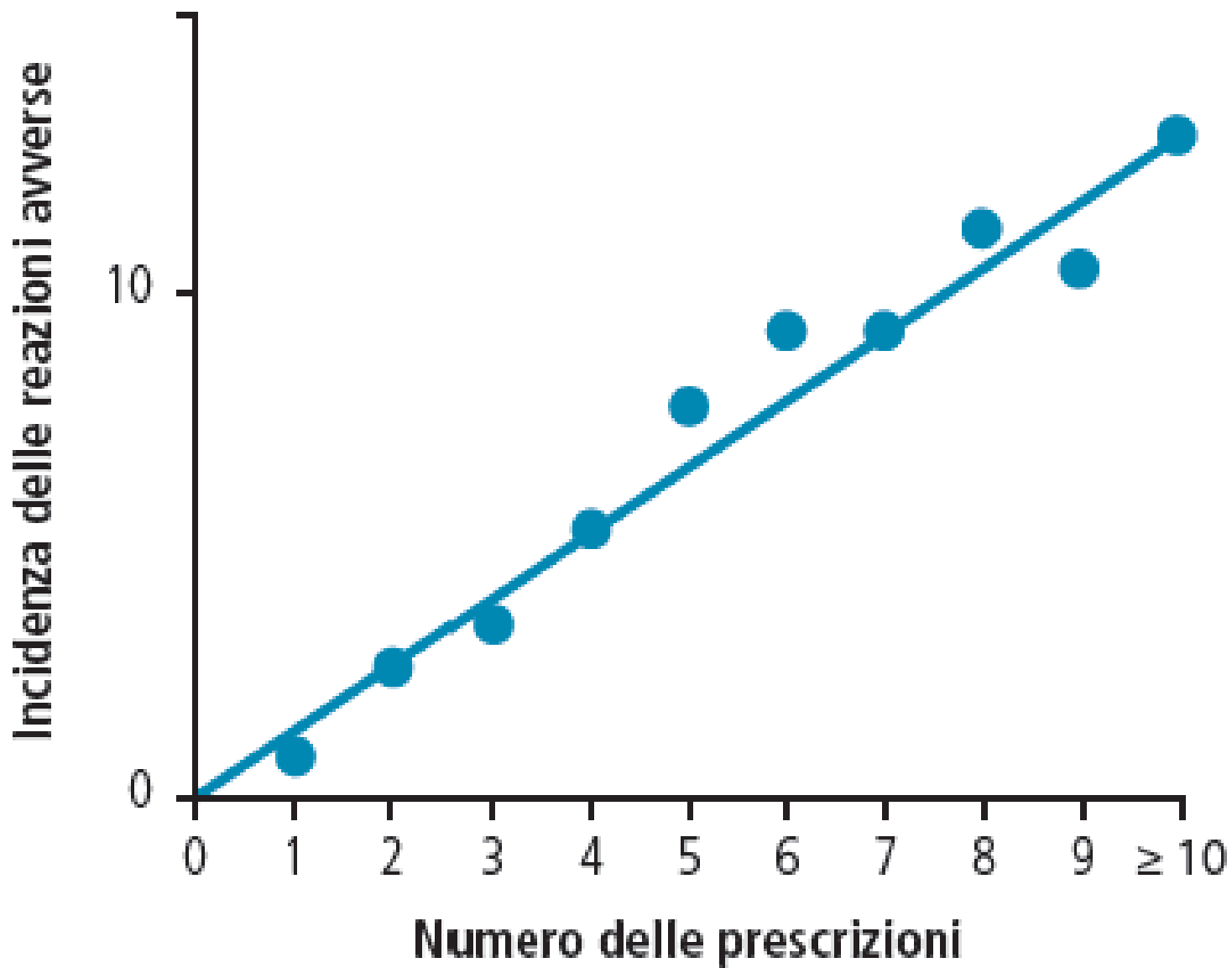




SCOMPENSO CARDIACO CRONICO: L'ANZIANO TRA POLIFARMACIA ED ADERENZA

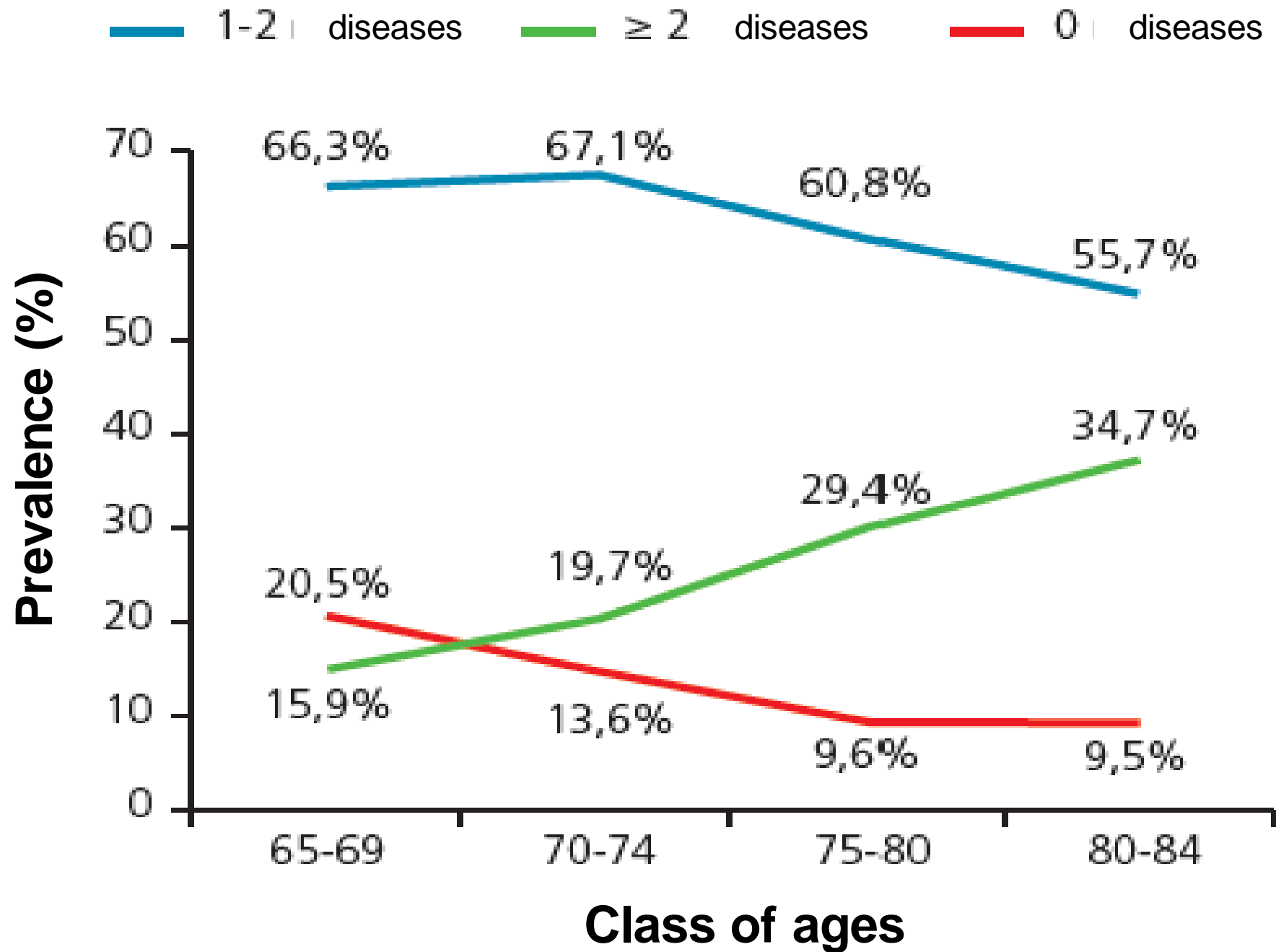
Nicola Ferrara, MD

*Dpt di Medicina e Scienze della Salute, Università degli Studi del Molise
Centro di Ricerca e Formazione in Medicina dell'Invecchiamento*

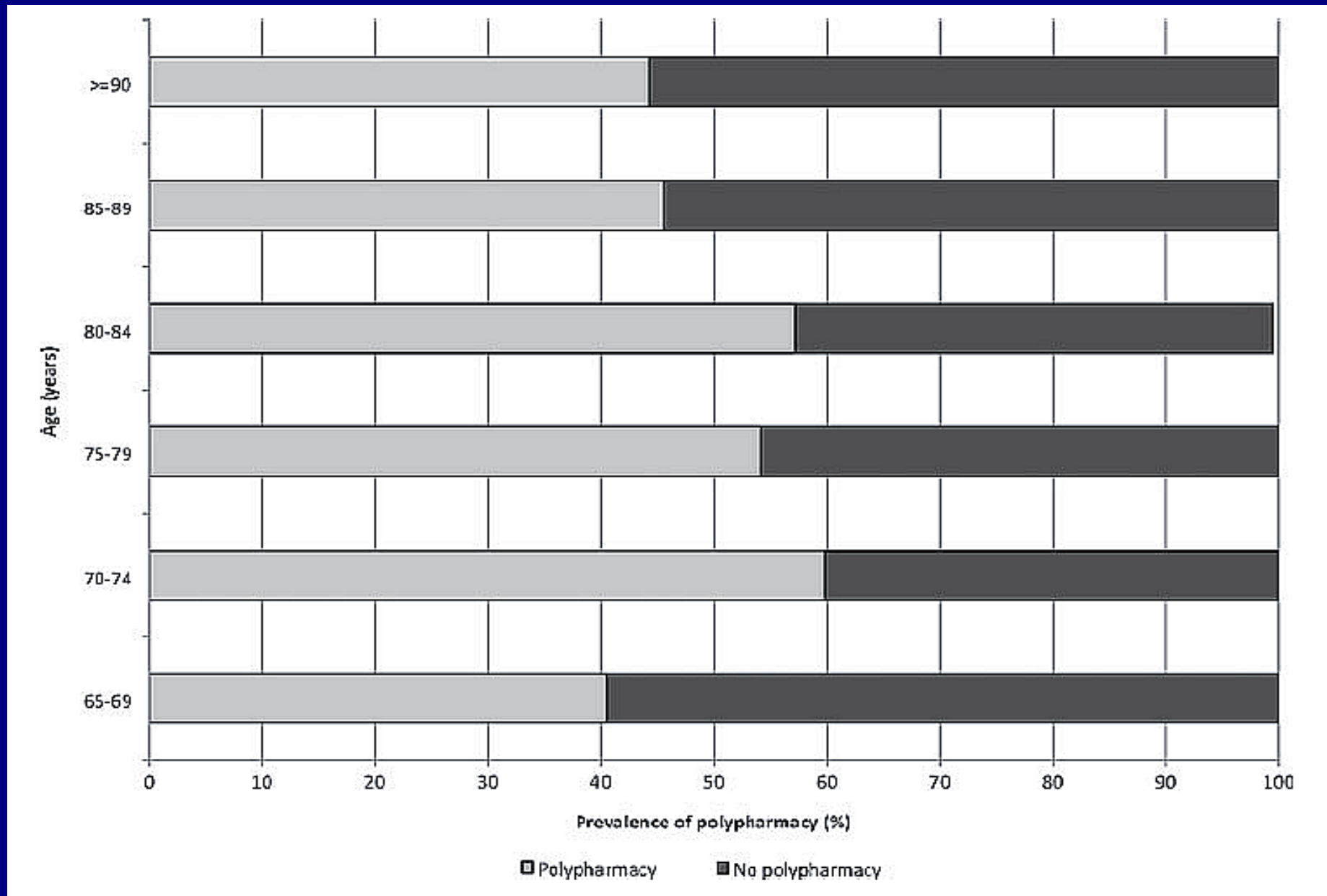


Data from GIFA, SIGG, Italy

Comorbidity in Italy



PREVALENCE OF POLYPHARMACY AT ADMISSION IN DIFFERENT AGE GROUPS: THE REPOSI STUDY



CONSUMATORI DI FARMACI* PER CLASSE DI ETÀ (1993-2010; x 1000)

	1993	1998	2003	2005	2008	2010
Fino a 14 anni	1.524	1.396	1.166	1.482	1.487	1.424
15-34 anni	2.753	2.626	2.636	2.773	2.873	2.728
35-64 anni	7.317	7.687	8.490	8.941	9.825	9.986
65 anni e più	5.986	6.933	7.730	8.460	9.377	9.477
Totale	17.580	18.643	20.022	21.656	23.563	23.614

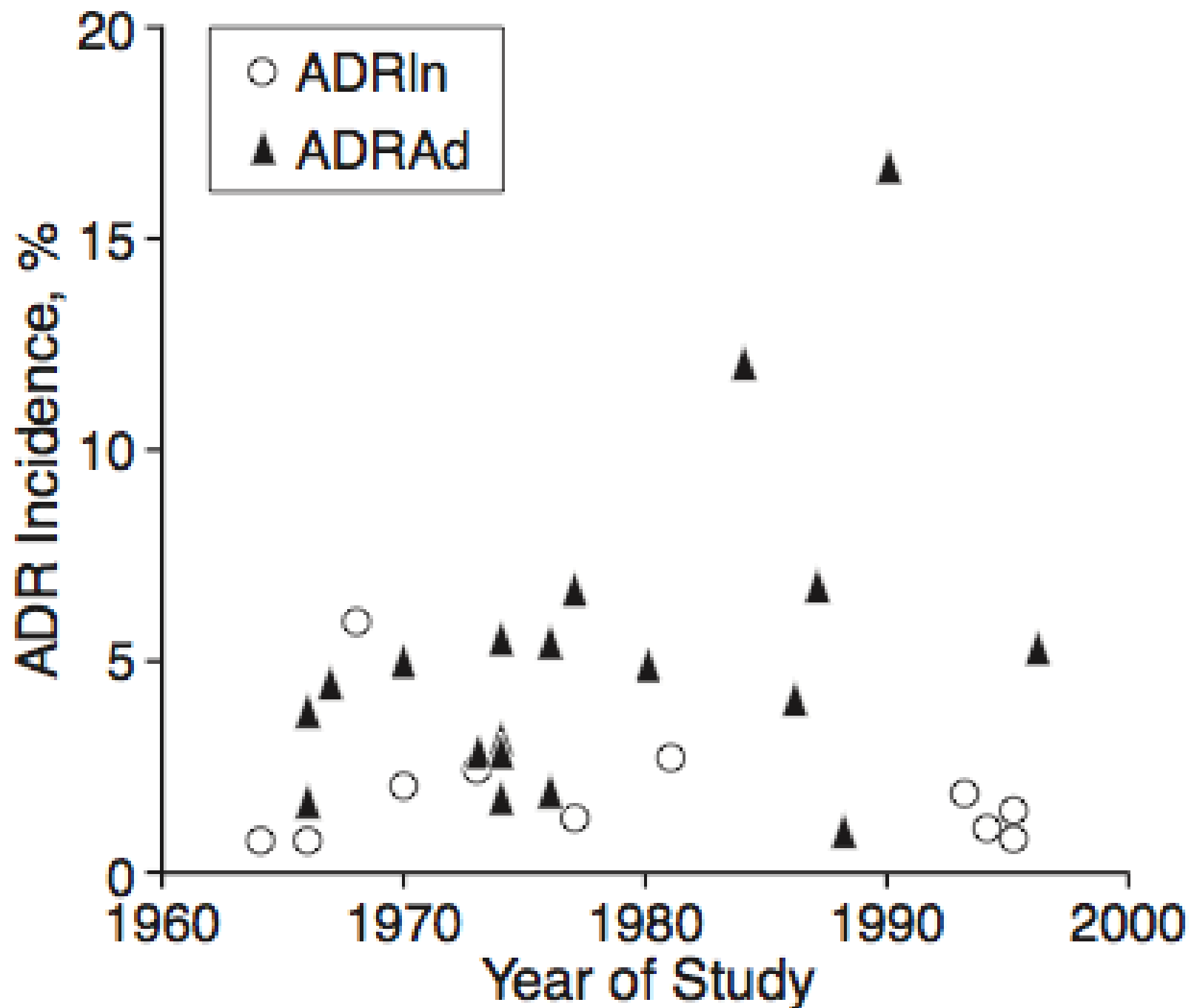
* nei due giorni precedenti l'intervista

ISTAT 2011

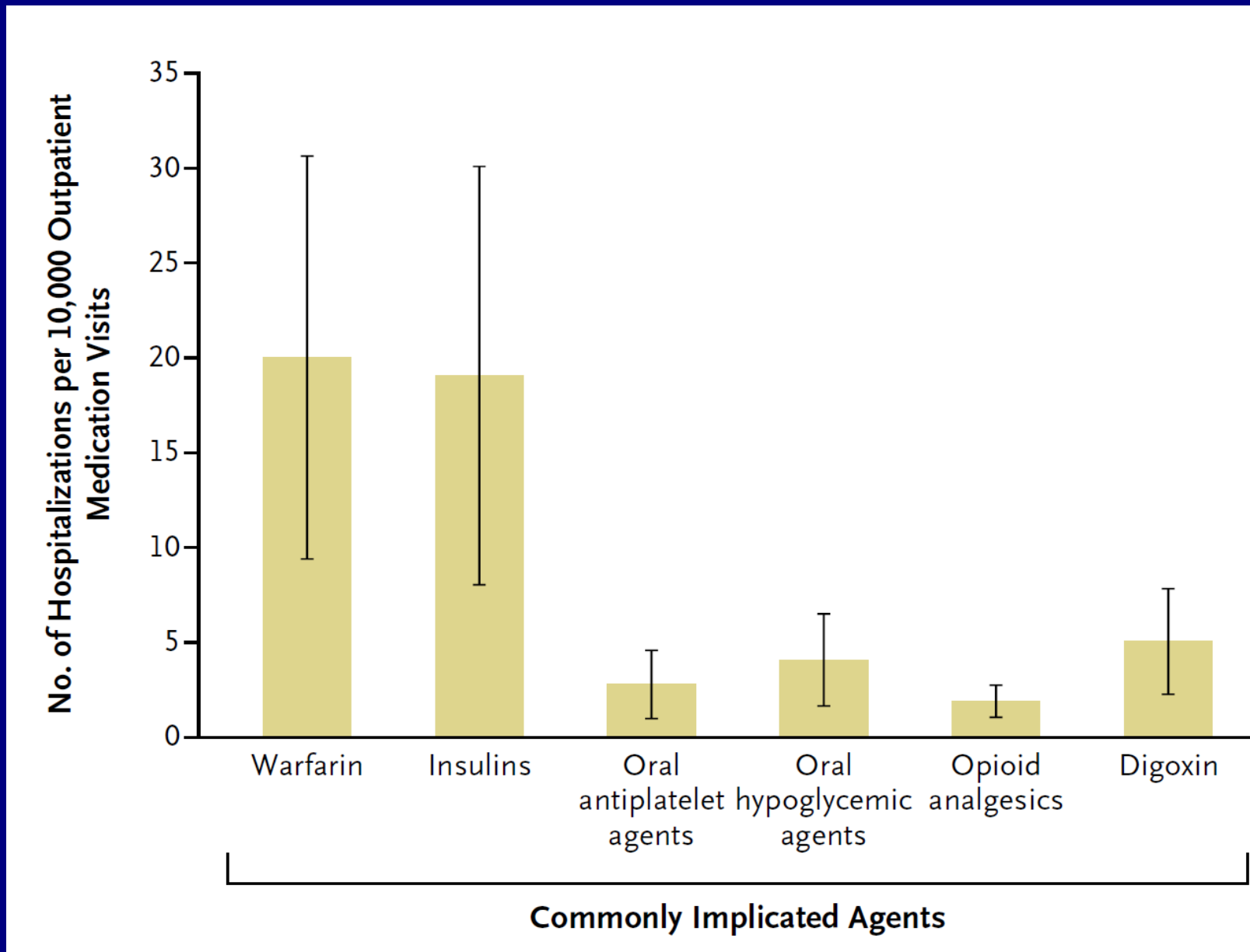
NUMERO DI INTERAZIONI

$$\frac{(n \text{ farmaci})^2 - 1}{2}$$

2



Stima della frequenza di ospedalizzazioni per eventi avversi da farmaci in anziani negli US, 2007–2009



- ✓ **Gli anziani ricevono in media 6-7 farmaci prescritti**

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- ✓ **Il 90% assume più di un farmaco**

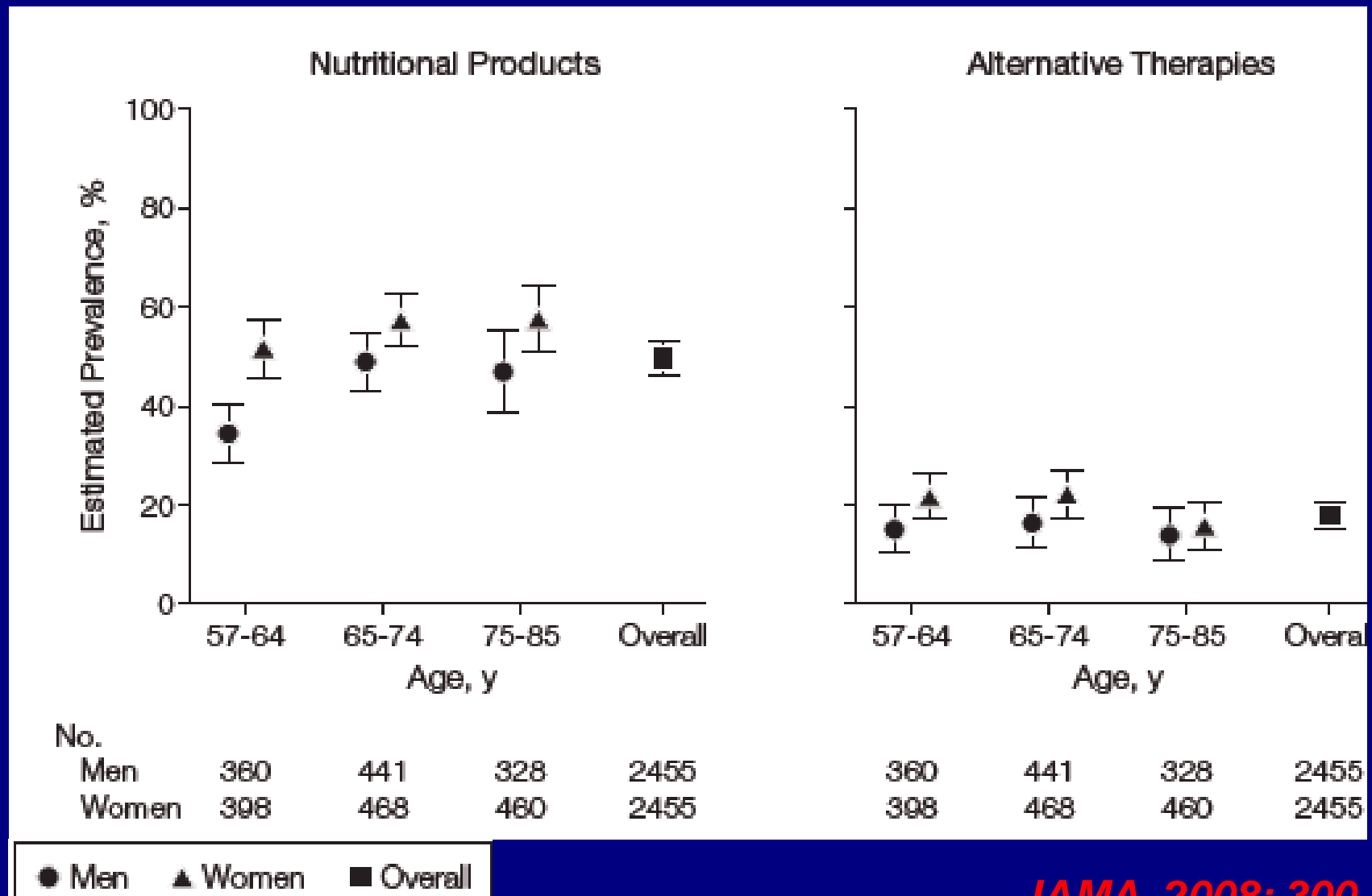
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- ✓ **Tra l' 11% ed il 14% prodotti di erboristeria**
- ✓ **Il 42% dei pazienti non informa il medico dell'assunzione dei prodotti da banco**

Weighted Prevalence Estimates of Nutritional and/or Alternative Therapies Among Prescription Medication Users by Age and Gender



Drug-Food Interactions

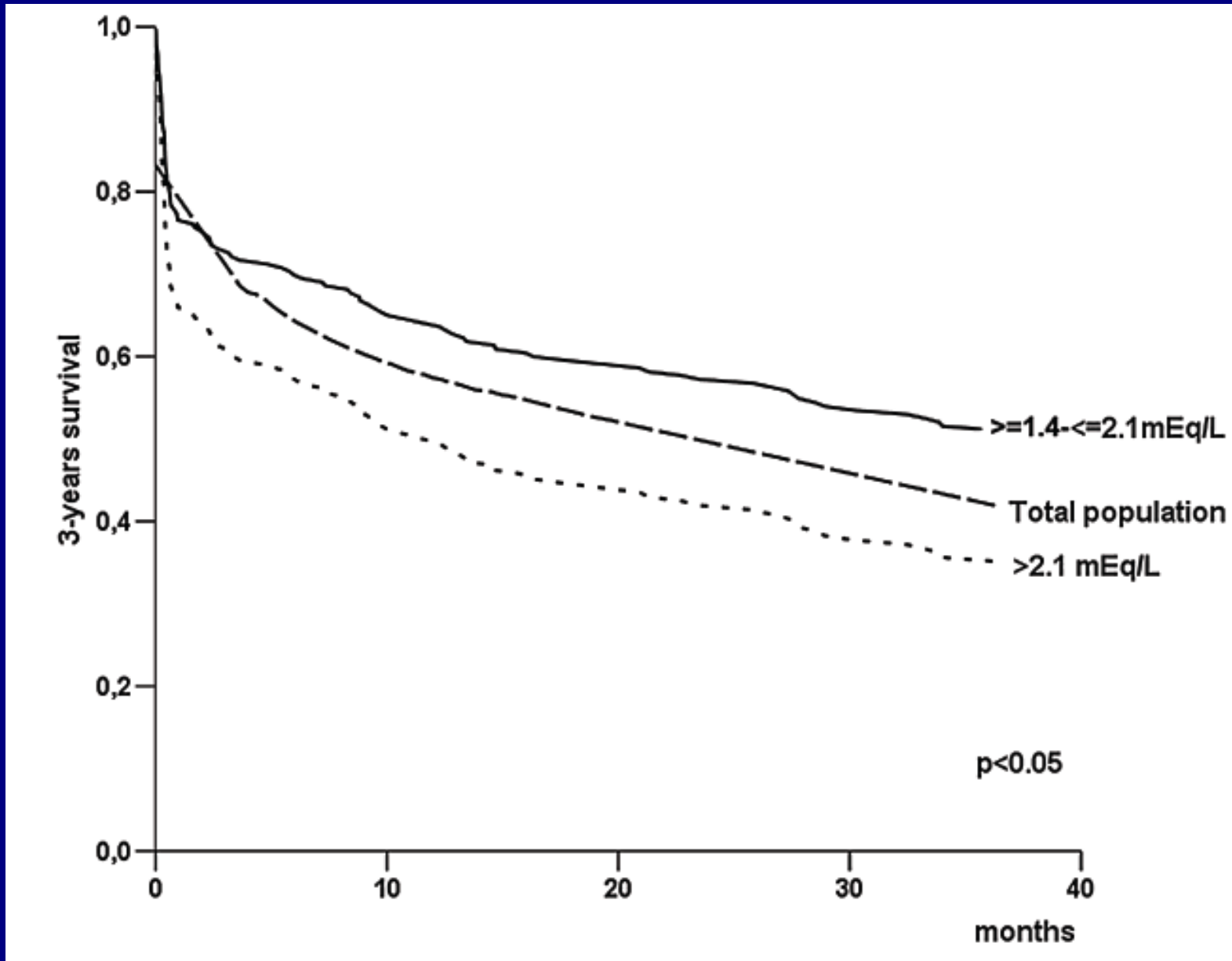
- Tetracycline and milk products
- Warfarin and vitamin K-containing foods
- Grapefruit juice

Drug-Herbal Interactions

St. John's Wort with:

- Indinavir
- Cyclosporine
- Digoxin
- Tacrolimus
- Possibly many others

Cox regression model in the 3-year follow-up



Corbi G, Acanfora D, Iannuzzi GL, Longobardi G, Cacciatore F, Furgi G, Filippelli A, Rengo G, Leosco D, Ferrara N. *Rejuvenation Res.* 2008;11(1):129-38.

DRUGS USED IN THE TOTAL STUDY POPULATION AND IN THE TWO MAGNESIUM GROUPS

	<i>Total population</i>	<i>Magnesium levels</i>		<i>p</i>
		$\geq 1.4 - \leq 2.1$	> 2.10	
Number of drugs	4.73 \pm 2.03	4.74 \pm 2	4.71 \pm 2.11	0.905
Amiodarone (%)	25 (12.6)	18 (12.8)	7 (12.1)	0.895
Other antiarrhythmic drugs (%)	11 (5.5)	9 (6.4)	2 (3.4)	0.410
Antiaggregants (%)	52 (26.1)	32 (22.7)	20 (34.5)	0.085
Anticoagulants (%)	20 (10.1)	12 (8.5)	8 (13.8)	0.260
Digoxin (%)	121 (60.8)	87 (61.7)	34 (58.6)	0.686
Beta blockers (%)	13 (6.5)	12 (8.5)	1 (1.7)	0.078
Ca ²⁺ -antagonists	59 (29.6)	38 (27)	21 (36.2)	0.194
Diuretics (%)	114 (57.3)	85 (60.3)	29 (50)	0.183
ACE-inhibitors	95 (47.7)	72 (51.1)	23 (39.6)	0.143
Antialdosterons (%)	19 (9.5)	13 (9.2)	6 (10.3)	0.806
Vasodilators (%)	91 (45.73)	61 (43.3)	30 (51.7)	0.254
Nitrates (%)	74 (37.2)	51 (36.2)	23 (39.7)	0.644
Aminofillin (%)	42 (21.1)	28 (19.9)	14 (24.1)	0.501
Bronchodilators (%)	21 (10.6)	14 (9.9)	7 (12.1)	0.655
Mucolytics (%)	22 (11.1)	15 (10.6)	7 (12.1)	0.770
Insulin (%)	17 (8.5)	14 (9.9)	3 (5.2)	0.275
Oral hypoglycemic drugs (%)	31 (15.6)	22 (15.6)	9 (15.5)	0.988
Antacids and laxatives (%)*	83 (41.7)	35 (24.8)	48 (82.7)	<0.0001
Other drugs (%0	138 (69.3)	102 (72.3)	36 (62.1)	0.153

*Antacids and laxatives containing magnesium.

Corbi G, Acanfora D, Iannuzzi GL, Longobardi G, Cacciatore F, Furgi G, Filippelli A, Rengo G, Leosco D, Ferrara N. *Rejuvenation Res.* 2008 Feb;11(1):129-38.

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Multivariate analysis of predictors of polypharmacy at discharge among 1,155 patients

Variables	Odds ratio ^a (95% CI)	<i>P</i> value
Females	1.00 (0.75-1.32)	0.98
Age (years), mean	0.96 (0.94-0.98)	<0.0001
Number of drugs at admission, mean	2.32 (1.96-2.74)	<0.0001
Adverse clinical events (one or more)	1.08 (0.72-1.63)	0.70
Hypertension	1.84 (1.34-2.53)	<0.0001
Ischemic heart disease	1.72 (1.18-2.50)	0.005
Heart failure	3.77 (1.77-8.01)	0.001
Atrial fibrillation	1.09 (0.66-1.82)	0.61
Diabetes mellitus	0.88 (0.54-1.43)	0.70
COPD	1.93 (1.33-2.79)	0.001
Dementia	0.69 (0.29-1.66)	0.41
Cerebrovascular disease	0.93 (0.62-1.39)	0.73
Liver disease	0.90 (0.49-1.63)	0.72
GI disorders	0.99 (0.59-1.66)	0.98
Osteoporosis/osteoarthritis	1.44 (0.84-2.46)	0.18
Chronic renal failure	0.98 (0.51-1.89)	0.96
Anemia	0.88 (0.56-1.40)	0.59
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L'insufficienza cardiaca cronica nel mondo dei "trials" e nel mondo "reale"

Variabili Mondo dei "trials"

Età 50-65

M > F

Singola malattia

Terapia specifica

Aderenza Alta

Rischio di disabilità basso

Mondo "reale"

≥ 75

F > M

Comorbilità

Polifarmacoterapia

Aderenza Bassa

Rischio di disabilità alto

Associazione negativa tra condizioni patologiche e terapia farmacologica nell'insufficienza cardiaca cronica nell'anziano

Condizione patologica

Insufficienza renale

BPCO

Deficit cognitivo e depressione

Ipotensione ortostatica

Incontinenza urinaria

Deprivazione sensoriale

Implicazioni cliniche

Aggravamento da uso di ACE-I e diuretici

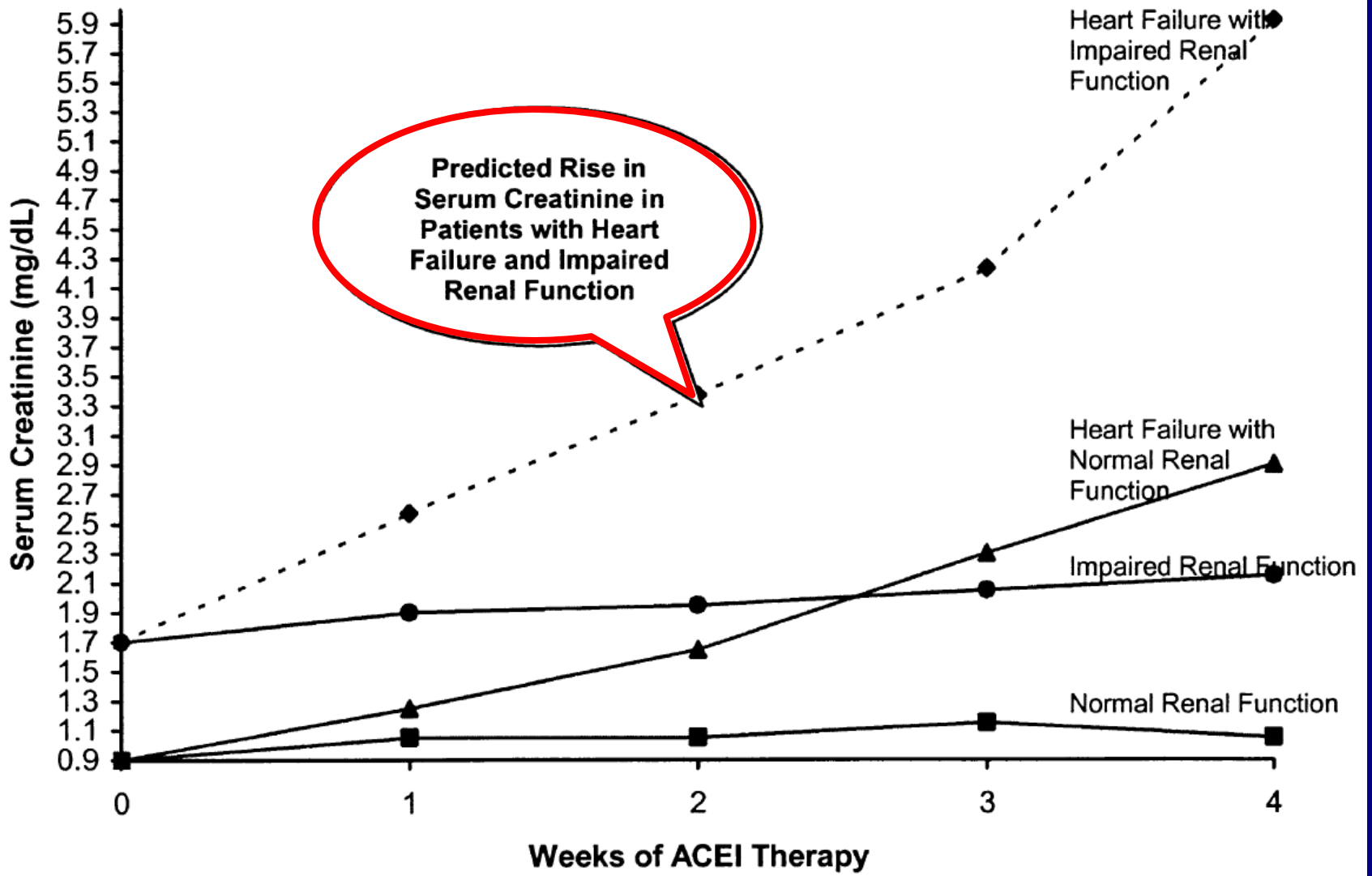
Interferenza con B-bloccanti

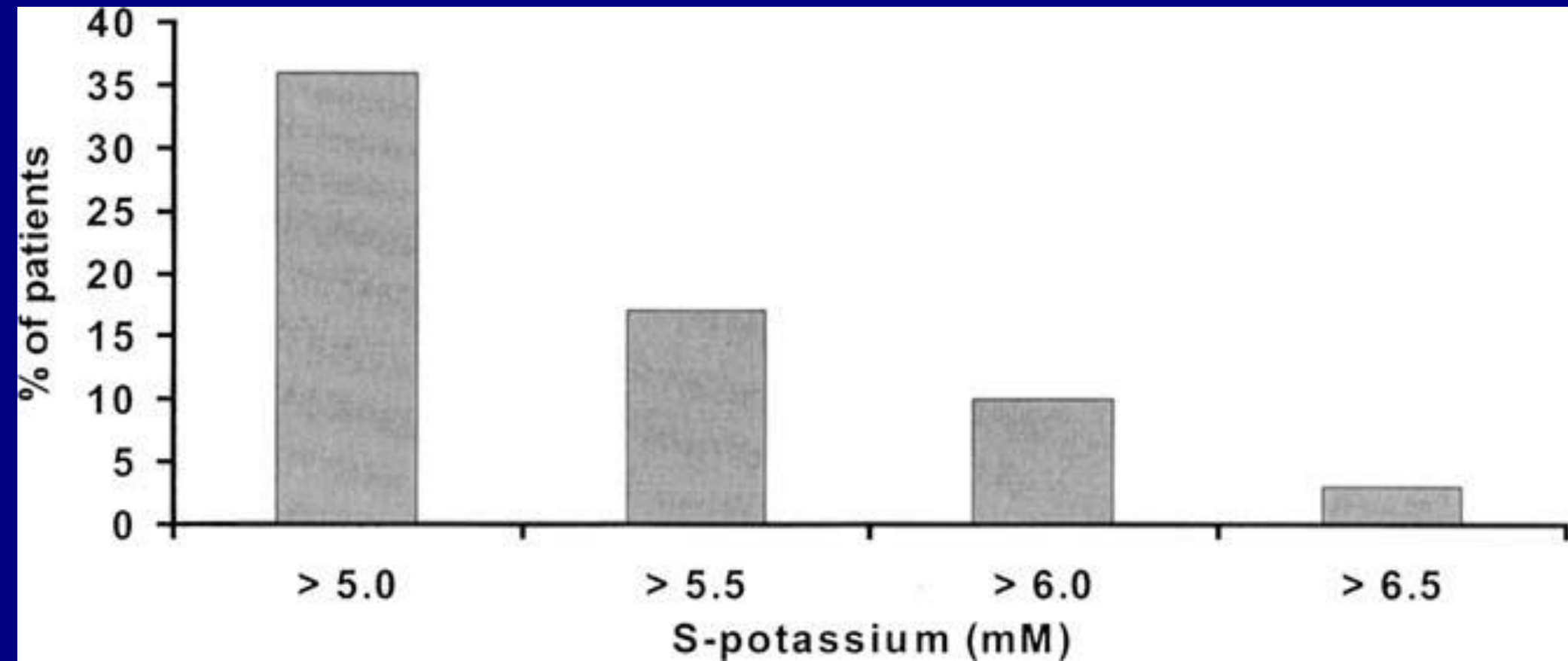
Interferenza con l'aderenza alla terapia

Aggravamento da uso di ACE-I, diuretici, β -bloccanti e vasodilatatori

Aggravamento da uso di diuretici

Interferenza con l'aderenza alla terapia





Svensson M. et al., Journal of Cardiac Failure Vol. 10 No. 4 2004

A Case Series of Hospitalized Patients with Elevated Digoxin Levels

Paul E. Marik, MD, Laurie Fromm, PharmD

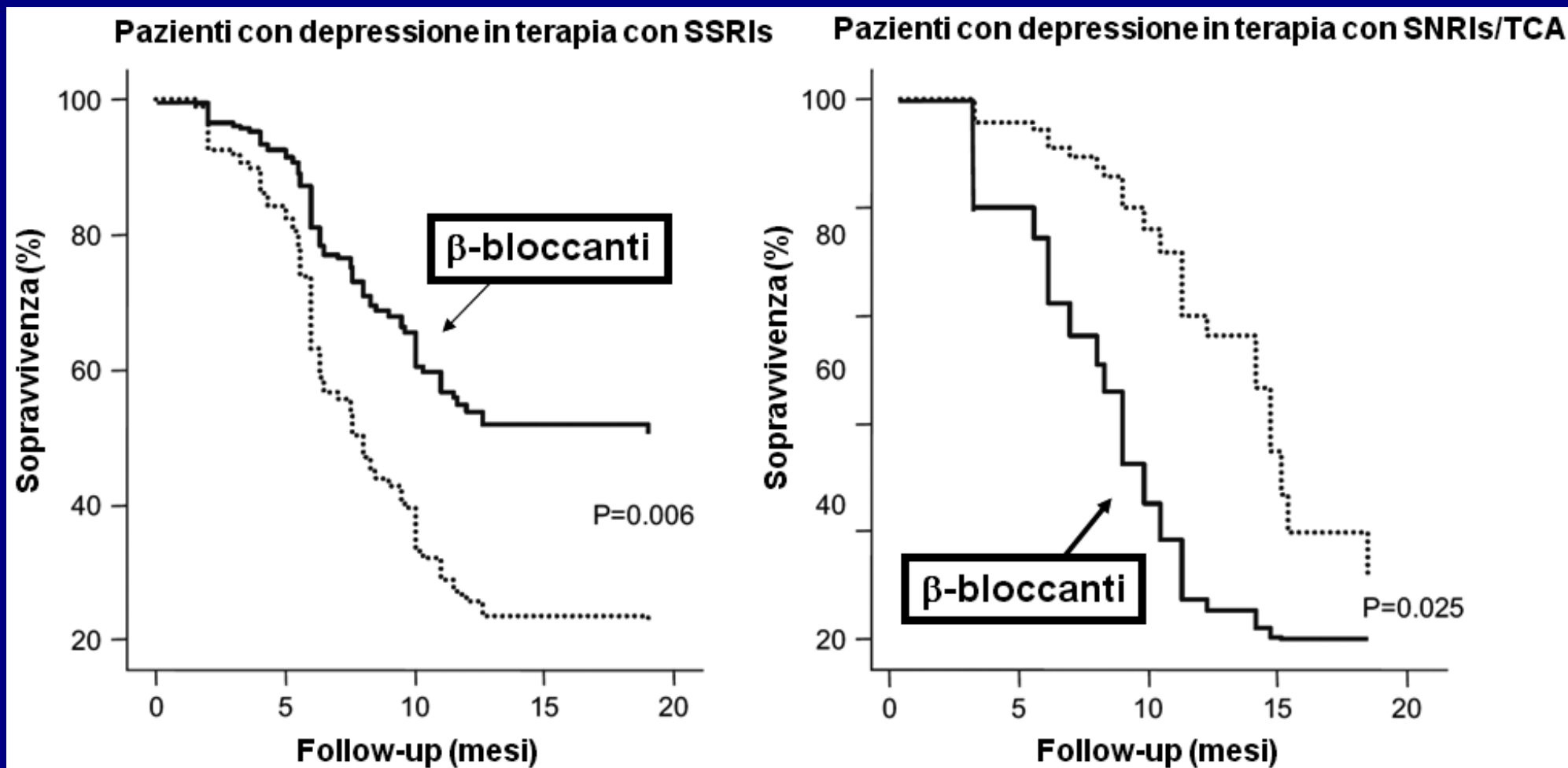
PURPOSE: Although there is renewed enthusiasm for the use of digoxin in patients with heart failure, current dosing guidelines are based on a nomogram published in 1974. We studied the incidence of and risk factors for elevated digoxin levels in patients admitted to a community hospital, and compared their dosage regimens to published guidelines.

SUBJECTS AND METHODS: We reviewed the charts of all patients who had serum digoxin levels greater than 2.4 ng/mL during a 6-month period. We collected demographic and clinical data, indications for digoxin use, digoxin dosage, concurrent medications, laboratory data, and clinical and electrocardiographic features of digoxin toxicity.

RESULTS: Of the 1,433 patients with digoxin assays, 115 (8%) patients had elevated levels. Of the 82 patients with complete records and correctly timed digoxin levels, 59 (72%) had electrocardiographic or clinical features of digoxin toxicity. Patients with serum digoxin levels >2.4 ng/mL were slightly older (78 ± 8 versus 73 ± 9 years of age; $P = 0.12$) and had greater serum creatinine levels (3.1 ± 7.3 versus 1.4 ± 0.3 mg/dL; $P = 0.01$) than those with levels ≤ 2.4 ng/mL. Forty-seven patients had elevated digoxin levels on admission, including 21 patients admitted for digoxin toxicity. Impaired or worsening renal func-

tion contributed to high levels in 37 patients, and a drug interaction was a contributory factor in 10 cases. Twenty (43%) of these patients were taking the recommended maintenance dose based on the scheme employed in the Digitalis Investigation Group study. Thirty-five patients developed high digoxin levels while in hospital. In 26 patients, this followed a loading dose of digoxin for the control of rapid atrial fibrillation. Impaired renal function was implicated in all of these patients. Despite the elevated digoxin level, rate control was achieved in only 11 patients of these patients.

CONCLUSIONS: Elevated digoxin levels and clinical toxicity remains a common adverse drug reaction. Elderly patients, particularly those with impaired renal function and low body weights, are at the greatest risk. As published digoxin nomograms often result in toxicity, clinical variables need to be monitored. In patients with congestive heart failure and normal sinus rhythm the potential benefit of digoxin is small; thus, patients should receive a dose that minimizes the risk of toxicity. For patients with new onset atrial fibrillation, other agents may be preferable for rate control. *Am J Med.* 1998;105:110-115. ©1998 by Excerpta Medica, Inc.



Inibitori “selettivi” della ricaptazione della serotonina (SSRI) modificano positivamente, mentre quelli “selettivi” per la norepinefrina (SNRI)/antidepressivi triciclici (TCA) modificano negativamente l’effetto dei β-bloccanti sulla sopravvivenza a lungo termine in pazienti con insufficienza cardiaca cronica e grave depressione.

Modificato da Tousoulis et al.

Summary of studies on reducing polypharmacy in older adults (ie, those aged >65 years).

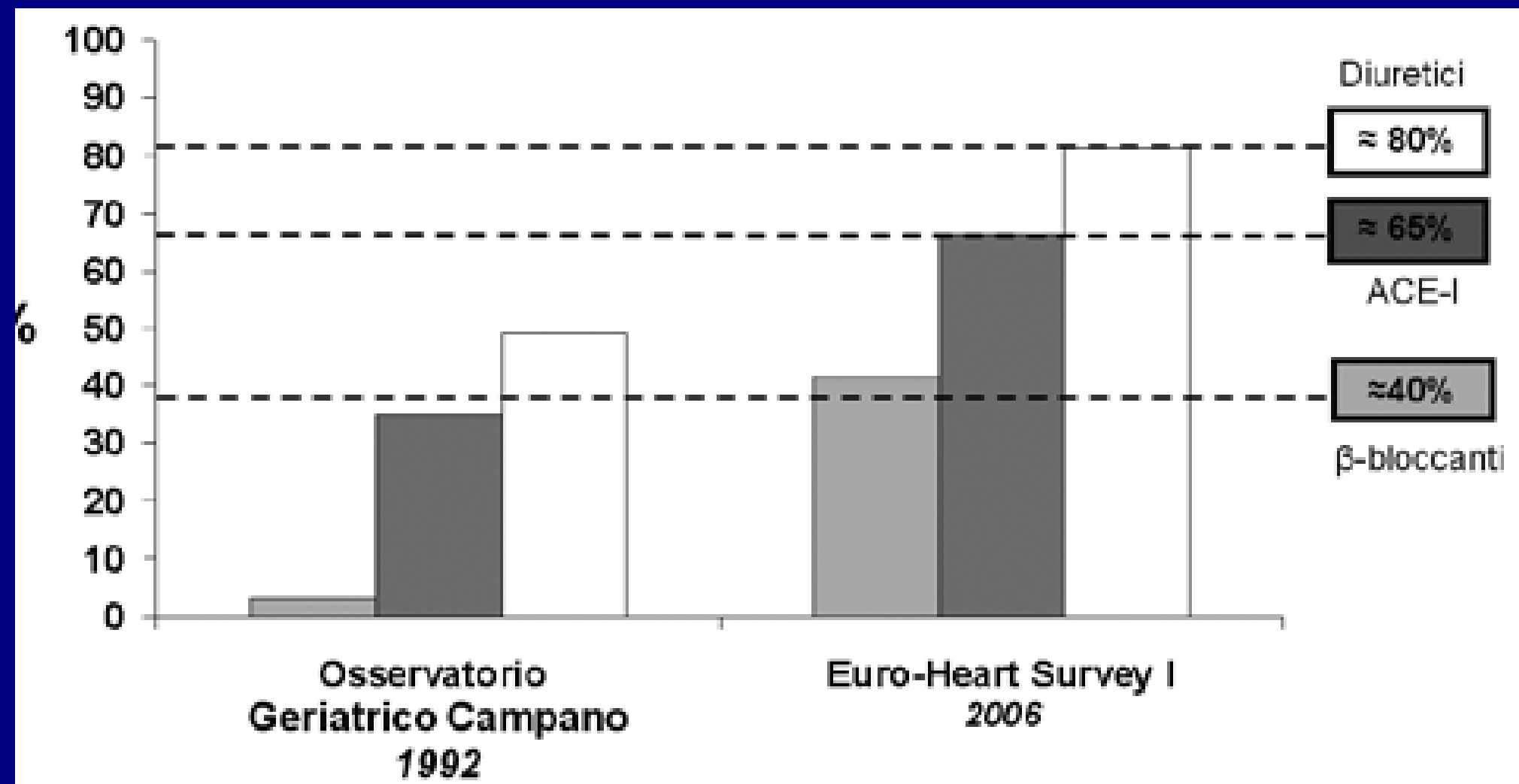
Author/Year	Setting	Intervention	Results
Muir et al, 2004 ⁵⁶	General medicine inpatient service	Medication grid provided to admitting residents that listed all medications and administration times for 1 week.	Medication grid reduced number of medications per patient in the intervention group (0.92) compared with the control group (1.65) ($P < 0.001$).
Fillit et al, 1999 ⁵⁴	Medicare managed care organization	Mailing to elderly Medicare managed care members at risk for polypharmacy urging them to meet with their physicians and bring medications with them for review.	Of the 42% of the population at risk who had a medication review with their physician, 20% reported having a medication discontinued.
Fick et al, 2004 ⁵⁵	Medicare + Choice southeastern managed care organization	Physicians were mailed a list of patients taking potentially inappropriate medications.	Overall, 12.5% of potentially inappropriate medications were discontinued.
Zarowitz et al, 2005 ²⁰	Outpatient, managed care	Clinical pharmacy medication review with physician education.	Overall, polypharmacy event rate decreased from 29.01 to 9.43 events/1000 patients after the first mailing and from 27.99 to 17.07 events/1000 patients after the second mailing.
Schmader et al, 2004 ²⁸	Inpatient and outpatient care for veterans	Inpatient or outpatient GEM.	Unnecessary and inappropriate drug use was reduced in inpatients receiving GEM care ($P < 0.05$).

GEM = geriatric evaluation and management.

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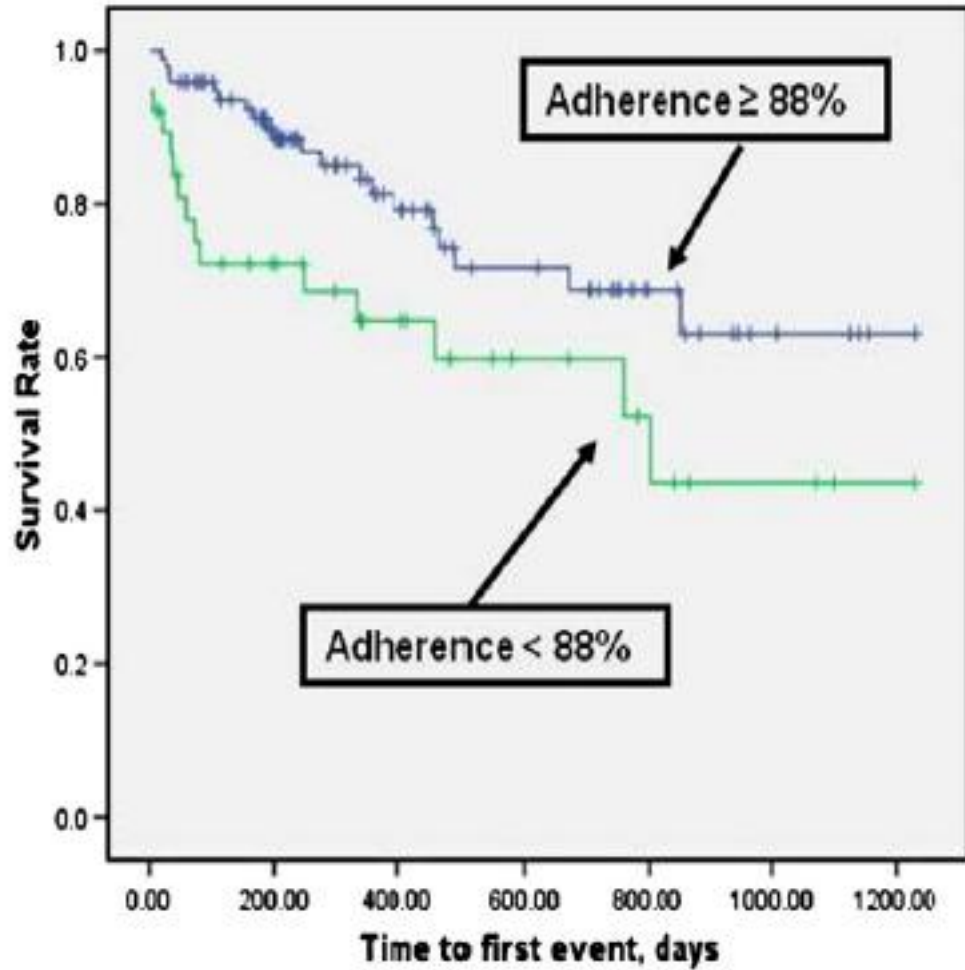
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HOW TO MEASURE THE ADHERENCE

- ◆ Patient report
- ◆ Pill count
- ◆ Refill adherence
- ◆ Electronic monitoring using bar code-microchip technologies

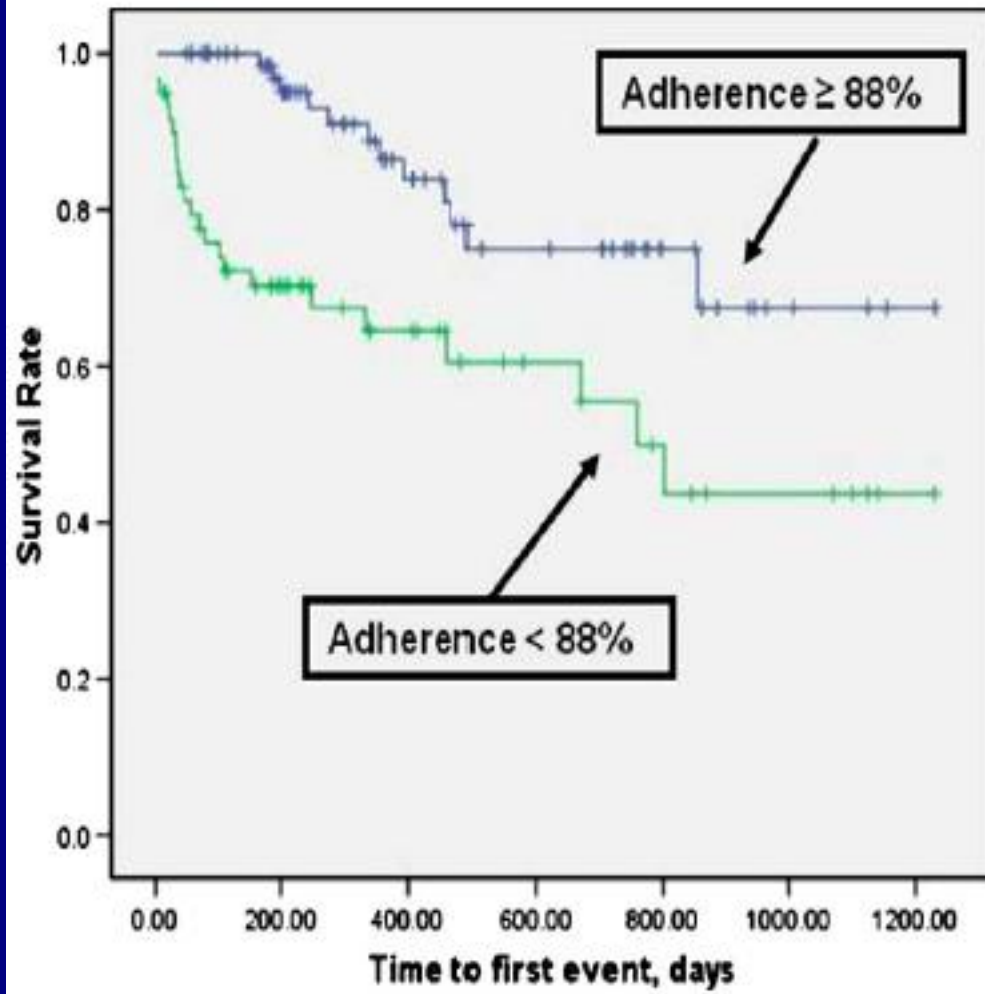
Kaplan Meier Survival Plot: Dose-count



DOSE COUNT

(% of prescribed doses taken)

Kaplan Meier Survival Plot: Dose-day



DOSE DAYS

(% of days the correct number of doses was taken)

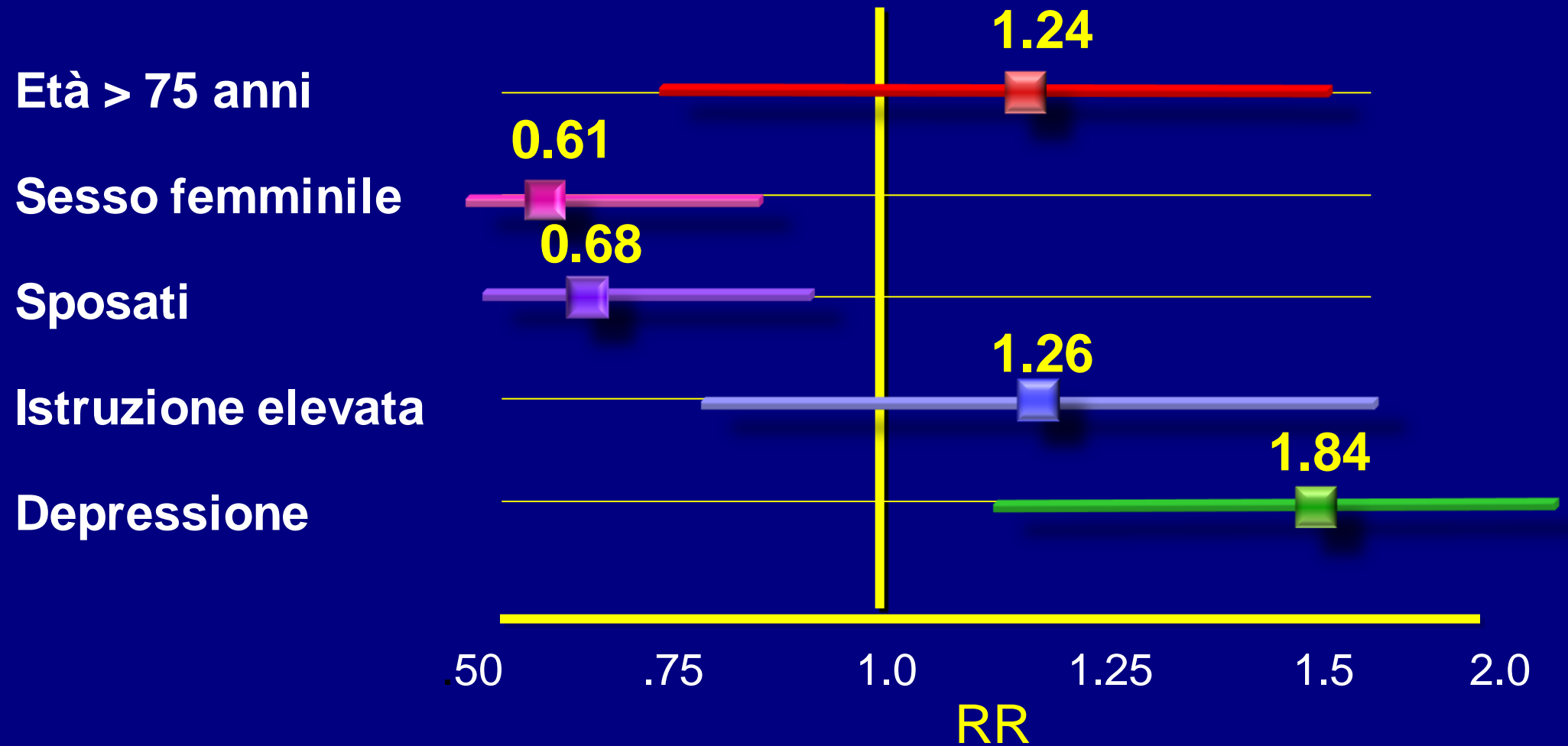
Percentage of patients adhering to selected recommendations for the treatment of HF

Weighing behavior (%)	
Daily	14
Weekly	17
Monthly	22
Never	47
Knowledge of symptoms of worsening HF (%)	
Knew ≥ 2 symptoms	16
Knew at least 1 symptom	53
Did not know any symptoms	31
Monitored for symptoms of worsening HF (%)	9
Medication adherence (%)	
Taking all medications as prescribed and not taking unprescribed medications	34
Taking all prescribed medications plus ≥ 1 not prescribed	12
Not taking all prescribed medications and not taking unprescribed medications	28
Not taking all prescribed medications and taking medications not prescribed	26
Low-sodium diet adherence (%)	
Stated their physician did not prescribe a low-sodium diet	20
Followed a low-sodium diet and could calculate sodium content	8
Followed a low-sodium diet but could not calculate sodium content	5
Did not follow a low-salt diet, but could calculate sodium content	12
Did not follow a low-salt diet and could not calculate sodium content	55

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Predittori di ridotta "adherence" in anziani ipertesi





Agenzia Italiana del Farmaco

- ↪ Incidenza di reazioni avverse al farmaco (ADR)*
- ↪ Numero di prescrizioni inappropriate, definite secondo criteri di Beers e quelli di Zhan*
- ↪ Numero di prescrizioni potenzialmente interagenti mediante software dedicato (NoV®Farma, Infologic SrL, Padova), che utilizza la libreria DrugReax di Micromedex®.*

EVALUATION OF AN EDUCATIVE/INFORMATIVE STRATEGY ON DRUGS USE IN ELDERLY POPULATION WITH CHRONIC-DEGENERATIVE DISEASES IN SEVERAL CARE SETTING: A CONTROLLED STUDY

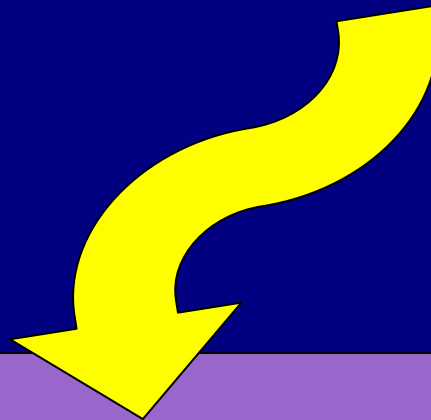
Study Design

Control

usual care

Intervention

usual care + educative/informative instruments



Caregivers



Relatives



Patients





NARANJO Algorithm

Naranjo CA, et al. A method for estimating the probability of adverse drug reactions. Clin. Pharmacol. Ther. 1981;30 (2): 239-45.

English

1- Are there previous conclusive reports on this reaction?

Yes No Do not know or not done

2- Did adverse event appear after the suspected drug was given?

Yes No Do not know or not done

3- Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?

Yes No Do not know

4- Did the adverse reaction appear again on rechallenge?

Yes No Do not know

5- Are there alternative causes that could have caused the reaction?

Yes No Do not know

6- Did the reaction reappear when the drug was given again?

Yes No Do not know

7- Was the drug detected in any body fluids?

Yes No Do not know

8- Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?

Yes No Do not know or not done

9- Did the patient have a similar reaction to the same or similar drugs in any previous exposure?

Yes No Do not know or not done

10- Was the adverse event confirmed by any objective evidence?

Yes No Do not know or not done

DEFINITA ≥ 9
PROBABILE 5-8
POSSIBILE 1-4
DUBBIA ≤ 0

Farmaco

Amiodarone

◀ III ▶

Farmaco

Amiodarone

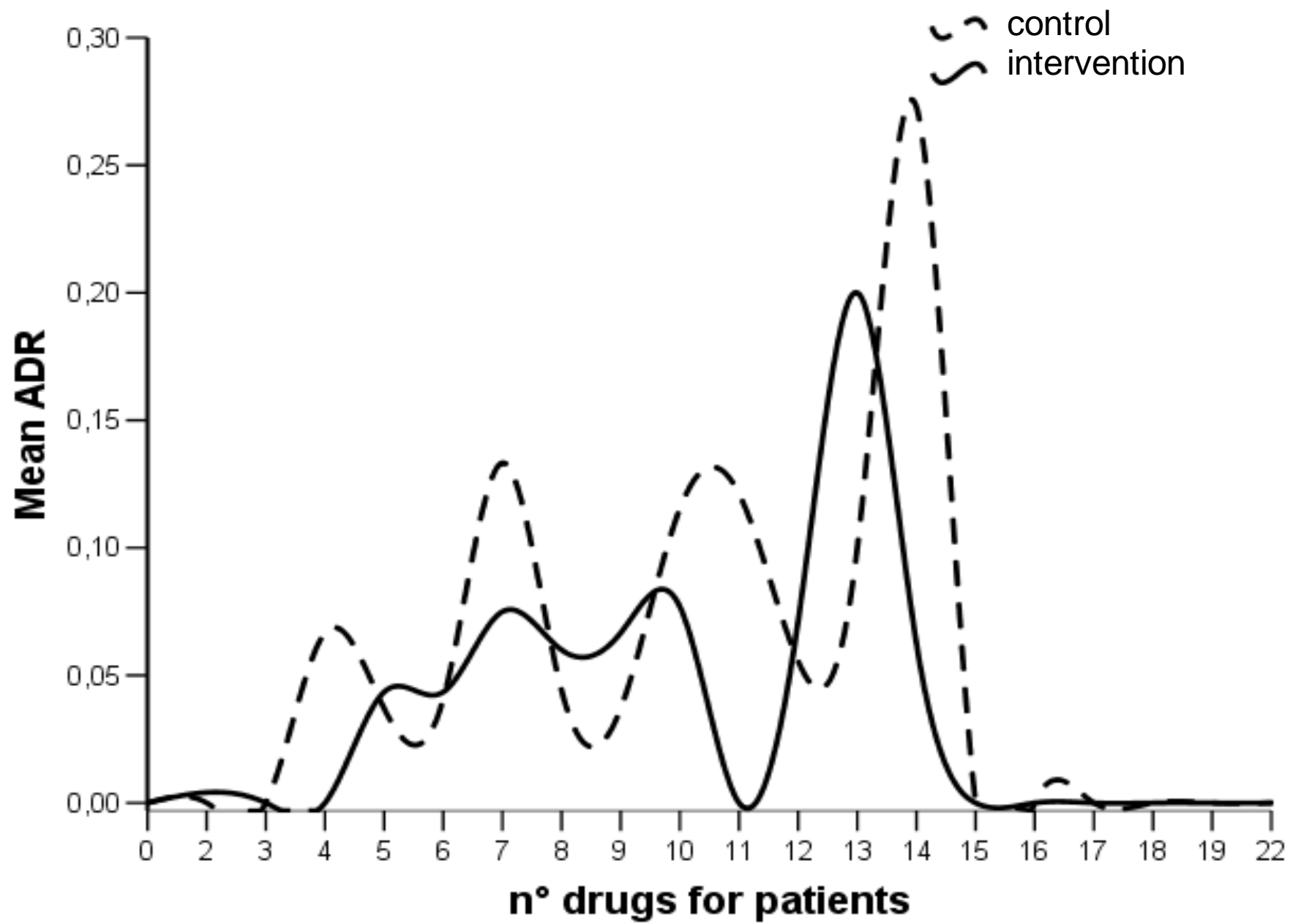
Causa inapproprietezza

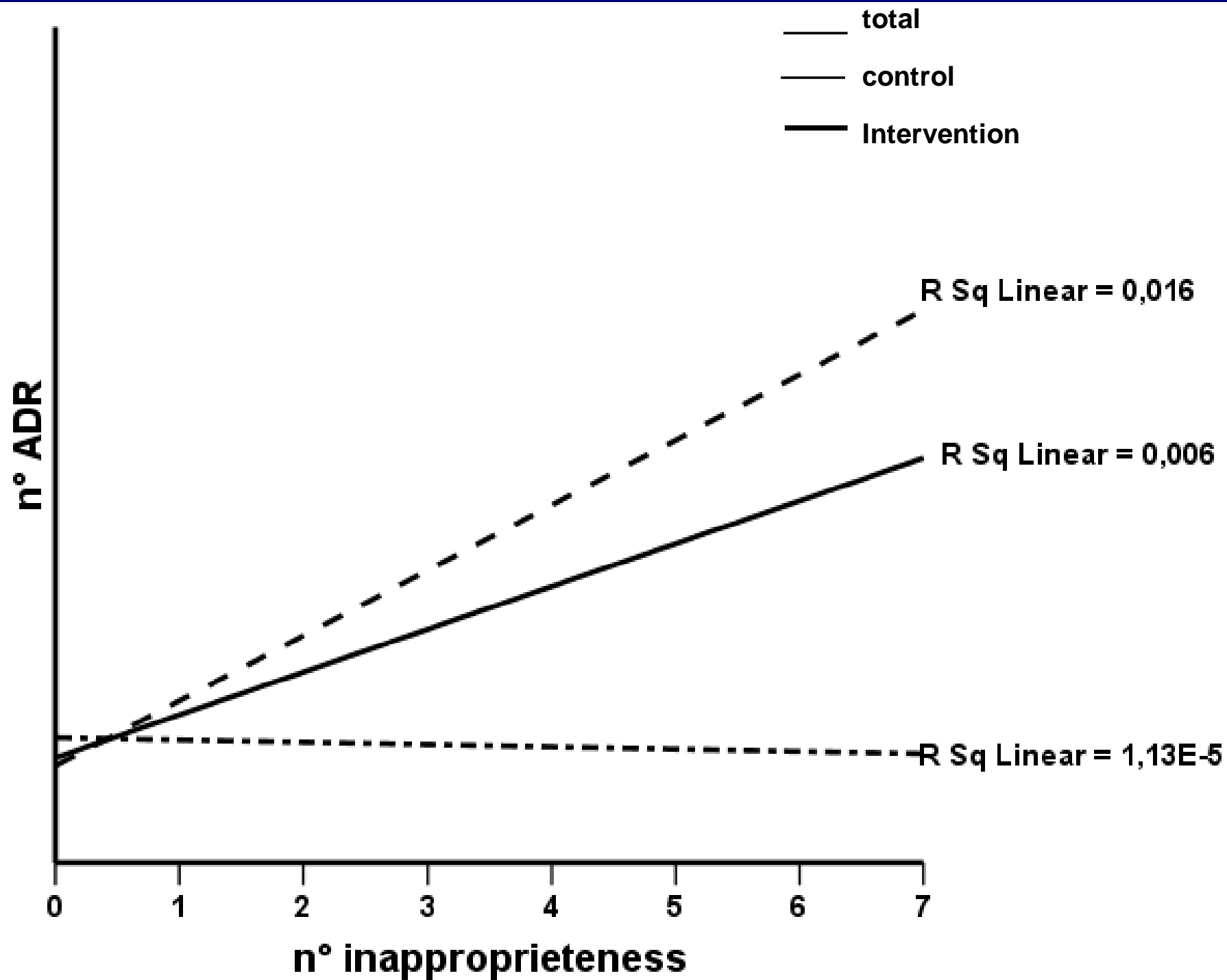
Associato con problemi del QT e rischio di provocare torsade des pointes.

Diagnosi

SEVERITA': **Alta**







Conclusioni

Il nostro strumento educativo/informativo è stato capace di:

- Ridurre il numero di prescrizioni inappropriate
- Ridurre la probabilità di ADR associata a inappropriatezza

dieta

Restrizione acqua e sale

Peso corporeo giornaliero

Aderenza al trattamento

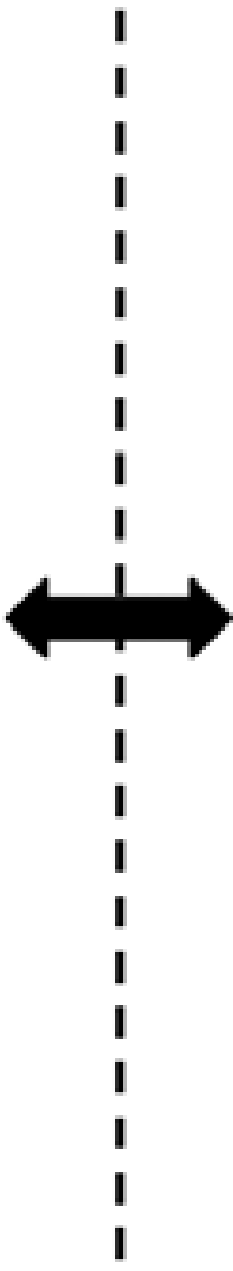
**GESTIONE PERSONALE
paziente e/o caregiver**

Sintomi ricorrenti

Consumo di alcool

Abolizione del fumo

Attività fisica



Specialista di cure palliative

Internista

Cardiologo

Geriatra

**Team
MULTIDISCIPLINARE**

Infermiere professionale

Dietista

Assistente sociale

Fisioterapista