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Management geriatrico delle malattie acido-correlate

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MALATTIE ACIDO-CORRELATE NELL'ANZIANO

MRGE

- Aspetti clinici
- Trattamento

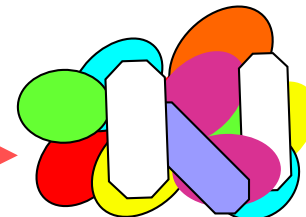


**ULCERA
PEPTICA**

**H
pylori**



FANS

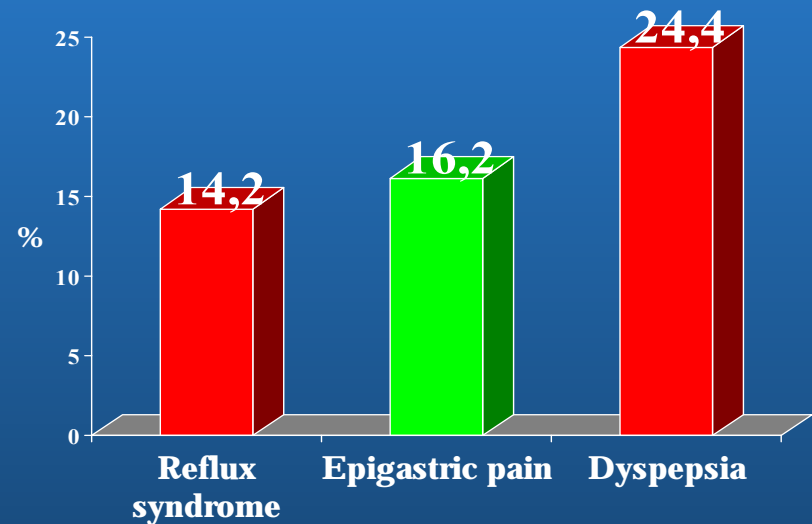
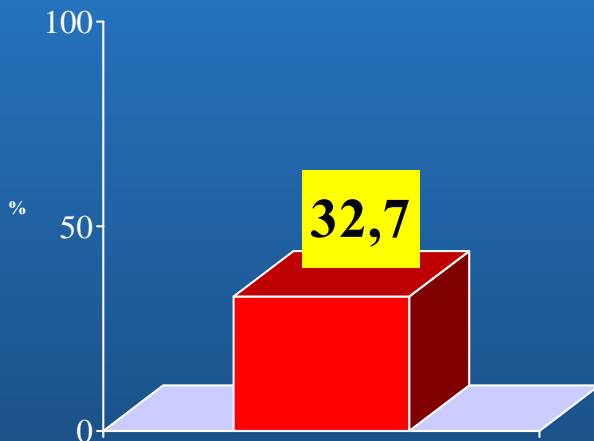




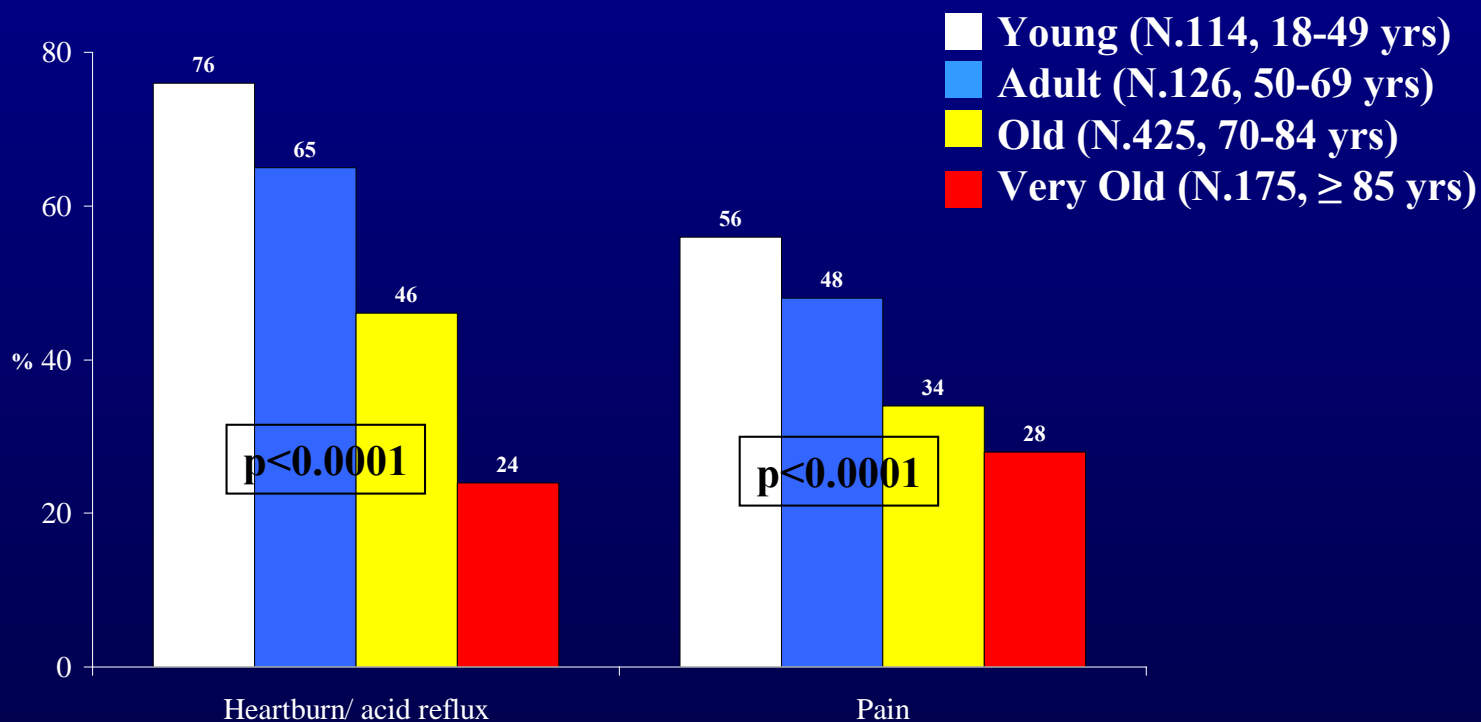
SOFIA Project
FIRI - SIGG

Prevalence of upper GI symptoms

24 UO Geriatric Units/133 GPs, 5515 outpatients
mean age: 75.0 ± 6.2 years, range: 65-100 years

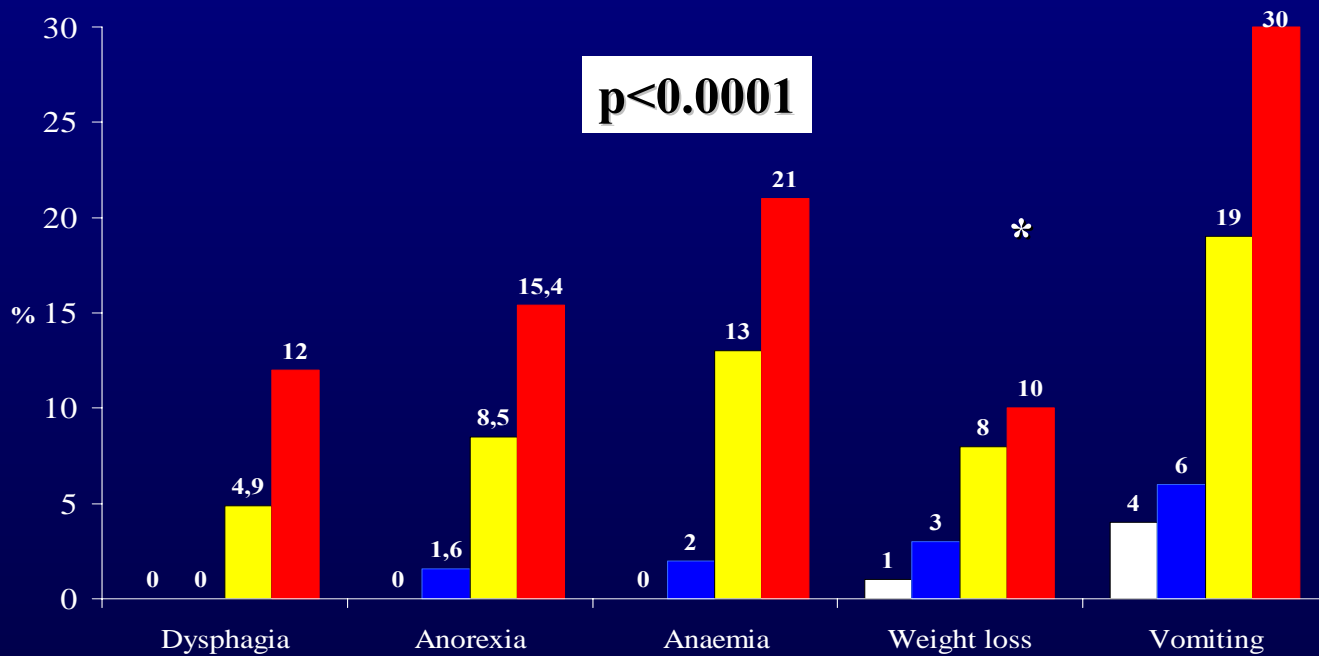


Prevalence of typical symptoms in 840 subjects with esophagitis divided according to age



Prevalence of non-specific symptoms in 840 subjects with esophagitis divided according to age

■ Young (N.114, 18-49 yrs) ■ Adult (N.126, 50-69 yrs)
■ Old (N.425, 70-84 yrs) ■ Very Old (N.175, ≥ 85 yrs)





Consiglio Nazionale delle Ricerche
Sezione Invecchiamento

QUESTIONARIO PER LA VALUTAZIONE DEI SINTOMI DIGESTIVI NELL' ANZIANO “UGISQUE”: Development Cohort

206 soggetti anziani, M=89, F=117, età media=76.2, range =65–96 anni
DIAGNOSI ENDOSCOPICA: Eso, UP, GasEr, NLO

A)	Dolore addominale	1 dolore	2 dolore da fame			
B)	Sintomi da reflusso	3 pirosi	4 rigurgito acido			
C)	Maldigestione	5 nausea	6 brontolii allo stomaco	7 gonfiore di stomaco	8 aerofagia	
D)	Emorragia digestiva	9 ematemesi	10 melena			
E)	Sintomi non specifici	11 anemia (≥ 3 gr di Hb ultimi 3 mesi)	12 anoressia	13 perdita di peso	14 vomito	15 disfagia

Score : 1= assente, 2=lieve, 3=moderato, 4=severo

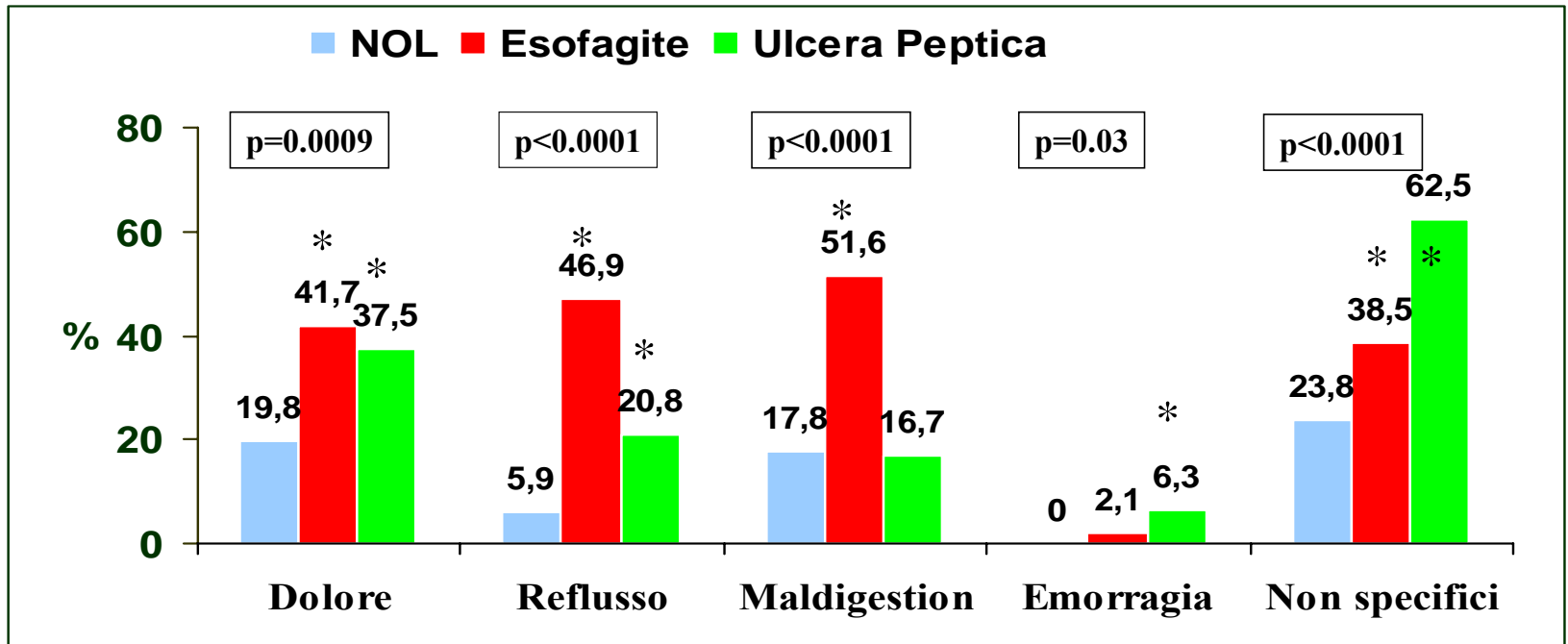


Consiglio Nazionale delle Ricerche
Sezione Invecchiamento

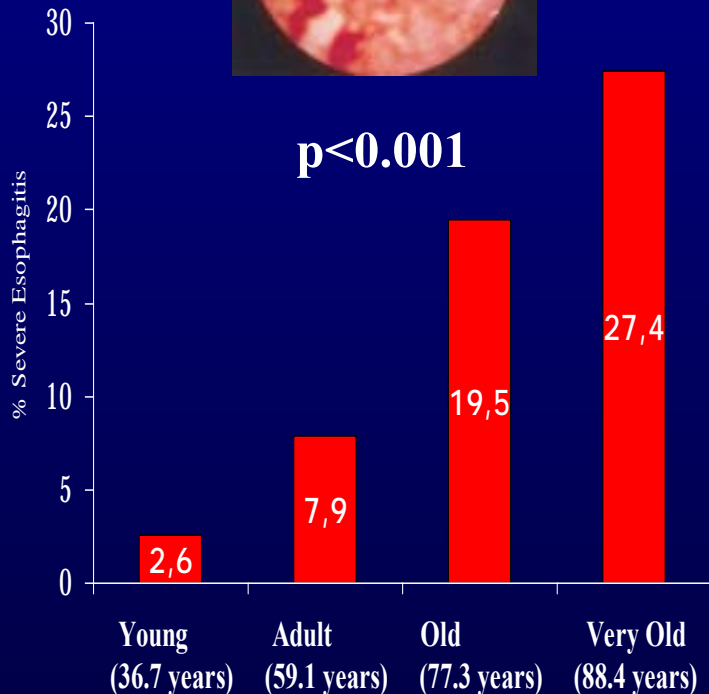
Prevalenza di classi di sintomi UGISQUE nelle malattie alte vie digestive: Validation Cohort

326 soggetti, età media=72.0±7.2, range=60–93 anni

DIAGNOSI ENDOSCOPICA: NLO, Esofagite, Ulcera Peptica

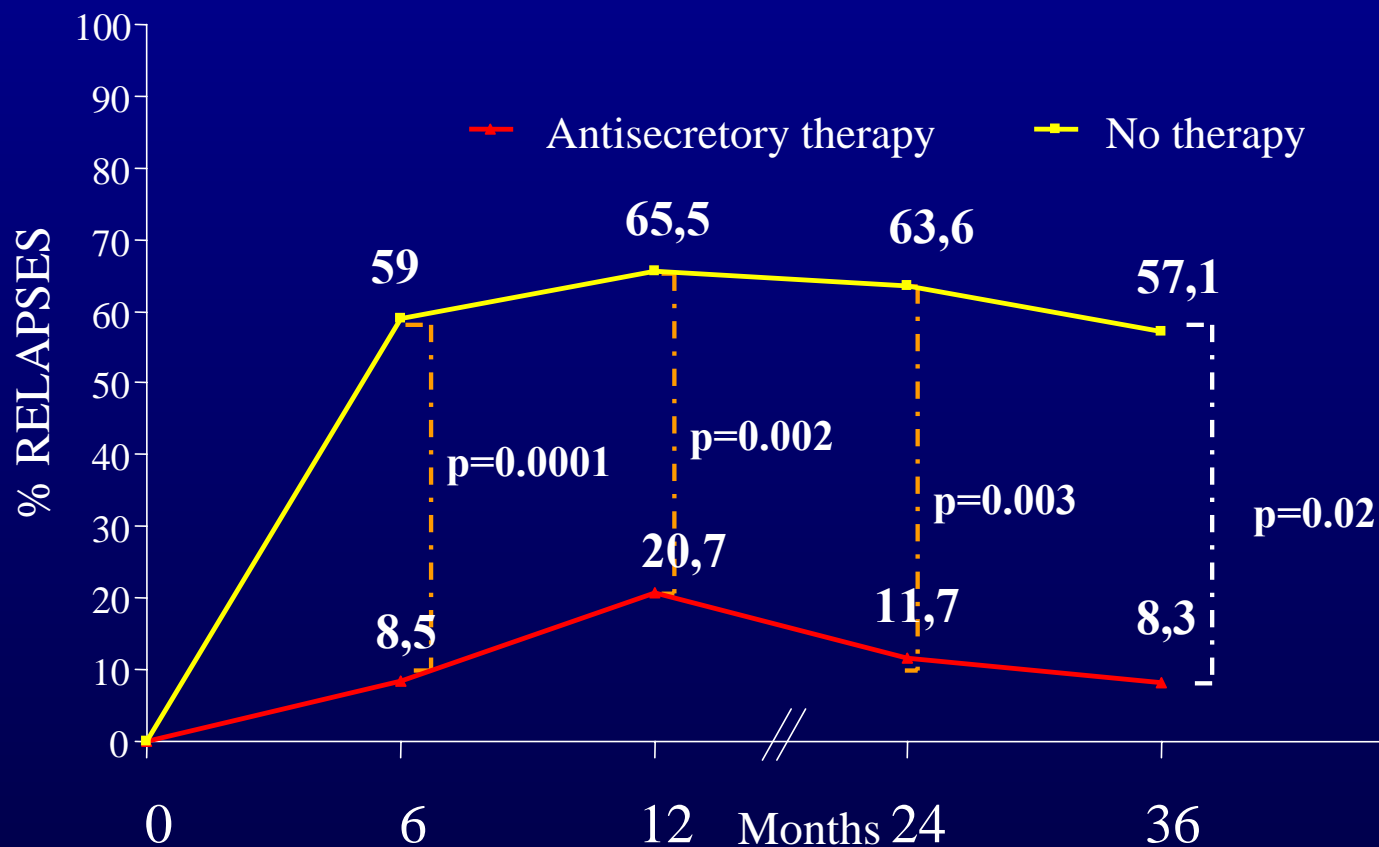


Percentages of severe esophagitis (grade 3-4 Savary-Miller class.) in 840 patients divided according to age



Risk Factor	OR	95% CI
> 65 years	2.66	1.38-5.12
> 85 years	4.57	2.15-9.71
HH > 3 cm	2.38	1.41-4.01
Male Sex	2.83	1.72-4.64

Long term clinical outcome of 138 elderly patients with reflux esophagitis: a three-year follow-up study



SAFETY OF LONG-TERM PPI TREATMENT

**230 patients, mean age=63 years (36% over 70 years)
treated with omeprazole 20-40 mg daily
follow-up: 11 years**

	Hp-positive	Hp-negative
Gastric atrophy/year	4.7%	0.7%
Dysplasia/neoplasms	none	none

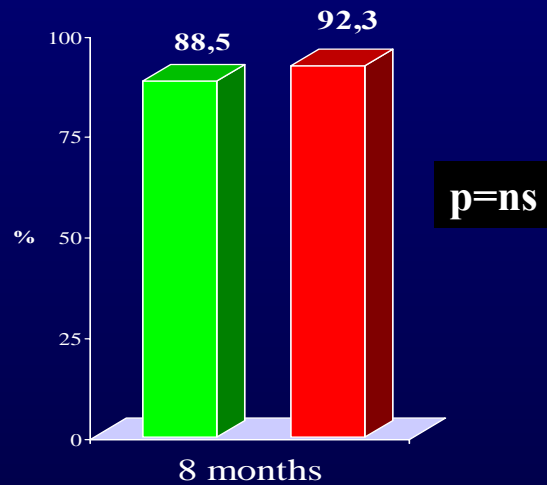
Treatment of esophagitis in H pylori-positive elderly patients

N° 61 patients, mean age= 72 years, range 65-85 years

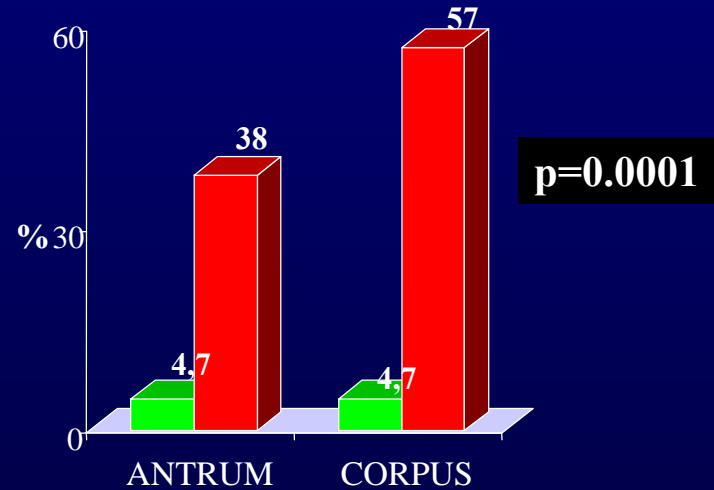
 PPI+CLA+AMO (31 p.ts)

 PPI (30 p.ts)

Healing rates of esophagitis

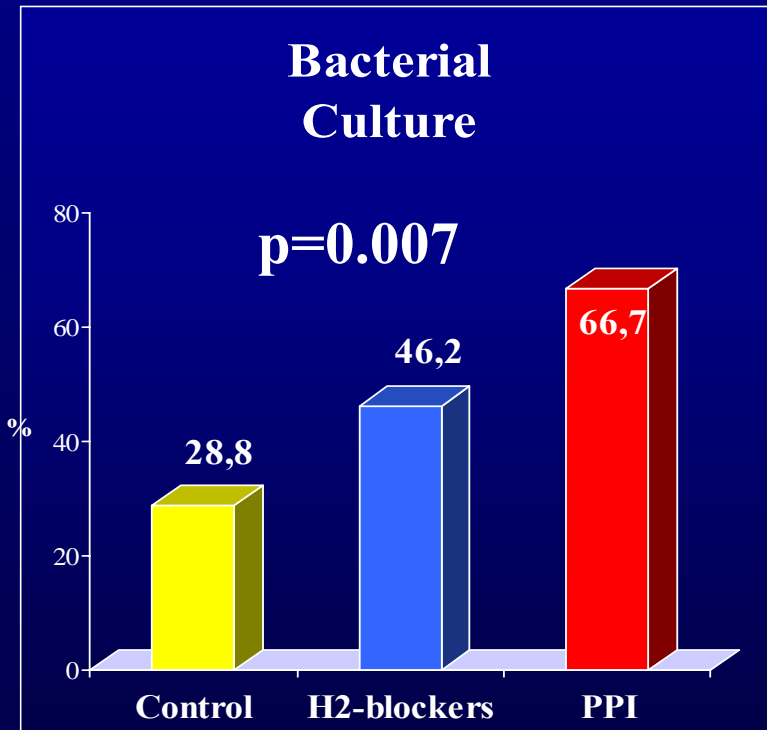


Activity of chronic gastritis



Antisecretory drugs and gastric microbial proliferation

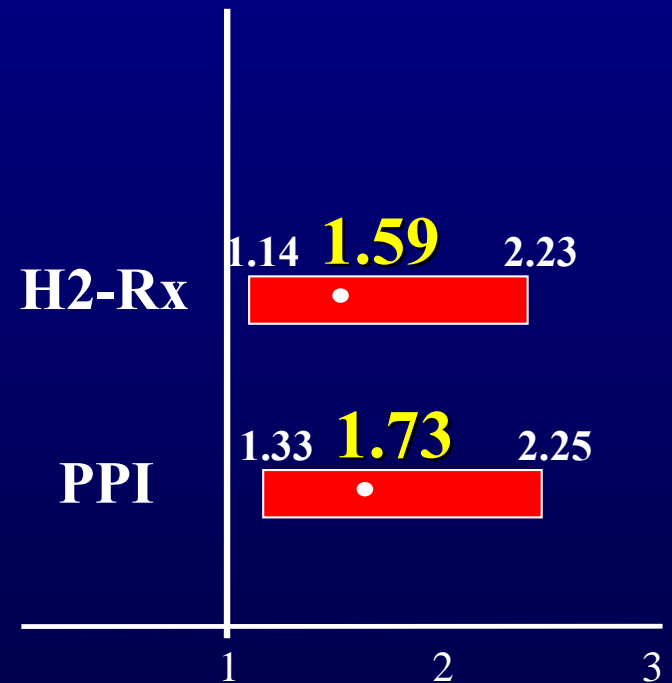
102 patients, Nov2000-Dec2002
26=H2Rx vs 24=PPIs vs 52=controls



Wang, Hepatogastroenterol 2004; 51:1540-3

Risk of Pneumonia and Use of Acid-Suppressive Drugs

364.683 subjects, 5.551 pneumonia
Primary Care Data, Jan1995-Dec2002

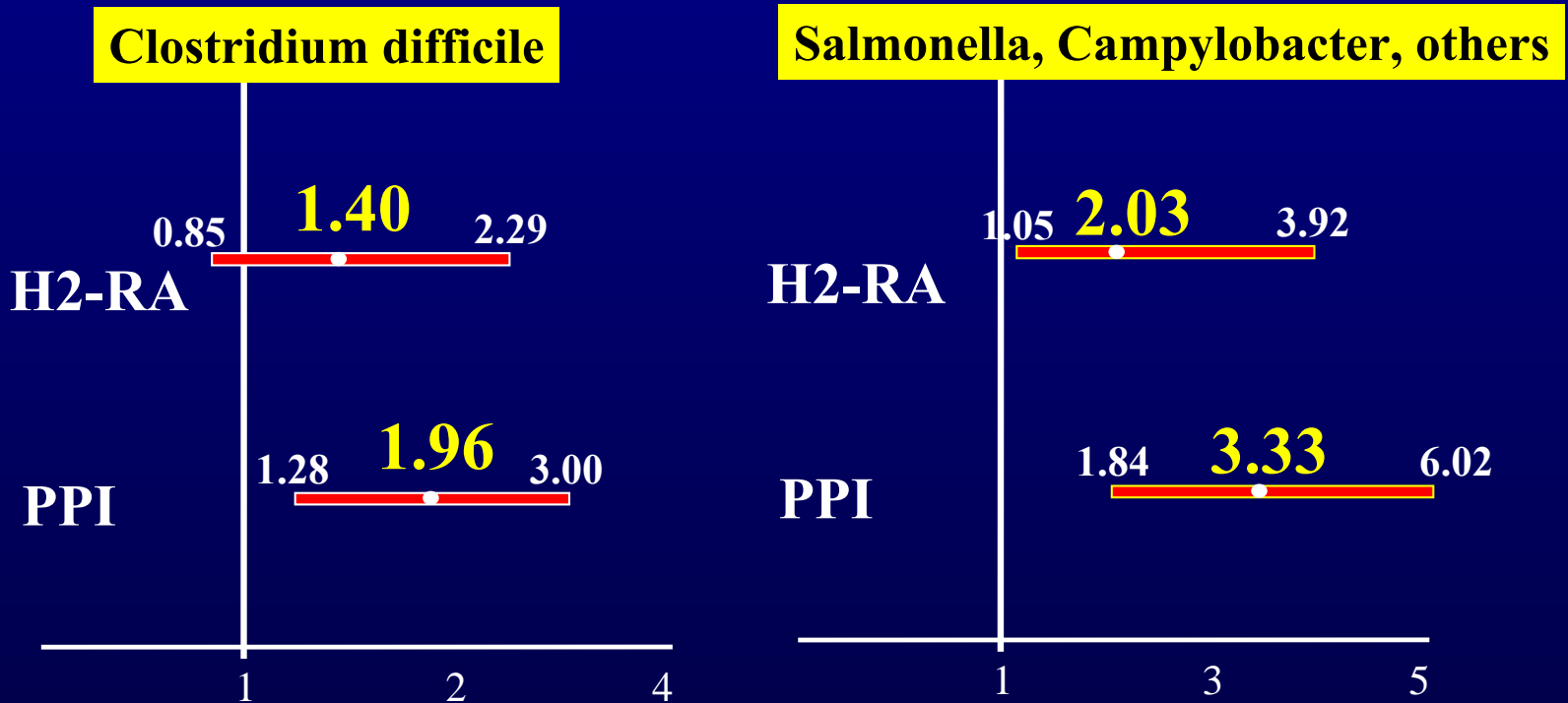


Laheij, JAMA 2004; 292:1955-60

Systematic review of the risk of enteric infections in patients taking acid suppression therapy

Clostridium difficile: 12 papers, 2948 patients

Salmonella, Campylobacter, other enteric infections: 6 papers, 11.280 patients





Diarrhea and drug use in the elderly: analisi multivariata

**5.551 subjects, 488 patients with diarrhea (GSRS score ≥ 2)
M=210, F=278, mean age=75.6 \pm 6.2 years, range=65-100 years**

Drug class	OR	Lower	Upper	p value
Antibiotics	4.57	2.00	10.42	.0001
Proton Pump Inhibitors	3.62	2.52	5.19	.0001
Allopurinol	2.08	1.21	3.58	.008
Psycholeptics	1.89	1.32	2.69	.0001
Selective Serotonin Reuptake Inhibitors	1.75	1.05	2.91	.033
Angiotensin II receptor blockers	1.46	1.09	1.96	.013

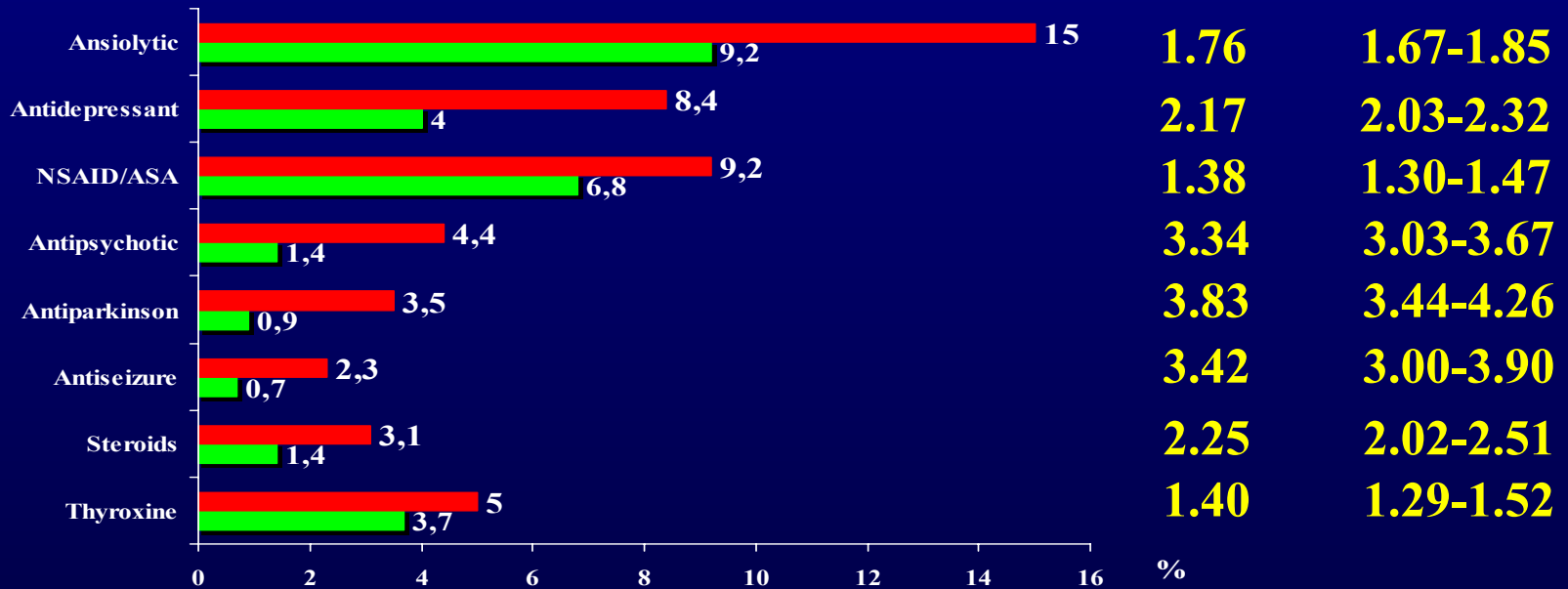
Long-term Proton Pump Inhibitor Therapy and Risk of Hip Fracture

13.556 hip fracture cases vs 135.386 controls

PROTON PUMP INHIBITORS > 1 year

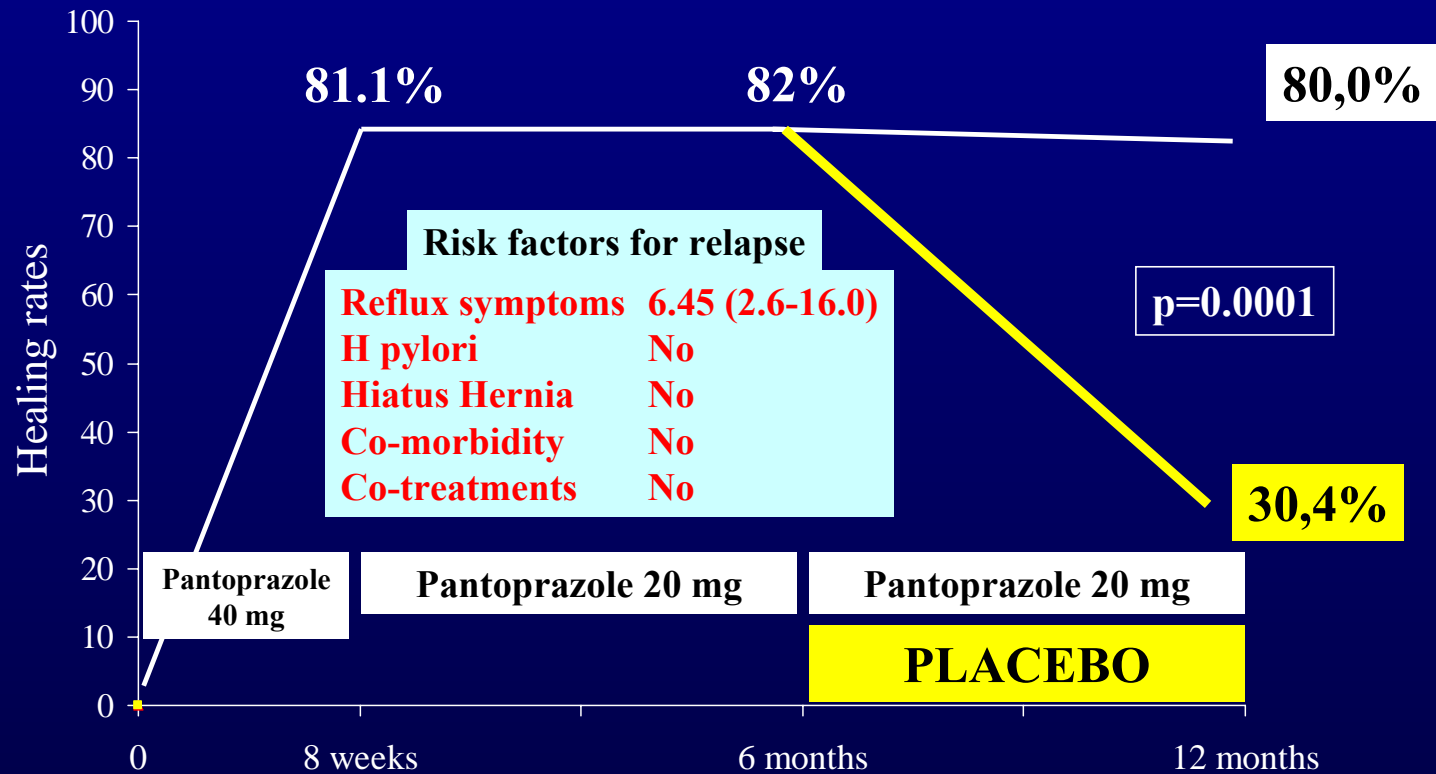
Crude OR 95%CI

1.82 1.67-2.00



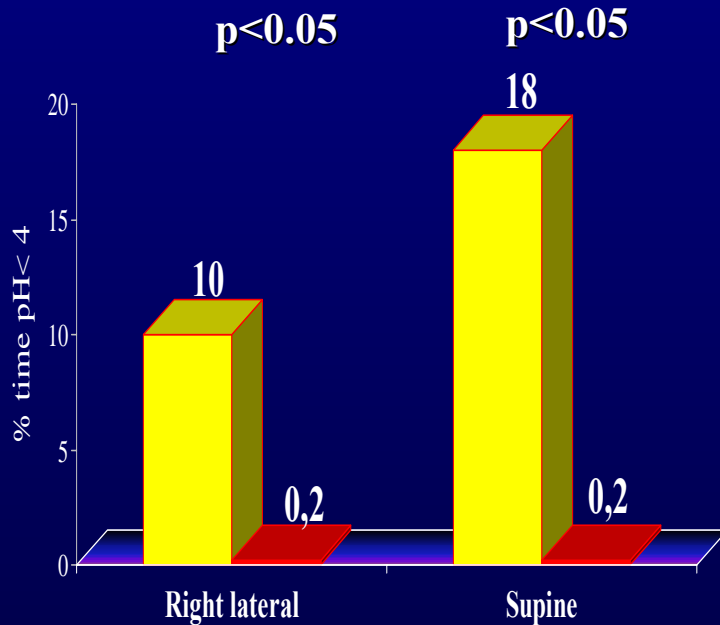
Short- and long-term therapy for reflux esophagitis in the elderly: a multi-centre, placebo-controlled study

164 patients, mean age=73 years, range 65-93 years

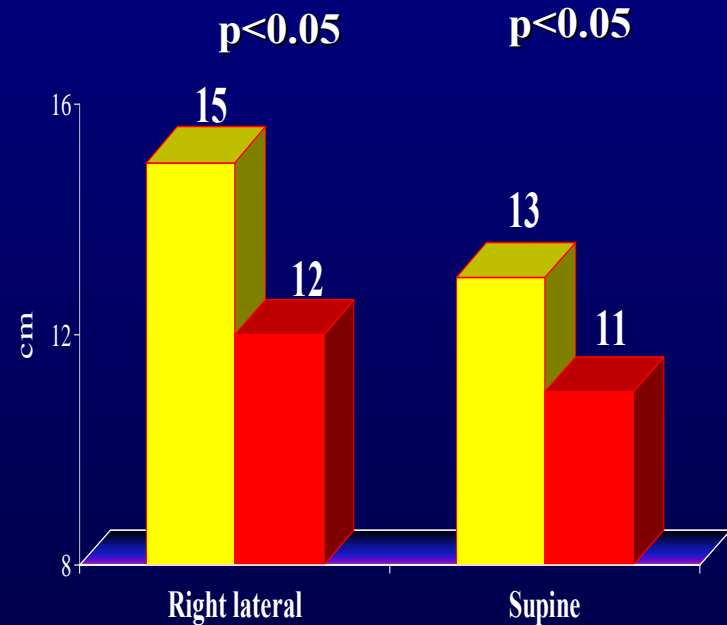


Antireflux properties of sodium alginate by multichannel intraluminal impedance and pH-metry

% time pH < 4 at baseline and after alginate in two decubitus positions



Proximal migration in cm of reflux events at baseline and after alginate



Take Home Message 1

MRGE NELL'ANZIANO

- 1. Sintomi “significativamente” diversi rispetto all’adulto-giovane**
- 2. Impiego di strumenti specifici per l’anziano: UGISQUE**
- 3. Esofagite più severa e recidiva frequente nell’anziano**
- 4. Sospendere la terapia con PPI dopo 6 mesi aumenta la recidiva**
- 5. Il 30% dei pazienti senza terapia antisecretiva non recidiva**
- 6. La terapia antisecretiva è ben tollerata**
- 7. Monitorare gli anziani con frequenti infezioni polmonari, malassorbimento intestinale, diarrea cronica e osteoporosi**

Gastric ulcer

n° 175

mean age = 81 years

range=65-98 years

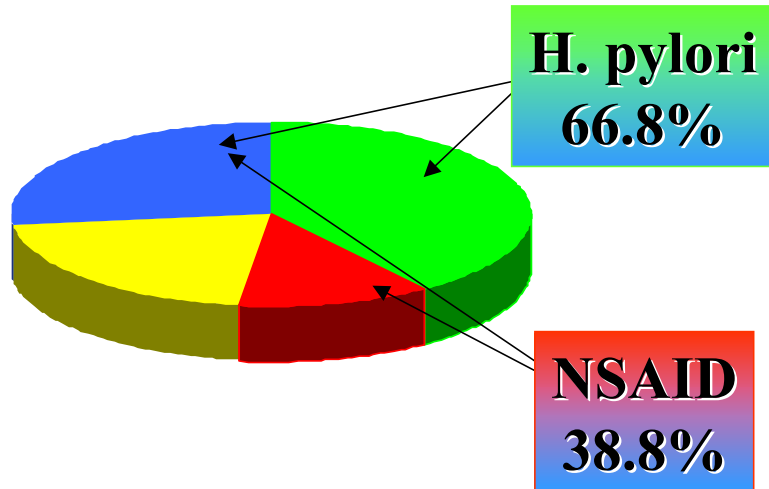
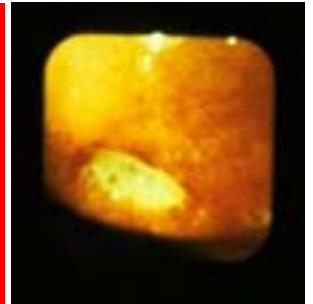


Duodenal ulcer

n° 345

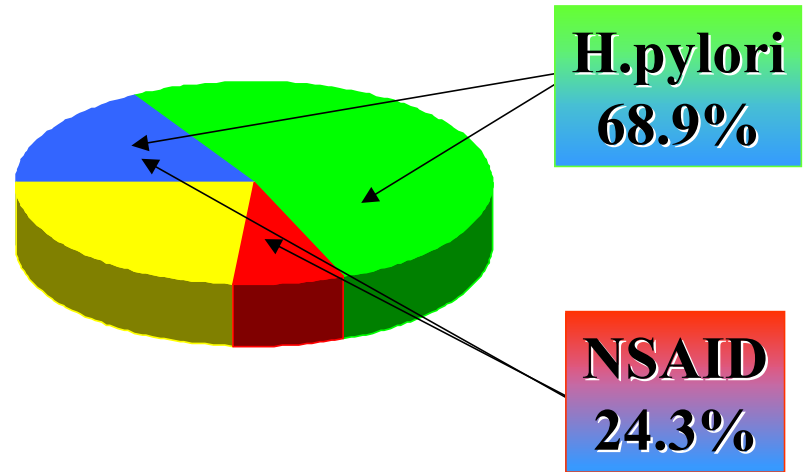
mean age = 81 years

range=65-99 years



■ H.pylori

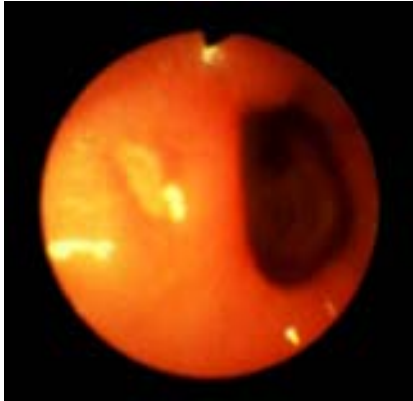
■ NSAID



■ H.pylori+NSAID

■ Other

STRATEGIES TO PREVENT NSAID-RELATED GASTROINTESTINAL DAMAGE



- **REDUCE DOSAGES OF NSAIDs**
- **USE LESS DAMAGING NSAIDs or COXIBs**

Risk of Upper GI Complications among Users of Traditional NSAIDs and Coxibs

Short half-life

Long half-time

Slow-release formulations

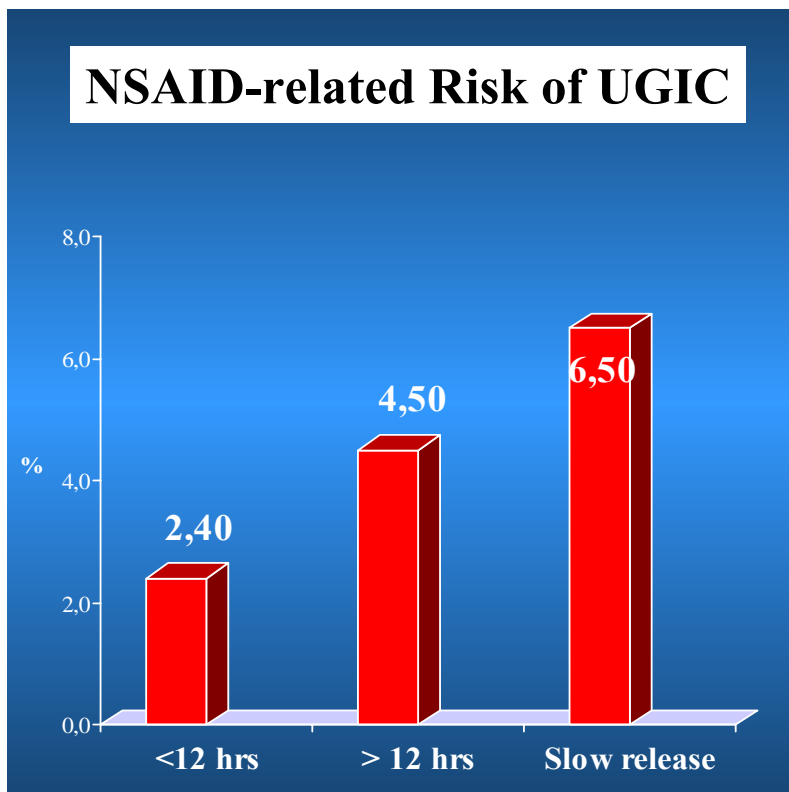
**Diclofenac
Etodolac**

**Ibuprofen
Indomethacin
Ketoprofen**

Apazone

**Meloxicam
Nabumetone
Naproxen
Piroxicam**

**Sulindac
Tenoxicam**



Risk of Peptic Ulcer in 3111 elderly patients: 676 treated with NSAIDs vs 2435 controls

Non Users

Acute NSAIDs alone

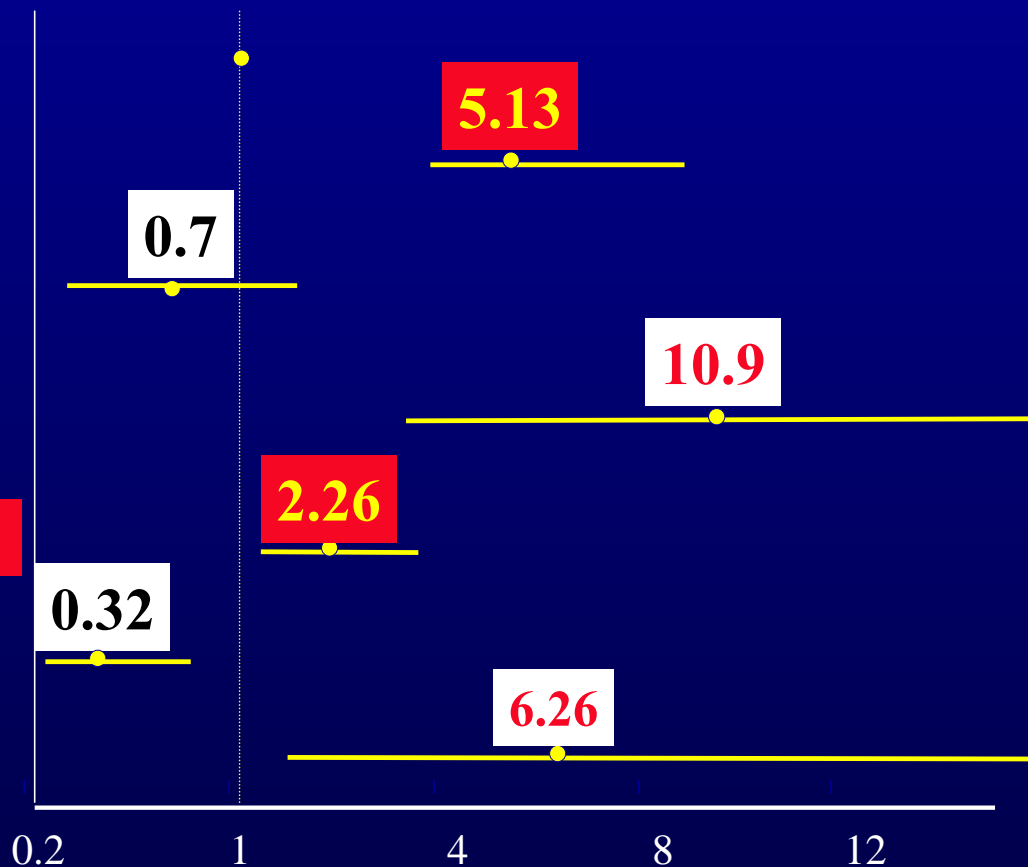
NSAID + PPI

NSAID + H2RA

Chronic NSAIDs alone

NSAID + PPI

NSAID + H2RA

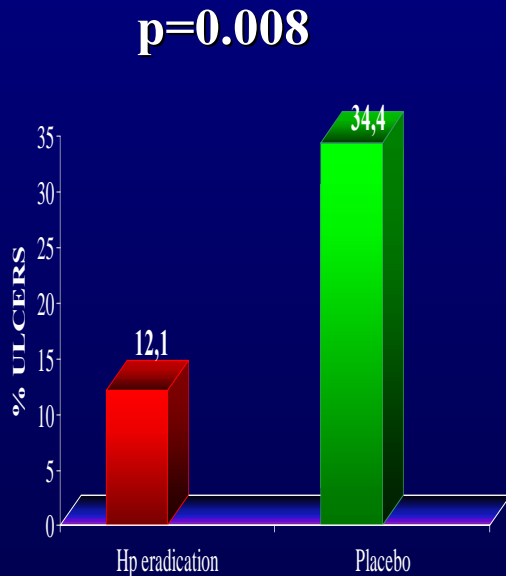


PREVENTION OF ULCER COMPLICATIONS IN H PYLORI-POSITIVE PATIENTS TREATED WITH NSAIDS OR ASA

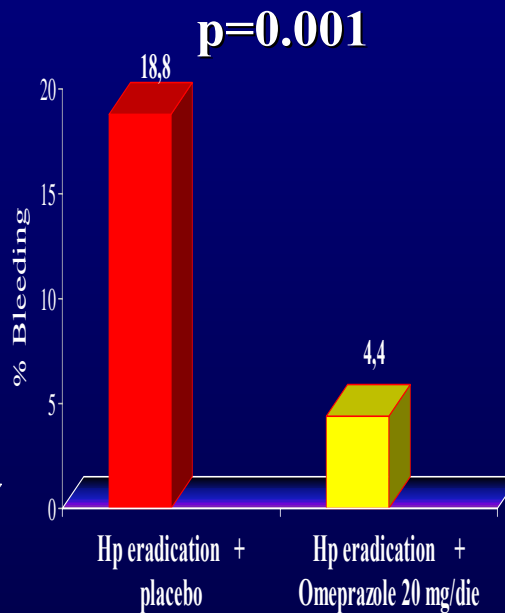
Diclofenac 100 mg /6 months
n° 100, mean age= 62.5 years

Naproxen 500 mg bid /6 months
n° 150, mean age= 67±13 years

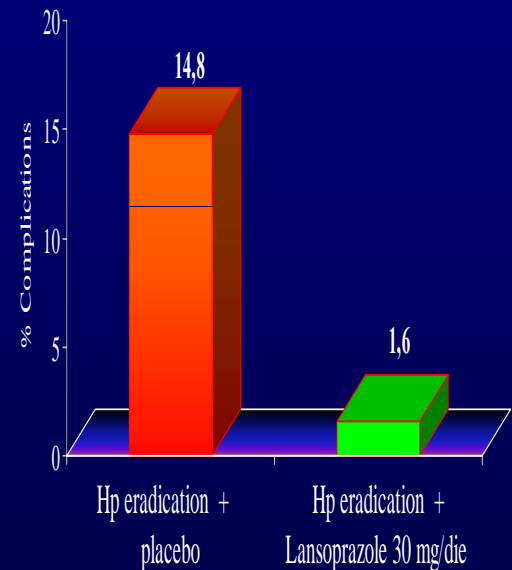
Aspirin 100 mg daily /1 year
n° 123, mean age= 71.5±8 years



Chan, Lancet 2002;359:9-13



Chan , NEJM 2001; 344: 967-73



Lai , NEJM 2002; 346: 2033-8



Current concepts in the management of *Helicobacter pylori* infection: the Maastricht III Consensus Report.

Eradication of *H pylori* infection

- may prevent peptic ulcer and bleeding in patients who are naïve users of non-steroidal anti-inflammatory drugs

Evidence: 1b, Recommendation: A

- in long term NSAID users is insufficient to prevent NSAID-related ulcer disease completely

Evidence: 1b, Recommendation: A

- is less effective than PPI treatment in preventing ulcer recurrence in chronic NSAID users

Evidence: 1b, Recommendation: A

STRATEGIES TO PREVENT NSAID-RELATED GASTROINTESTINAL DAMAGE

- **REDUCE DOSAGES OF NSAIDs**
- **USE LESS DAMAGING NSAIDs/COXIBs**
- **CO-PRESCRIPTION OF A PROTECTIVE DRUG**
- **H. PYLORI ERADICATION**

- **EDUCATION**

Criteria di Evitabilità di ADR (Hallas)

1756 patients, admitted to Geriatric Unit (Nov. 2004-Dec.2005)

ADR = 102 cases (5.8%) of all admissions

	Definitely avoidable		Possible avoidable
	17 (16.5%)	29 (28.4%)	32 (31.4%)
	<i>Inappropriate prescription</i>	<i>No gastroprotection</i>	<i>Inadequate monitoring</i>
NSAID/ASA	5 (29.4%)	29 (100%)	1 (3.1%)
Warfarin	3 (17.6%)	-	13 (40.6%)
Digoxin	1 (5.9%)	-	12 (37.5%)
Antidiabetics	-	-	2 (6.3%)
Amiodarone	1 (5.9%)	-	1 (3.1%)
Antihypertensive	4 (23.5%)	-	3 (9.4%)
Neurological	3 (17.6%)	-	-

STRATEGIES TO PREVENT NSAID-RELATED GASTROINTESTINAL DAMAGE

- **REDUCE DOSAGES OF NSAIDs**
- **USE LESS DAMAGING NSAIDs/COXIBs**
- **CO-PRESCRIPTION OF A PROTECTIVE DRUG**
- **H. PYLORI ERADICATION**
- **EDUCATION**
- **NEW PERSPECTIVES**

Drugs that are substrates for CYP 2C9

CYP 2C9

Celecoxib

Diclofenac

Naproxen

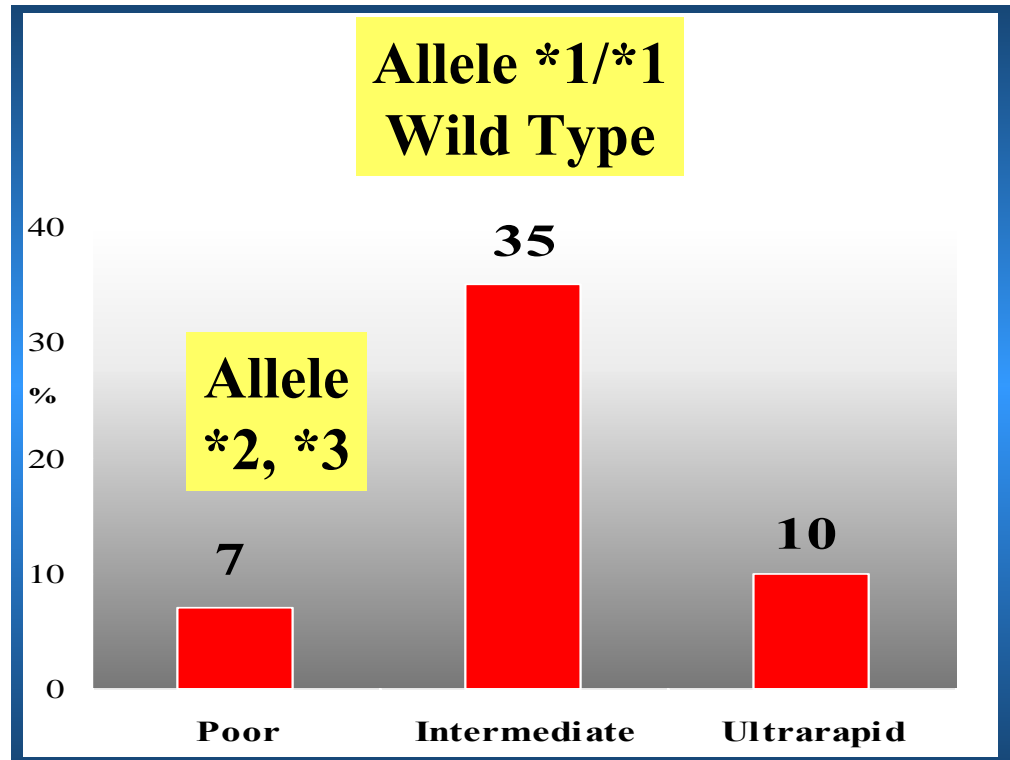
Nimesulide

Piroxicam

Tolbutamide

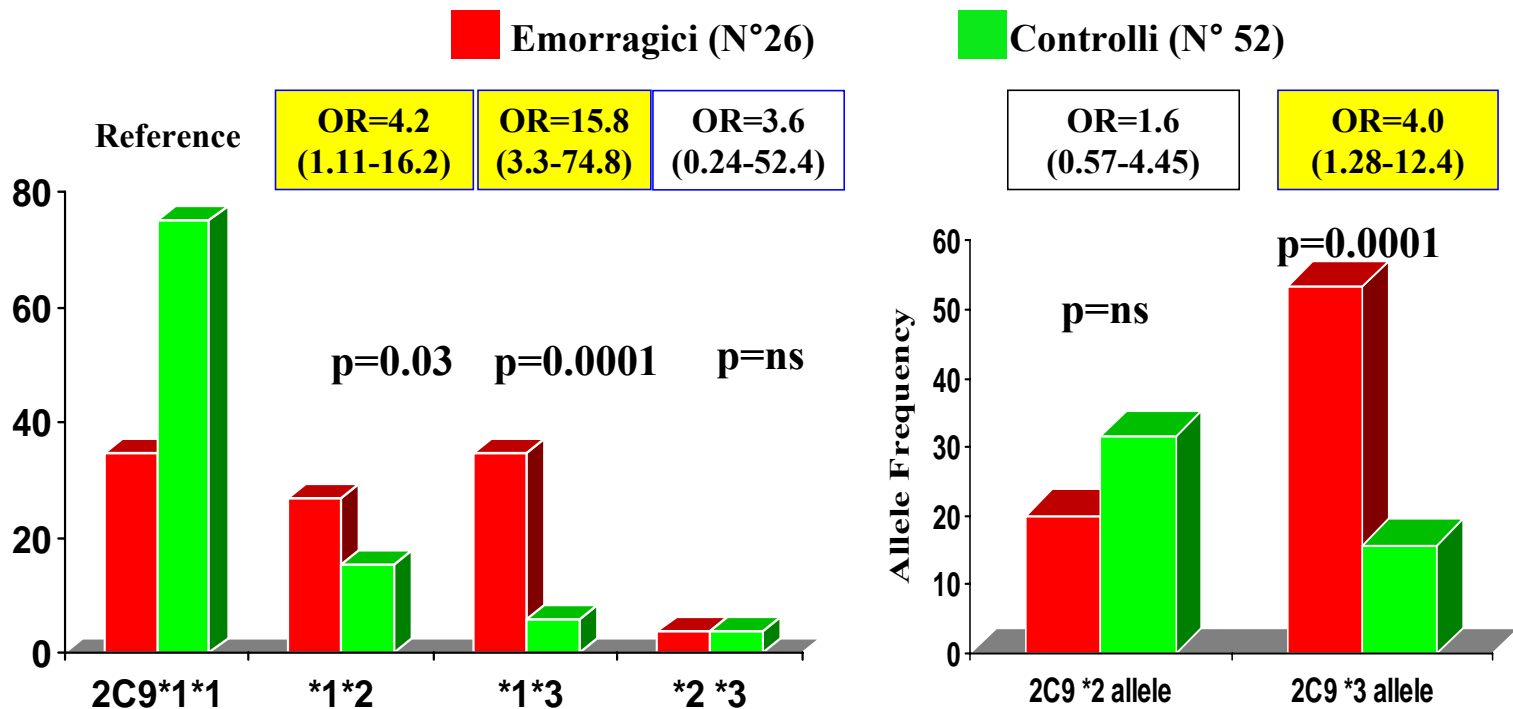
Glipizide

Warfarin



Rischio di emorragia gastroduodenale da FANS: ruolo dei polimorfismi genetici del Citocromo P450 2C9

Farmaci: celecoxib, diclofenac, nimesulide, naproxene, piroxicam < 30 giorni
H pylori negativi, no gastroprotezione





Multidimensional Prognostic Index for 1-year mortality in hospitalized older patients

Development Cohort:

838 pts, M/F=373/465, mean age=79.2±7.3, range=65-101

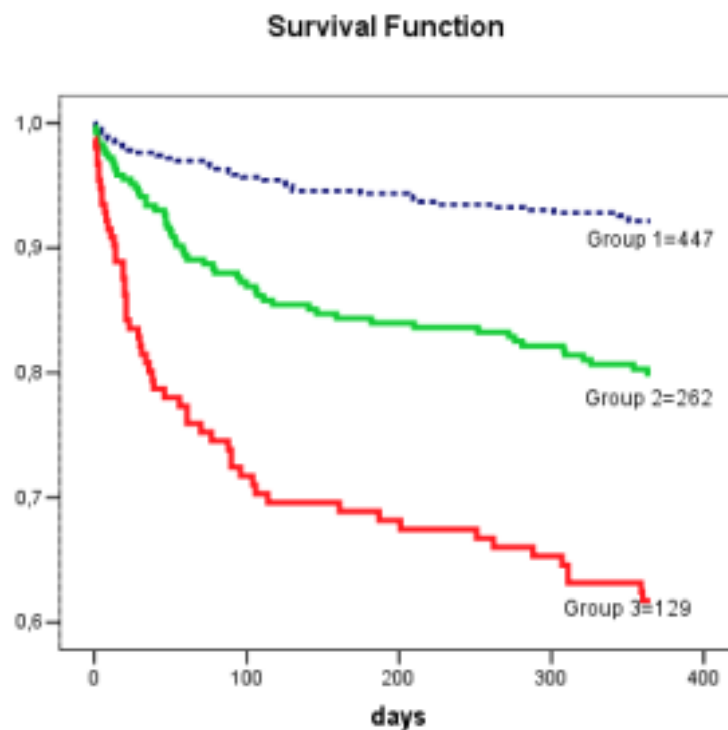
- Activities of Daily Living (ADL)	6	items
- Instrumental Activities of Daily Living (IADL)	8	items
- Short Portable Mental Status Questionnaire (SPMSQ)	10	items
- Mini-Nutritional Assessment (MNA)	18	items
- Exton-Smith Scale	5	items
- Cumulative Illness Rating Scale_comorbidity (CIRS)	14	items
- Number of drugs	1	
- Social index	1	
TOTAL	63	items

M. P. I.

	Mild	Moderate	Severe
SCORE	0.18±0.09	0.48±0.09	0.77±0.08
RANGE	0.00-0.33	0.34-0.66	0.67-1.0

1-Year Mortality by M.P.I. in hospitalized elderly patients *Development cohort*

838 patients, M=373, F=465, mean age=79.2±7.3, range=65-101



**Cumulative HR in the Validation Cohort
according to different grades of severity
of MPI after 180 days and 1-year of follow-up.**

MPI Grades	Time	Validation cohort			
		N° 857			
		Predicted Mortality	CI (95%)		Observed Mortality
Lower	Upper				
Low Risk MPI 1	6 months	4.1	0.023	0.059	4.2
	12 months	5.7	0.035	0.079	5.7
Moderate Risk MPI 2	6 months	17.7	0.132	0.222	17.1
	12 months	24.6	0.195	0.297	23.2
Severe Risk MPI 3	6 months	43.8	0.350	0.526	36.9
	12 months	55.9	0.469	0.649	45.1

Risk factors of 1-year mortality in hospitalized older patients: Validation Cohort

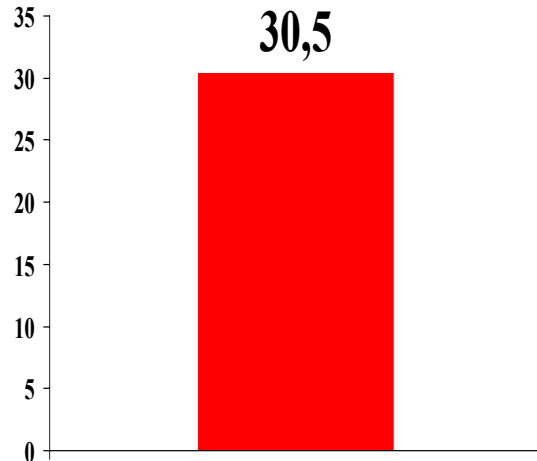
<i>Risk factors</i>	<i>Standardized β coefficient</i>	<i>OR</i>	<i>95% CI</i>	<i>p value</i>
Multidimensional Prognostic Index	9.954	3.647	2.827-4.705	.0001
Age	5.073	1.068	1.041-1.096	.0001
Sex (Male)	1.983	1.441	1.005-2.066	.047
ADL	8.533	1.386	1.286-1.494	.0001
IADL	8.100	1.320	1.234-1.411	.0001
SPMSQ	5.948	1.191	1.125-1.262	.0001
CIRS comorbidity	6.864	1.461	1.311-1.629	.0001
MNA	9.337	1.179	1.139-1.221	.0001
Exton Smith	9.575	1.300	1.232-1.372	.0001
No. of Drugs	3.697	1.135	1.061-1.213	.0001
Social support network	0.834	0.835	0.547-1.275	.404

Multidimensional Prognostic Index in anziani ospedalizzati con emorragia digestiva

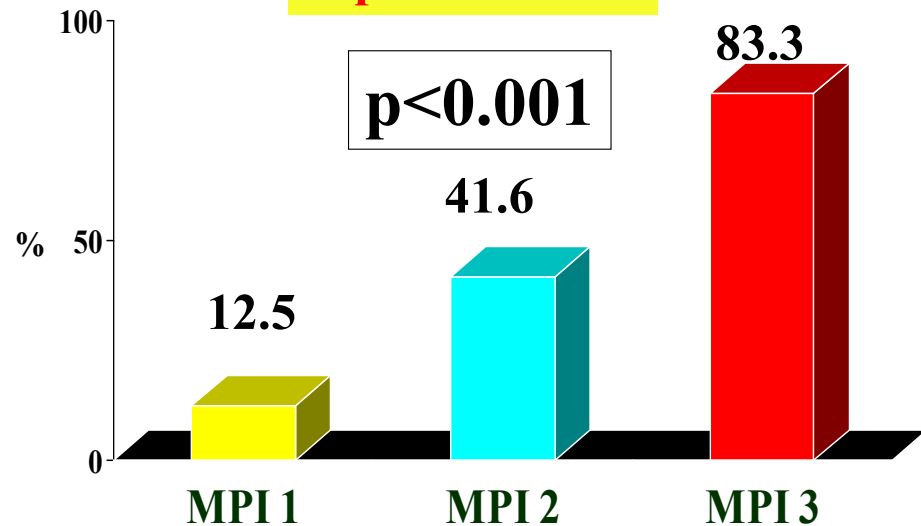
età media=82.8 ± 7.9, range=70-101 anni

Age/sex adjusted OR=10.4, 95%CI= 2.04-53.6

**MORTALITA'
A DUE ANNI**



**MORTALITA'
per M.P.I.**



Take Home Message 2

- **Circa il 40% delle GU e 25% delle DU sono FANS-correlate**
 - **Il rischio di danno GI è più elevato con l'uso acuto di FANS**
 - **Le strategie di prevenzione attualmente disponibili sono:**
 - **bassi dosaggi e formulazioni adatte di FANS**
 - **evitare prescrizioni inappropriate**
 - **prescrivere farmaci gastro-protettori (PPI)**
 - **eradicare l' H. pylori**
- ... NUOVE PROSPETTIVE NELL'ANZIANO...**
- **farmacogenetica del CYP**
 - **identificare il soggetto ad alto rischio (VMD e MPI)**

Grazie per l'attenzione



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