XXXII Congreso Nacional de la SEMI

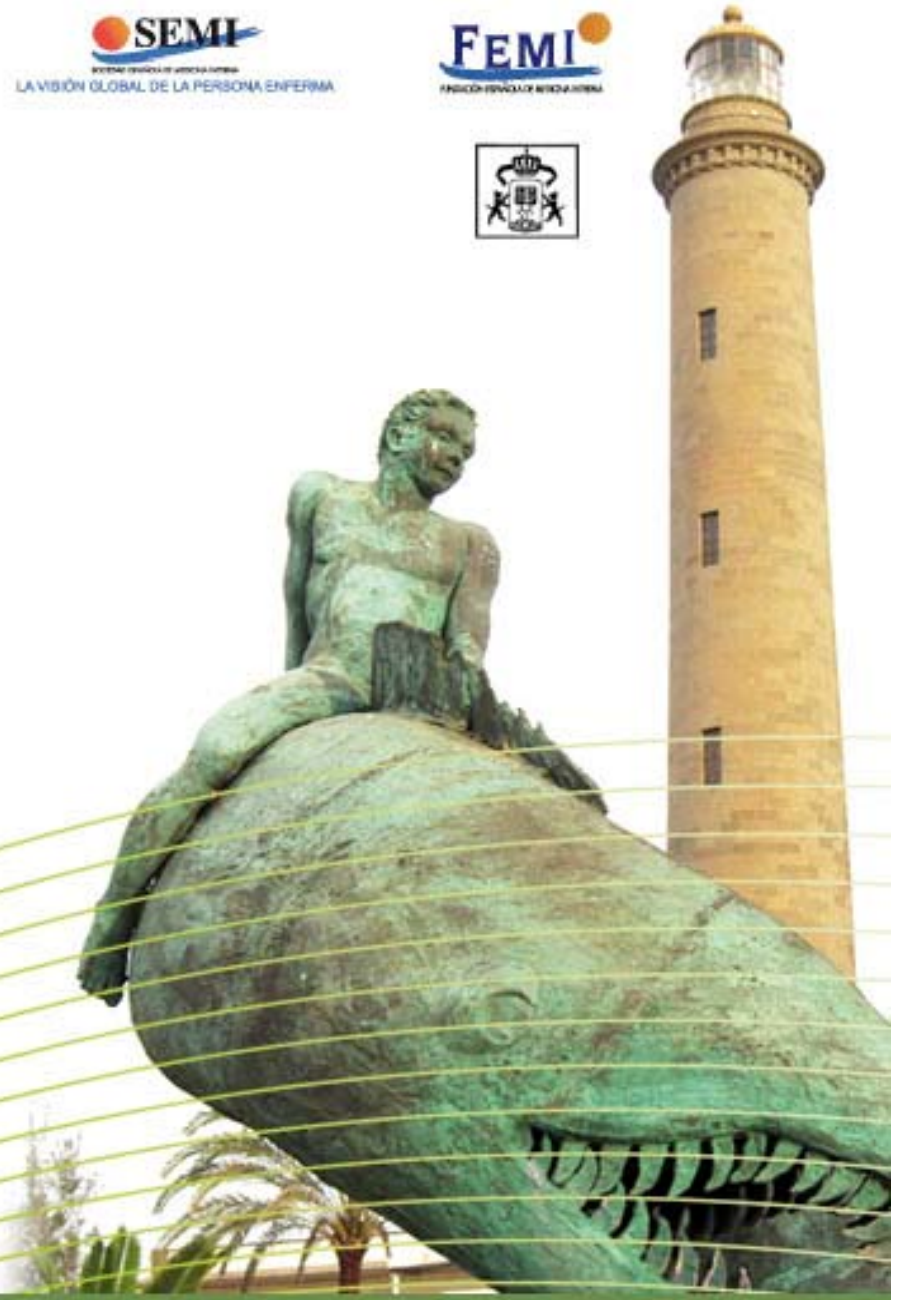
XIV Congreso de la Sociedad Canaria de Medicina Interna

26-28 Octubre 2011

Dr. J.M. Marrero Monroy
Presidente de la SCPD

Costa Meloneras

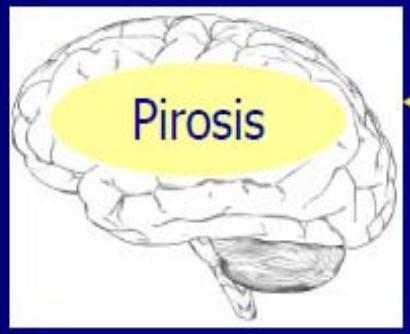
Palacio de Congresos Expomeloneras
Maspalomas. San Bartolomé de Tirajana
Gran Canaria. Las Palmas



Siglo XXI

La Dispepsia Funcional y la ERGE:
Las Enfermedades del Siglo XXI

PATOGENESIS DE LA ERGE

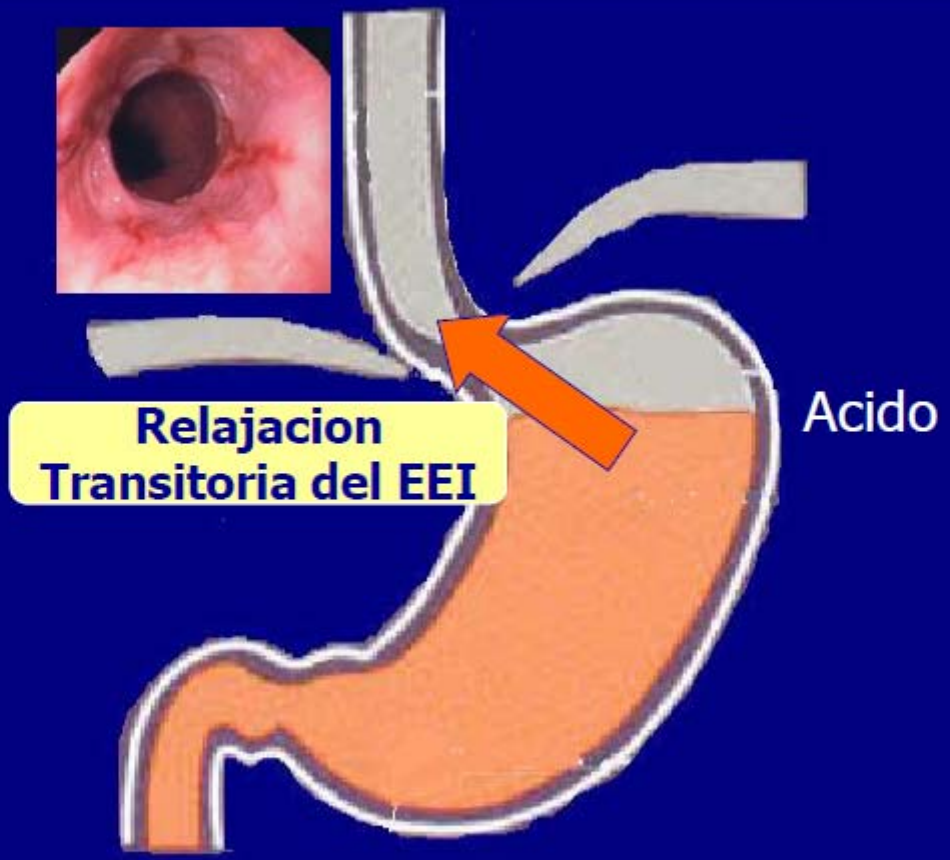


TRPV1 (receptor vaniloide 1)

Relajacion Transitoria del EEI

Acido

PATOGENESIS DE LA ERGE



Modificación del estilo de vida

Dejar de fumar

Reducir peso

Reducir consumo de alcohol

Con síntomas nocturnos

- evitar comer tres horas antes de acostarse
- elevación de cabecera de cama

Síntomas postprandiales

- consumir comidas pequeñas y mas frecuente
- evitar supino después de comer

Obesidad abdominal

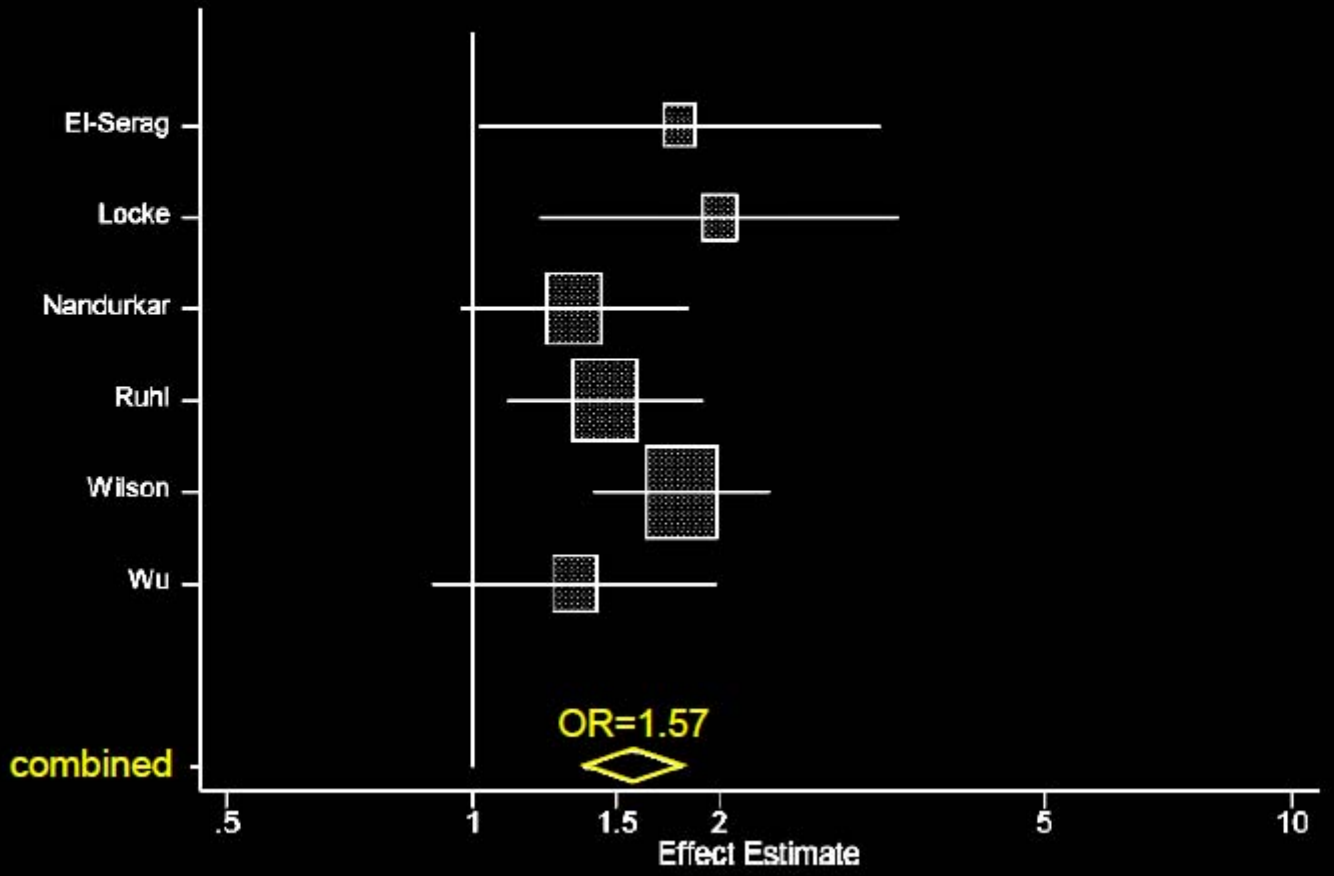
- evitar ropa apretada

Kahrilas PJ N Engl J Med 2008;359:1700-1707

Being overweight is associated with higher chance of GERD

GERD defined as symptoms, esophagitis or both

Overweight defined as BMI 25 - 28

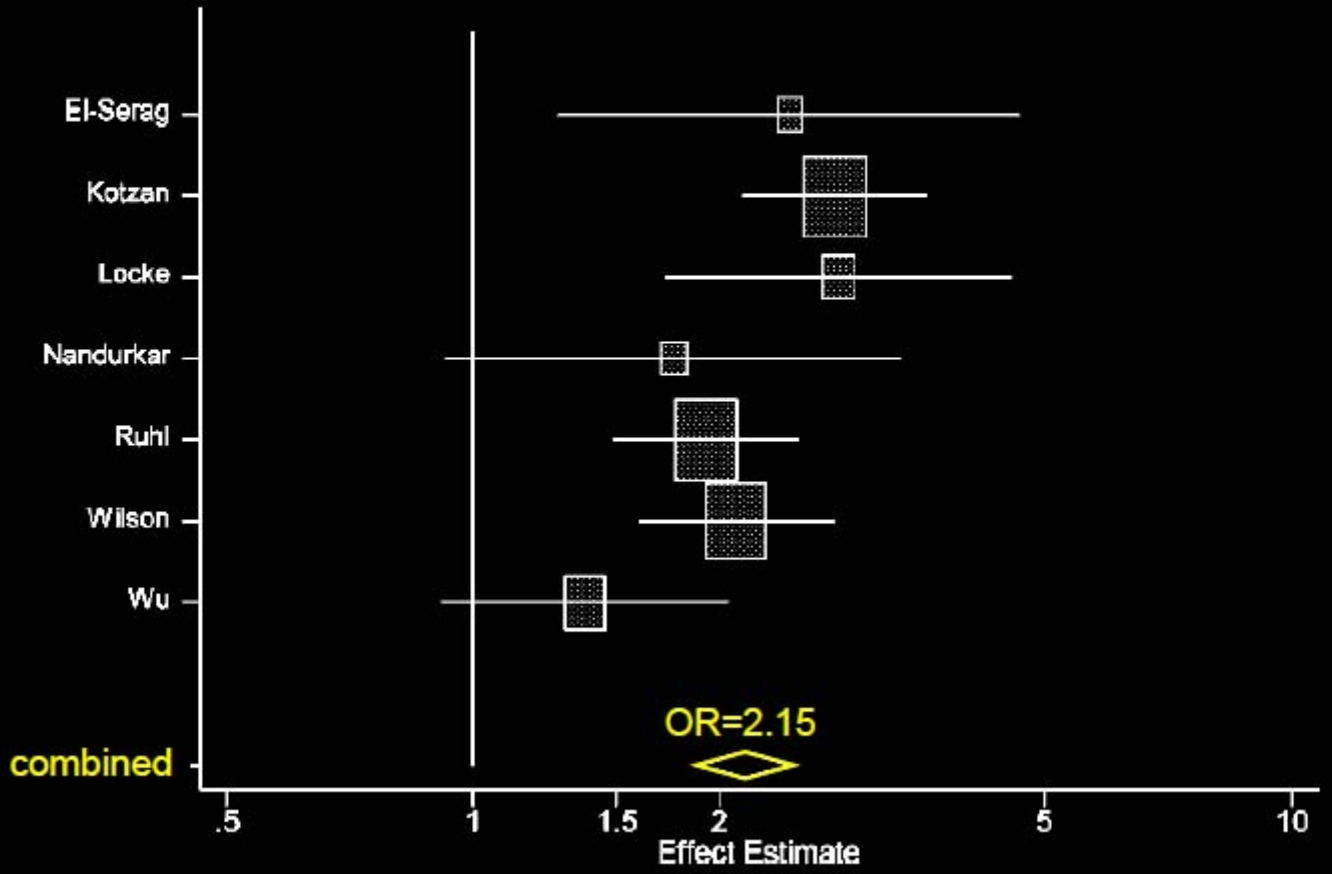


Corley DA *et al.* Am J Gastroenterol 2006;108:2619-2628

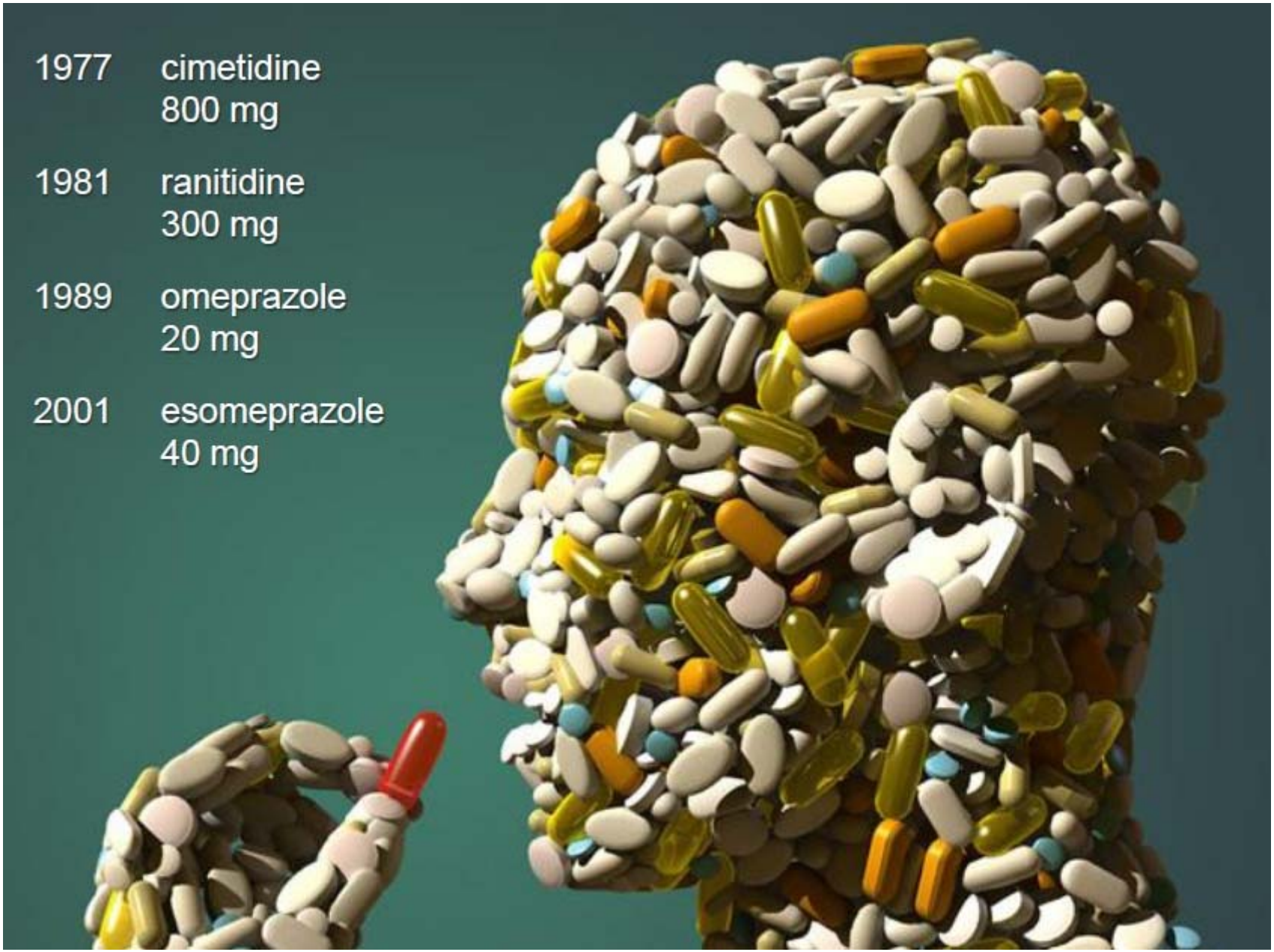
Being obese is associated with higher chance of GERD

GERD defined as symptoms, esophagitis or both

Obese defined as BMI>28



Corley DA *et al.* Am J Gastroenterol 2006;108:2619-2628

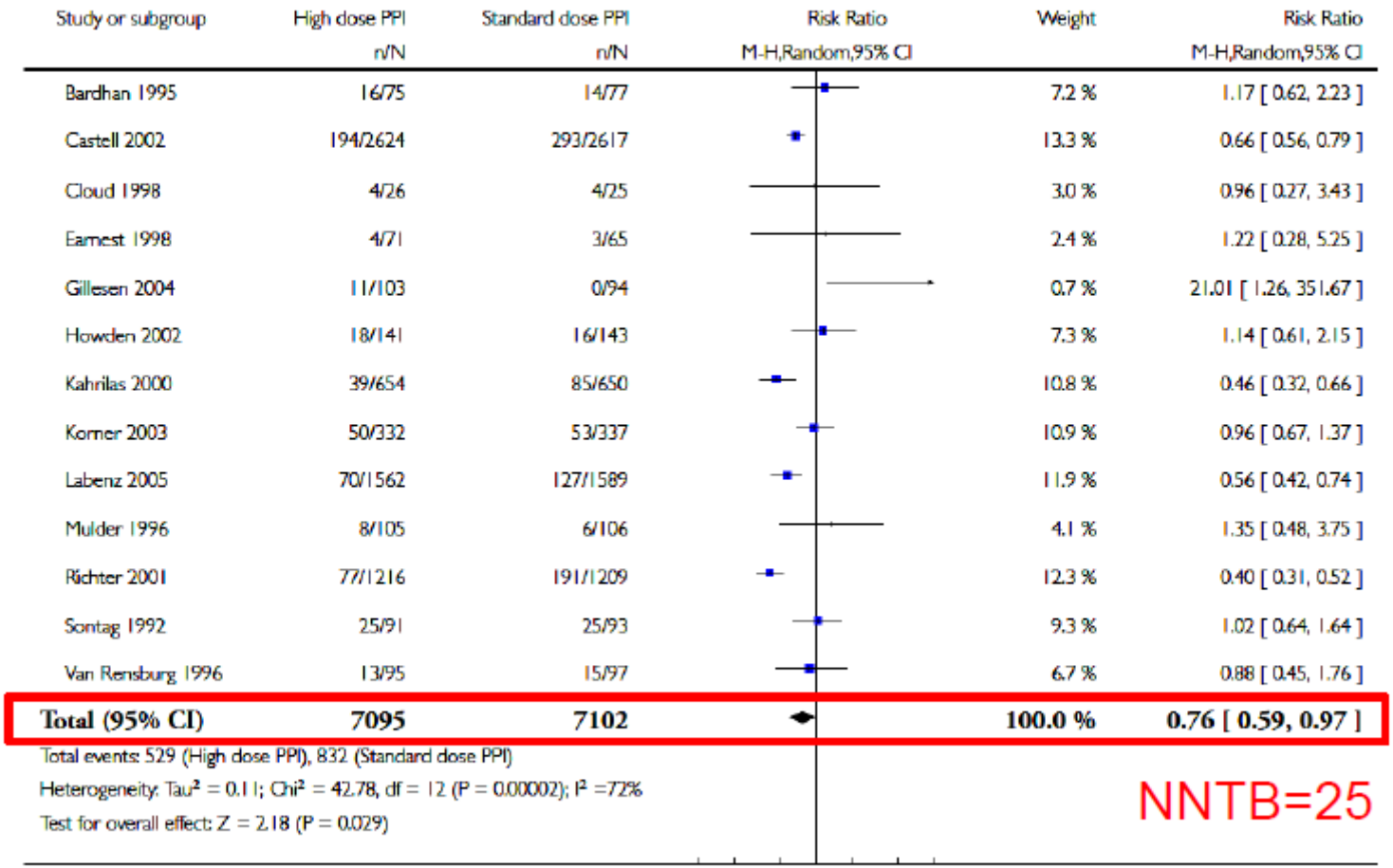

1977 cimetidine
800 mg
1981 ranitidine
300 mg
1989 omeprazole
20 mg
2001 esomeprazole
40 mg

Eficacia de los inhibidores de la secreción acida en dosis estándar

	PPI	H_2RA	Placebo
Healing of esophagitis	90%	52%	8%
Complete resolution of heartburn	40%	36%	15%

Aumentar las dosis mejora los resultados?

High dose PPI versus standard dose PPI
Effect on healing of esophagitis



Study or subgroup	High dose PPI n/N	Standard dose PPI n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Bardhan 1995	16/75	14/77		7.2 %	1.17 [0.62, 2.23]
Castell 2002	194/2624	293/2617		13.3 %	0.66 [0.56, 0.79]
Cloud 1998	4/26	4/25		3.0 %	0.96 [0.27, 3.43]
Earnest 1998	4/71	3/65		2.4 %	1.22 [0.28, 5.25]
Gillessen 2004	11/103	0/94		0.7 %	21.01 [1.26, 351.67]
Howden 2002	18/141	16/143		7.3 %	1.14 [0.61, 2.15]
Kahrilas 2000	39/654	85/650		10.8 %	0.46 [0.32, 0.66]
Korner 2003	50/332	53/337		10.9 %	0.96 [0.67, 1.37]
Labenz 2005	70/1562	127/1589		11.9 %	0.56 [0.42, 0.74]
Mulder 1996	8/105	6/106		4.1 %	1.35 [0.48, 3.75]
Richter 2001	77/1216	191/1209		12.3 %	0.40 [0.31, 0.52]
Sontag 1992	25/91	25/93		9.3 %	1.02 [0.64, 1.64]
Van Rensburg 1996	13/95	15/97		6.7 %	0.88 [0.45, 1.76]
Total (95% CI)	**7095**	**7102**		**100.0 %**	**0.76 [0.59, 0.97]**

Total events: 529 (High dose PPI), 832 (Standard dose PPI)

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 42.78$, df = 12 (P = 0.00002); $I^2 = 72\%$

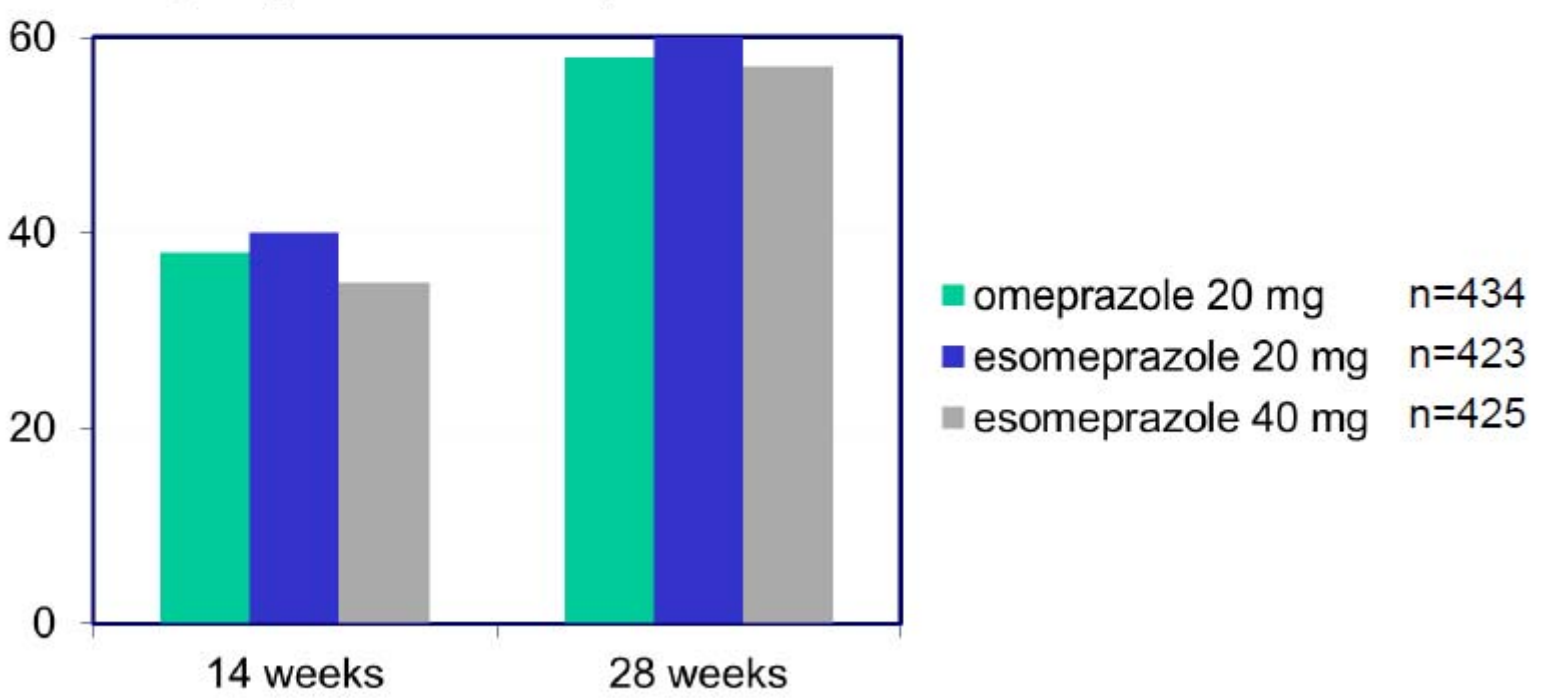
Test for overall effect: Z = 2.18 (P = 0.029)

NNTB=25

Moayyedi P et al. Cochrane Database Syst Rev 2010; CD003244

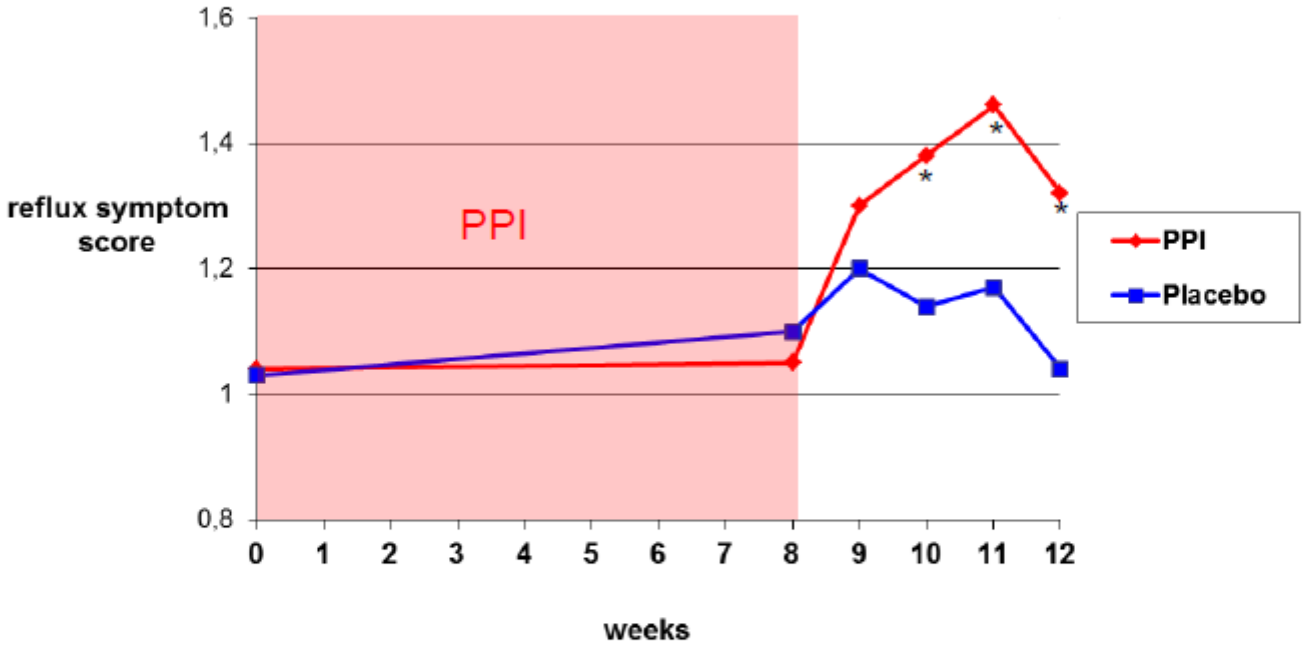
Mas no siempre es mejor
Efecto de los IBP en pacientes con ERG no erosiva

% de pacientes con resolución completa de la pirosis



Armstrong D *et al.* APT 2004;20:413-421

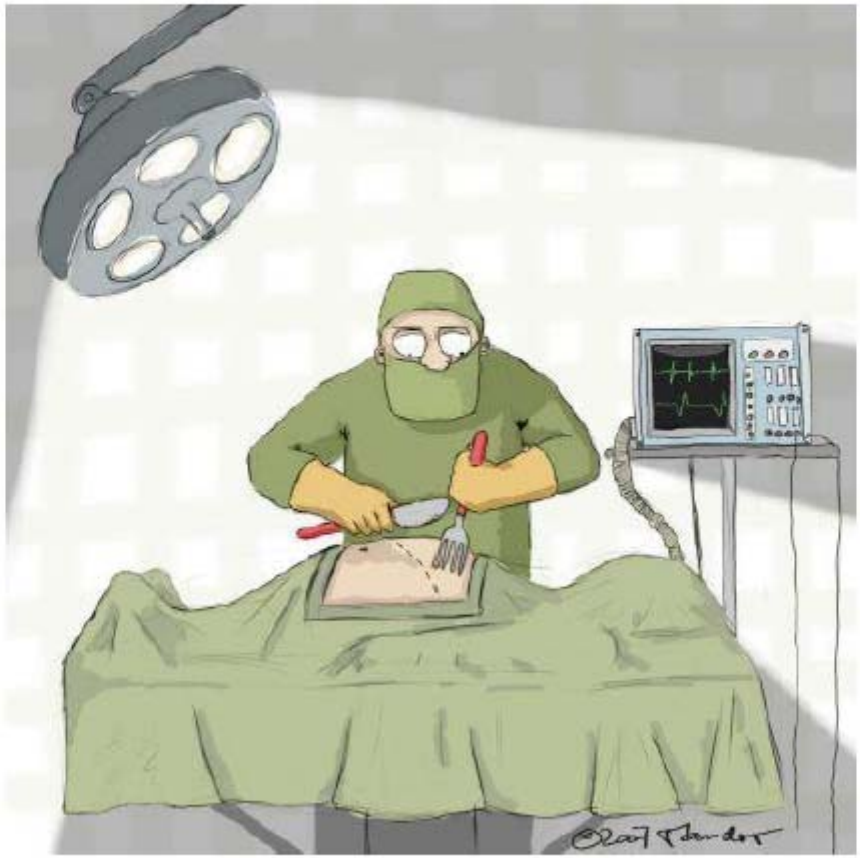
PPI induces reflux symptoms in healthy volunteers



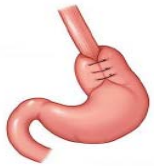
34% of those randomized to PPI reported relevant heartburn or regurgitation in weeks 9-12

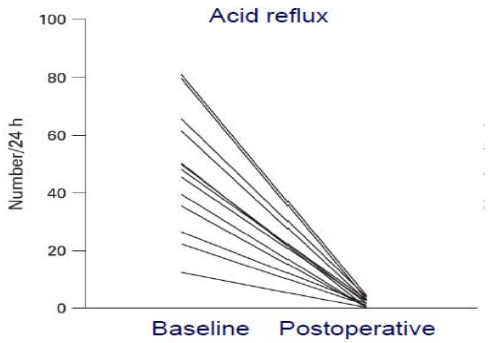
Reimer C *et al*. Gastroenterology 2009;137:80-87

Surgery



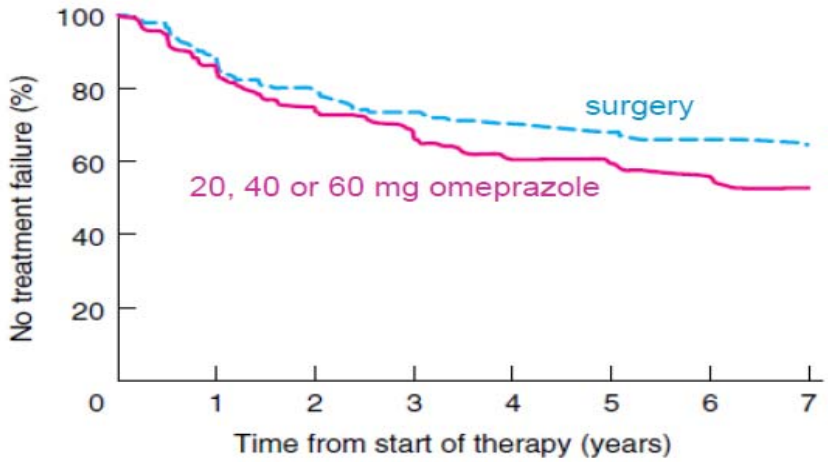
Effect of Nissen fundoplication on reflux events
24-hour esophageal pH-impedance monitoring





Bredenoord AJ *et al*. Gut 2008;57:161-166

Seven-year follow-up of a randomized clinical trial comparing PPI with surgical therapy for reflux esophagitis

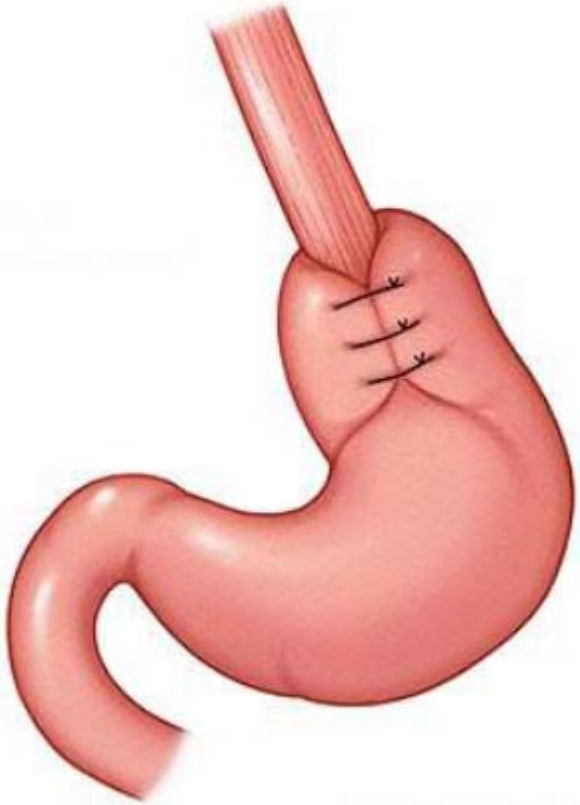


No. at risk					
Omeprazole	154	127	93	80	59
Surgery	144	122	98	81	60

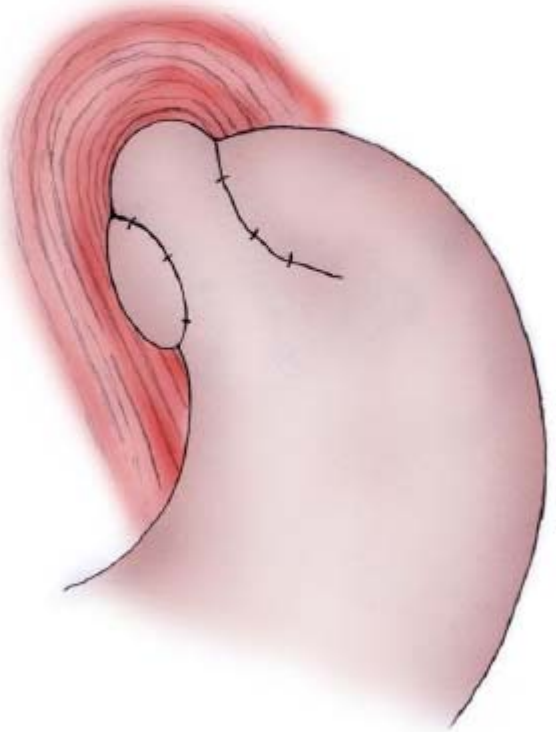
Lundell L *et al*. Br J Surg 2007;94:198-203

Nissen versus Toupet

Nissen
360 º posterior



Toupet
270 º posterior



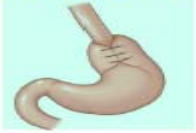
Meta-analysis of 7 RCTs comparing Nissen (n=404) and Toupet (n=388)

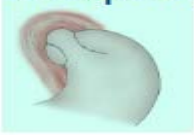
Undesired effects occur less frequently after Toupet

	RR	CI	P
Dysphagia	1.61	1.06 – 2.44	0.02
Dilatation for dysphagia	2.45	1.06 – 5.68	0.04
Surgical reintervention	2.19	1.09 – 4.40	0.03
Inability to belch	2.04	1.19 – 3.49	0.009
Gas bloating	1.58	1.21 – 2.05	0.001

Broeders JAJL *et al.* Brit J Surg 2010;97:1318-1330

Meta-analysis of 7 RCTs comparing Nissen (n=404) and Toupet (n=388)





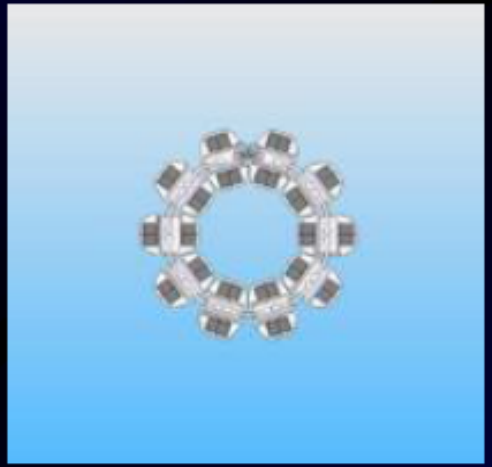
Efficacy of Toupet is similar to that of Nissen

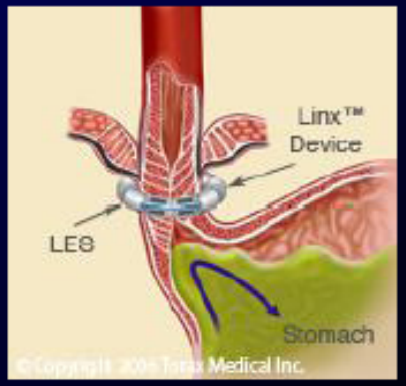
	RR	CI	P
Esophageal acid exposure	1.26	1.06 – 2.44	0.29
Esophagitis	1.20	0.78 – 1.85	0.40
Reflux symptoms	1.11	0.75 – 1.63	0.61
Patient satisfaction	1.01	0.95 – 1.06	0.77

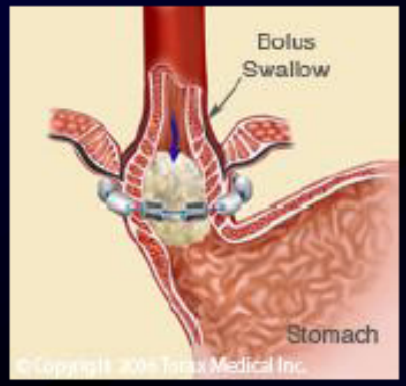
Broeders JAJL *et al.* Brit J Surg 2010;97:1318-1330

Magnetic bracelet sphincter augmentation

Linx ™ (Torax)







	pre-op n=44	1 yr post-op n=39	2 yr post-op n=20
time with pH < 4	11.9 %	3.1 %	2.4 %

"Early dysphagia occurred in 43% of the patients and self-resolved by 90 days. One device was laparoscopically explanted for persistent dysphagia."

Bonavina L *et al.* Ann Surg 2010;252:857–862

Endoscopic treatment of GERD

radio-frequency ablation

injection / implantation

suturing techniques

Stretta

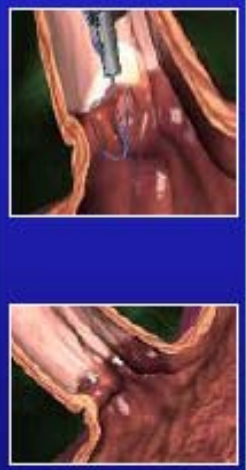
Enteryx

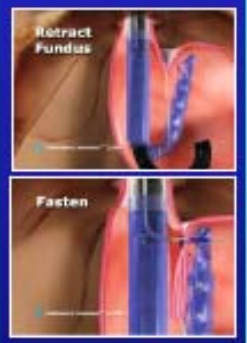
Gatekeeper

EndoCinch

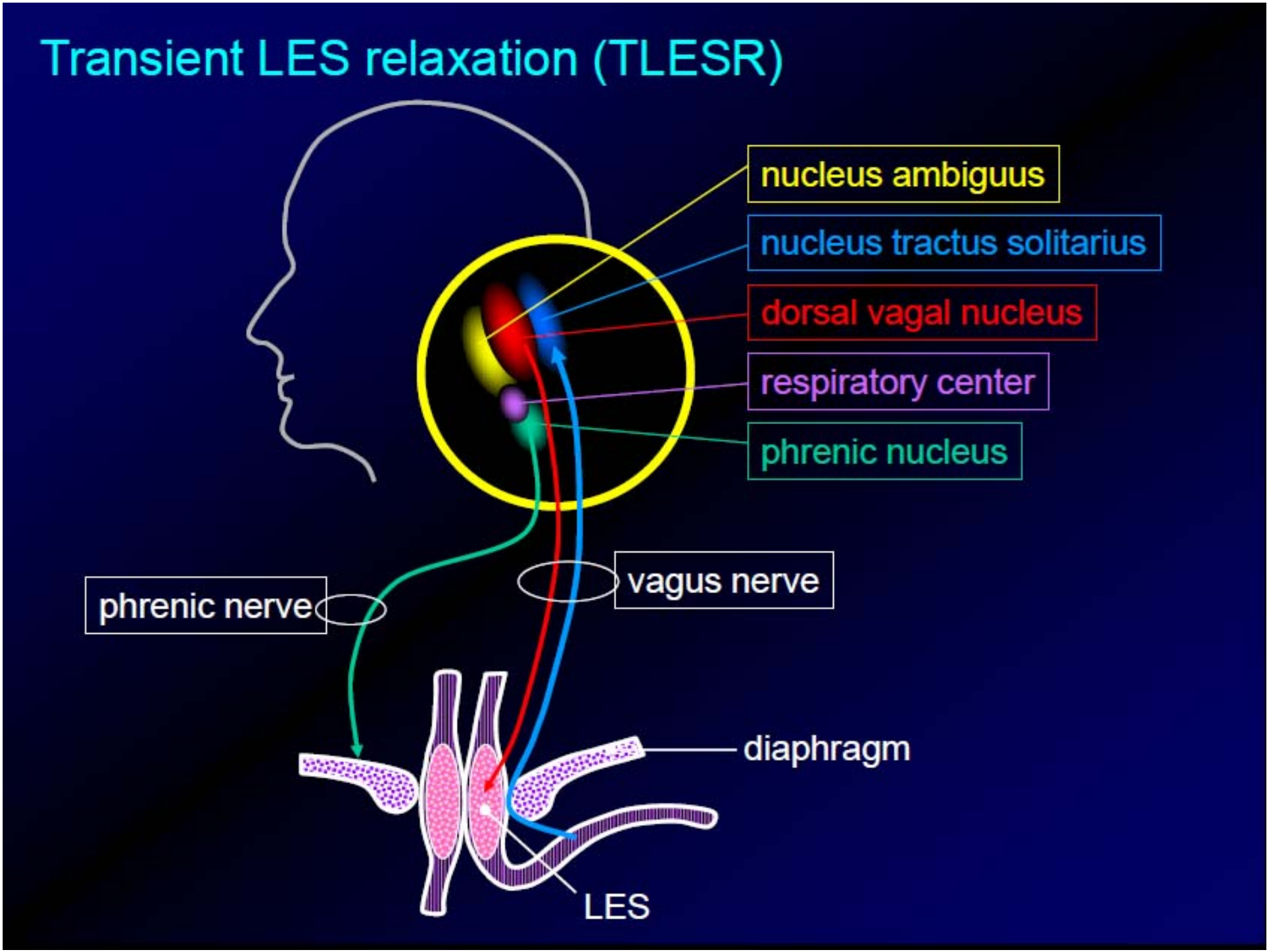
Plicator

EsophyX





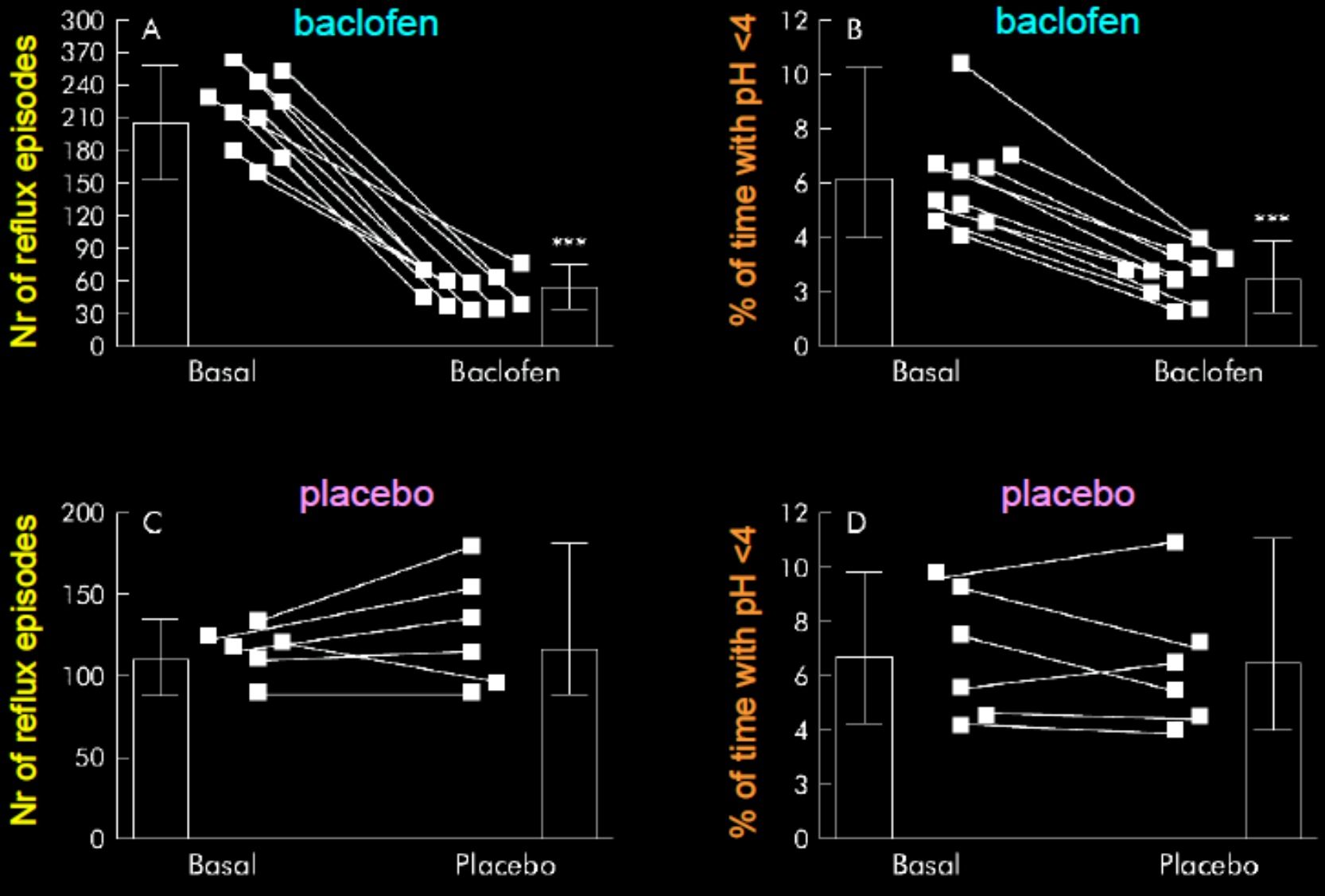
Transient LES relaxation (TLESR)



Pharmacological agents that reduce TLESR incidence

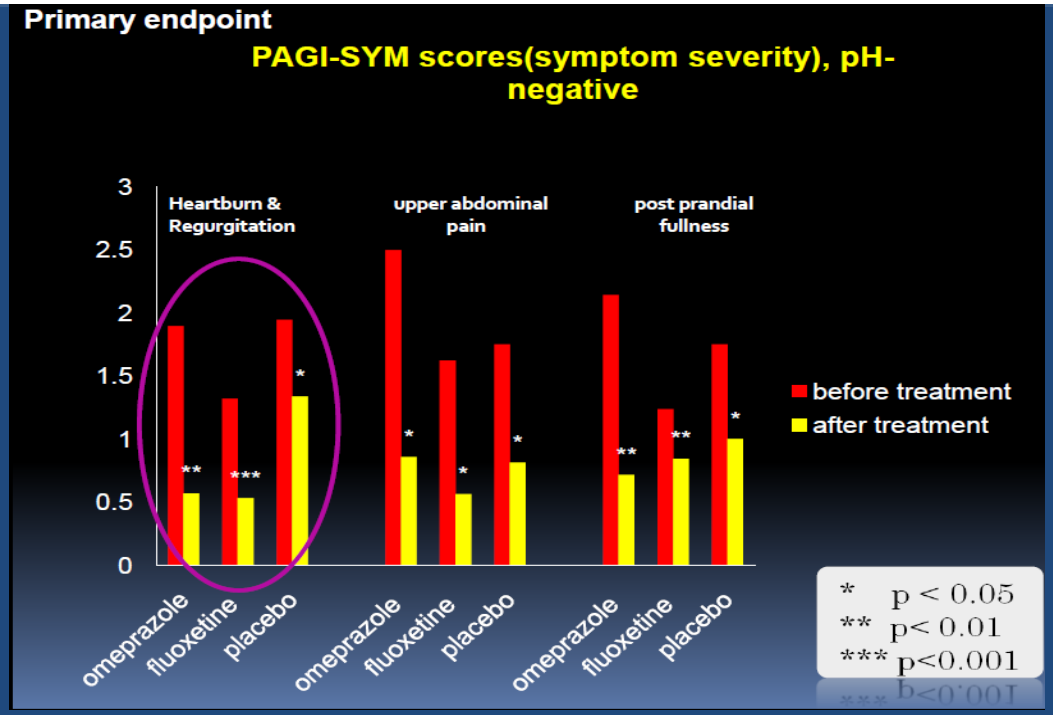
- nitric oxide synthase inhibitors
  L-NAME, L-NMMA
- CCK1 receptor antagonists
  loxiglumide, devazepide
- muscarinic receptor antagonists
  atropine
- μ opioid receptor agonists
  morphine
- CB1 receptor agonists
  WIN55, 212-2, D-9-tetrahydrocannabinol
- GABA-B receptor agonists
  baclofen, lesogaberan (AZD3355), arbaclofen placarbil
- mGluR5 receptor antagonists
  MTEP, MPEP, ADX10059, AZD2066

Long-term effect of baclofen (40 mg daily for 4 weeks) on acid reflux in patients with GORD



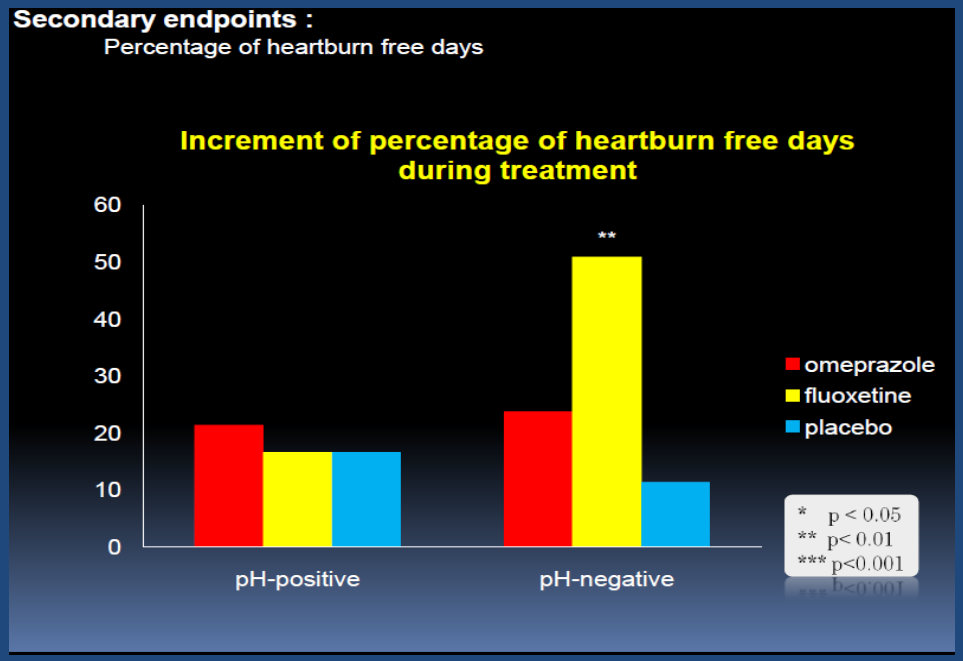
Ciccaglione AF and Marzio L Gut 2003;52:464-470

Primary endpoint



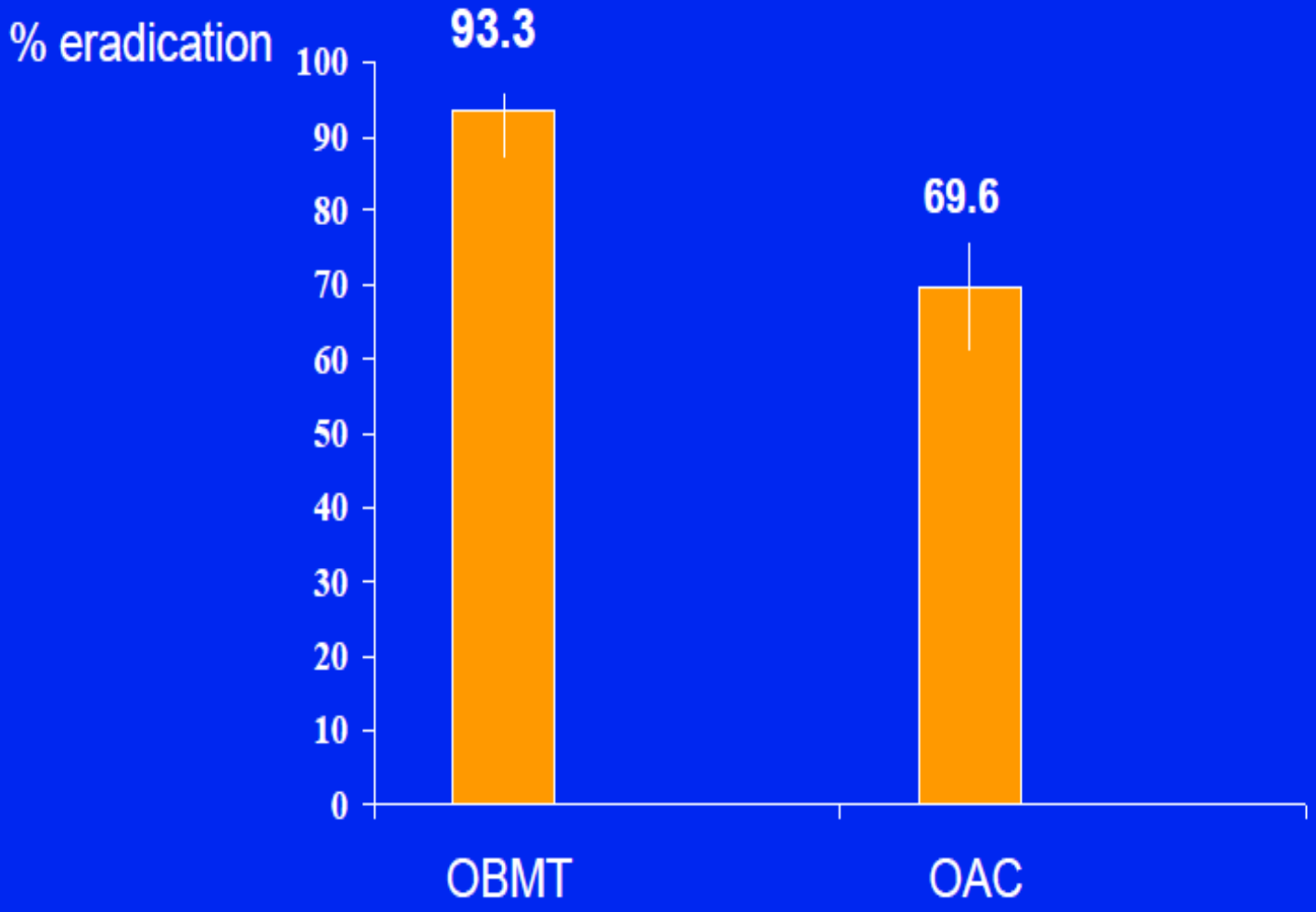
Secondary endpoints :

Percentage of heartburn free days

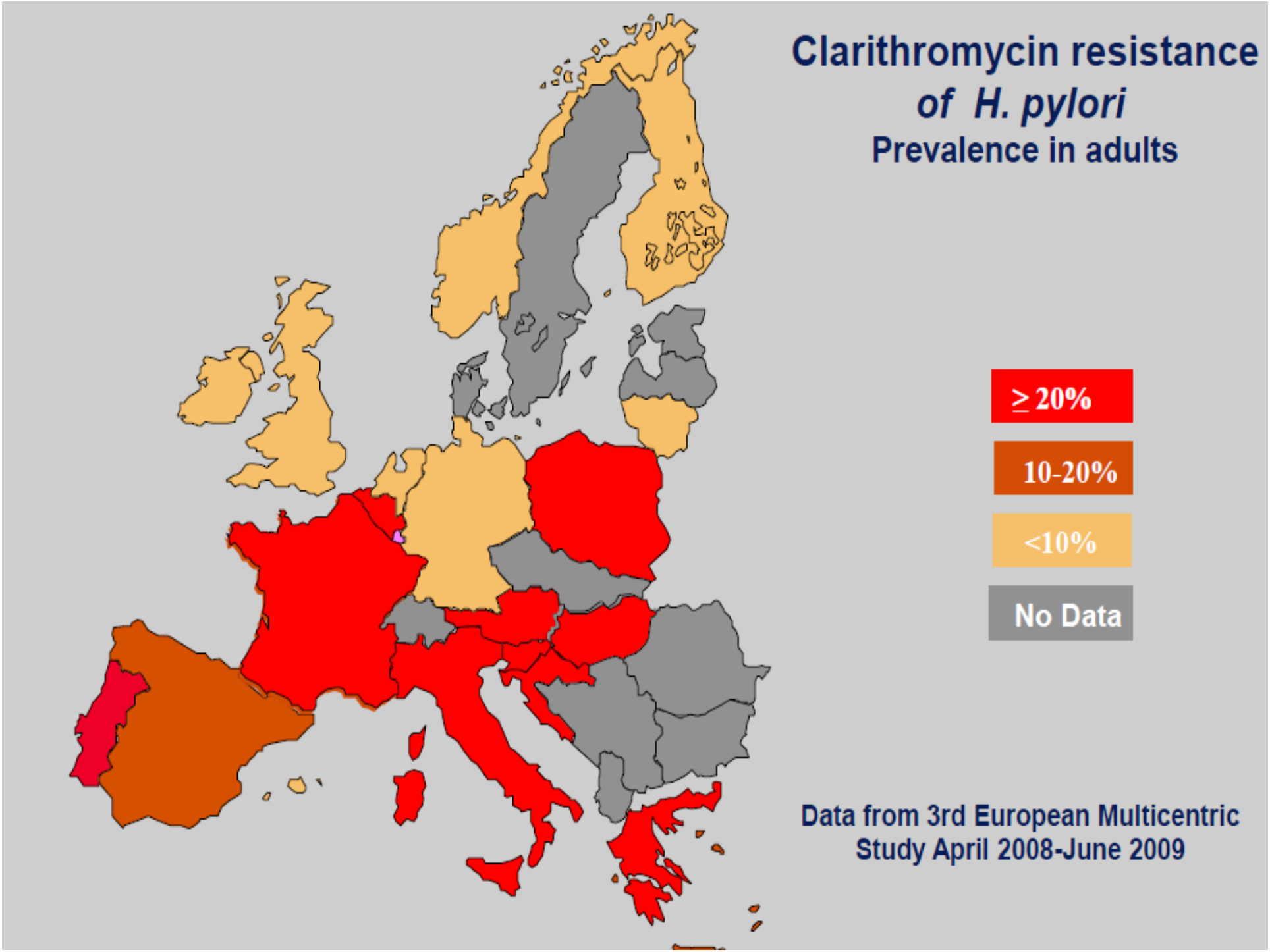


Helicobacter Pylori

Bismuth-based quadruple therapy
Results of the Pylera study (PP)



Malfertheiner et al., Lancet, 2011


Clarithromycin resistance
of H. pylori
Prevalence in adults
≥ 20%
10-20%
<10%
No Data
Data from 3rd European Multicentric
Study April 2008-June 2009

Sequential therapy

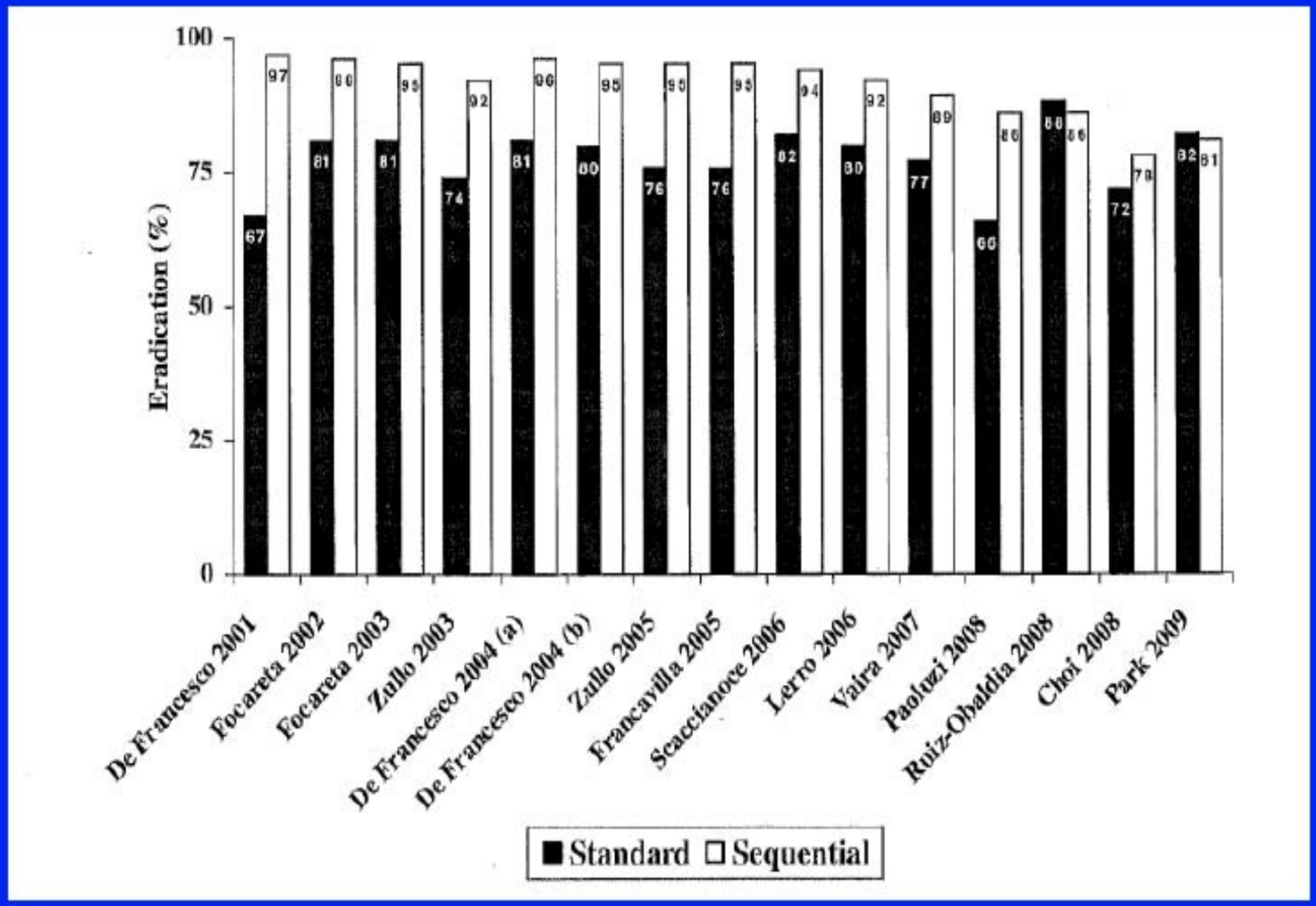
Regimen:

5 days Amoxicillin 1g + PPI bd

followed by 5 days of clarithromycin 500 mg + metronidazole 500 mg + PPI bd

Zullo et al. Aliment Pharmacol Ther 2000;14:715-8

Comparison of sequential therapy to standard triple therapy



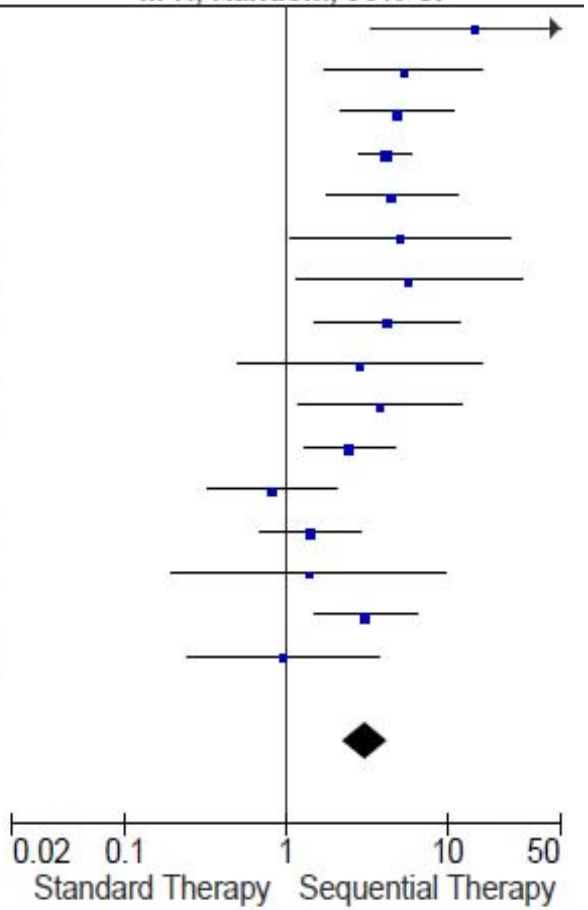
Gisbert et al., J Clin Gastroenterol 2010;44:313-25

Meta-analysis comparing *H. pylori* eradication efficacy (intention-to-treat) with sequential regimen *versus* standard triple therapy

Study or Subgroup	Sequential Events	Sequential Total	Standard Events	Standard Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
De Francesco 2001	61	63	43	64	3.7%	14.90 [3.32, 66.89]	2001
Focaretta 2002	90	94	75	93	5.5%	5.40 [1.75, 16.65]	2002
Focaretta 2003	166	174	149	184	8.2%	4.87 [2.19, 10.84]	2003
Zullo 2003	481	522	389	527	13.3%	4.16 [2.87, 6.05]	2003
De Francesco (b) 2004	110	116	93	116	6.9%	4.53 [1.77, 11.61]	2004
De Francesco (a) 2004	43	45	42	52	3.4%	5.12 [1.06, 24.77]	2004
Francavilla 2005	36	38	28	37	3.3%	5.79 [1.16, 28.94]	2005
Zullo 2005	84	89	72	90	6.1%	4.20 [1.49, 11.88]	2005
Lerro 2006	23	25	20	25	2.9%	2.88 [0.50, 16.48]	2006
Scaccianoce 2006	68	72	58	71	5.2%	3.81 [1.18, 12.33]	2006
Vaira 2007	134	150	116	150	9.9%	2.45 [1.29, 4.67]	2007
Ruiz-Obaldia 2008	65	76	72	82	7.1%	0.82 [0.33, 2.06]	2008
Choi 2008	60	77	58	81	9.0%	1.40 [0.68, 2.89]	2008
Kalach 2008	11	13	12	15	2.4%	1.38 [0.19, 9.83]	2008
Paoluzi 2008	77	90	59	90	8.9%	3.11 [1.50, 6.46]	2008
Park 2009	21	26	22	27	4.2%	0.95 [0.24, 3.78]	2009
Total (95% CI)		**1670**		**1704**	**100.0%**	**3.10 [2.23, 4.29]**	
Total events	1530		1308				

Heterogeneity: Tau² = 0.17; Chi² = 27.45, df = 15 (P = 0.03); I² = 45%

Test for overall effect: Z = 6.77 (P < 0.00001)



Gisbert et al., J Clin Gastroenterol 2010;44:313-25

Tratamiento del la infección por H. pylori

-La terapia secuencial es, con la terapia cuádruple basado con bismuto, el tratamiento de elección para la erradicación del la infección por H. pylori en el 2011.

-En áreas de baja resistencia a la claritromicina (<10%), es posible continuar con el uso de la terapia triple estándar.

-En áreas de alta resistencia a la claritromicina (>20%), es mandatorio no utilizar la terapia triple estándar o utilizar test de susceptibilidad previo al tratamiento.

Chemoprevention in Barrett's esophagus with NSAIDs and statins

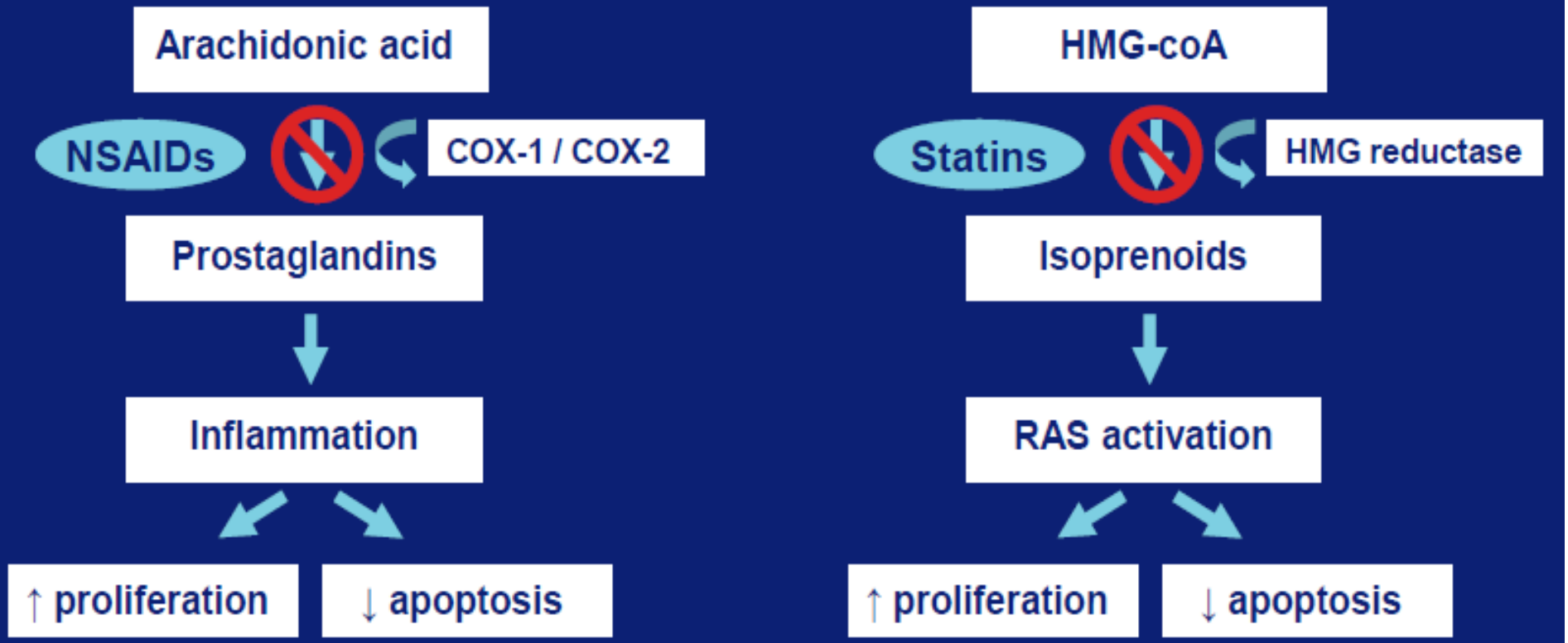
Results of a Large Multicenter Prospective Cohort Study

F. Kastelein[1], M.C.W. Spaander[1], K. Biermann[2], E.W. Steyerberg[3], H. Geldof[5], P.C.J. ter Borg[6], W. Lesterhuis[7], E.C. Klinkenberg[8], F. ter Borg[9], J.J. Kolkman[10], B. den Hartog[11], A.J.P. van Tilburg[12], T.G. Tan[13], F.T.M. Peters[14], B.E. Schenk[15], L.G.J.B. Engels[16], E.J. Kuipers[1,4] and M.J. Bruno[1]

Department of Gastroenterology & Hepatology[1], Pathology[2], Public health[3] and Internal medicine[4], Erasmus MC, Rotterdam; Department of Gastroenterology & Hepatology, IJsselland[5], Capelle a/d IJssel; Ikazia[6], Rotterdam, Albert Schweitzer[7], Dordrecht; VUMC[8], Amsterdam; Deventer Hospital[9], Deventer; MST[10], Enschede; Rijnstate[11], Arnhem; St. Franciscus Gasthuis[12], Rotterdam; ZGT[13], Hengelo; UMCG[14], Groningen; Isala Clinics[15] Zwolle; Orbis MC[16], Sittard, the Netherlands

Chemoprevention

Chemoprevention with NSAIDs and statins is effective in the prevention of cancer

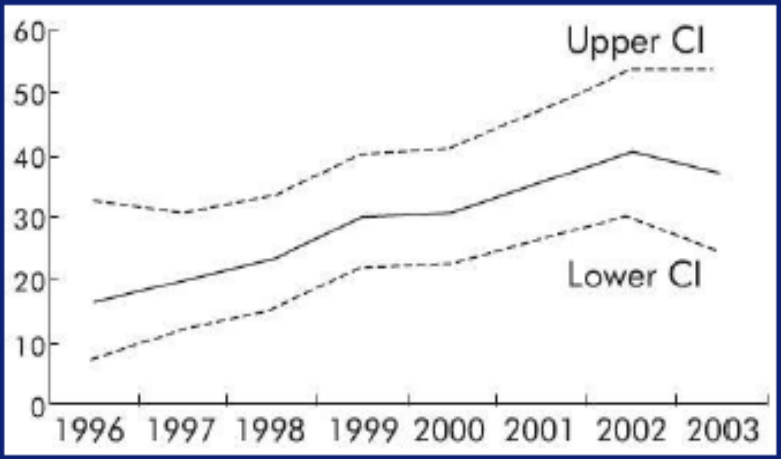


Barrett's esophagus

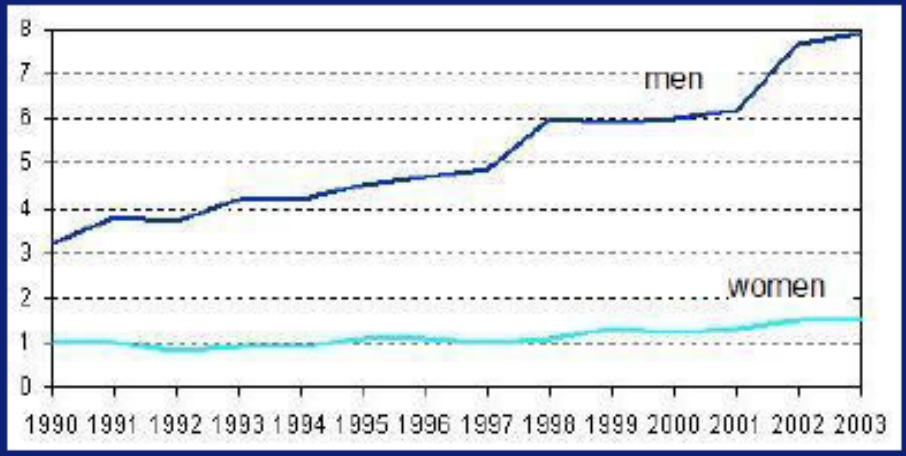
Barrett's esophagus (BE):

- Is a premalignant condition
- Increased risk of esophageal adenocarcinoma (EAC)
- Incidence of 0.5% per year

The incidence of BE and EAC has risen in the Netherlands:

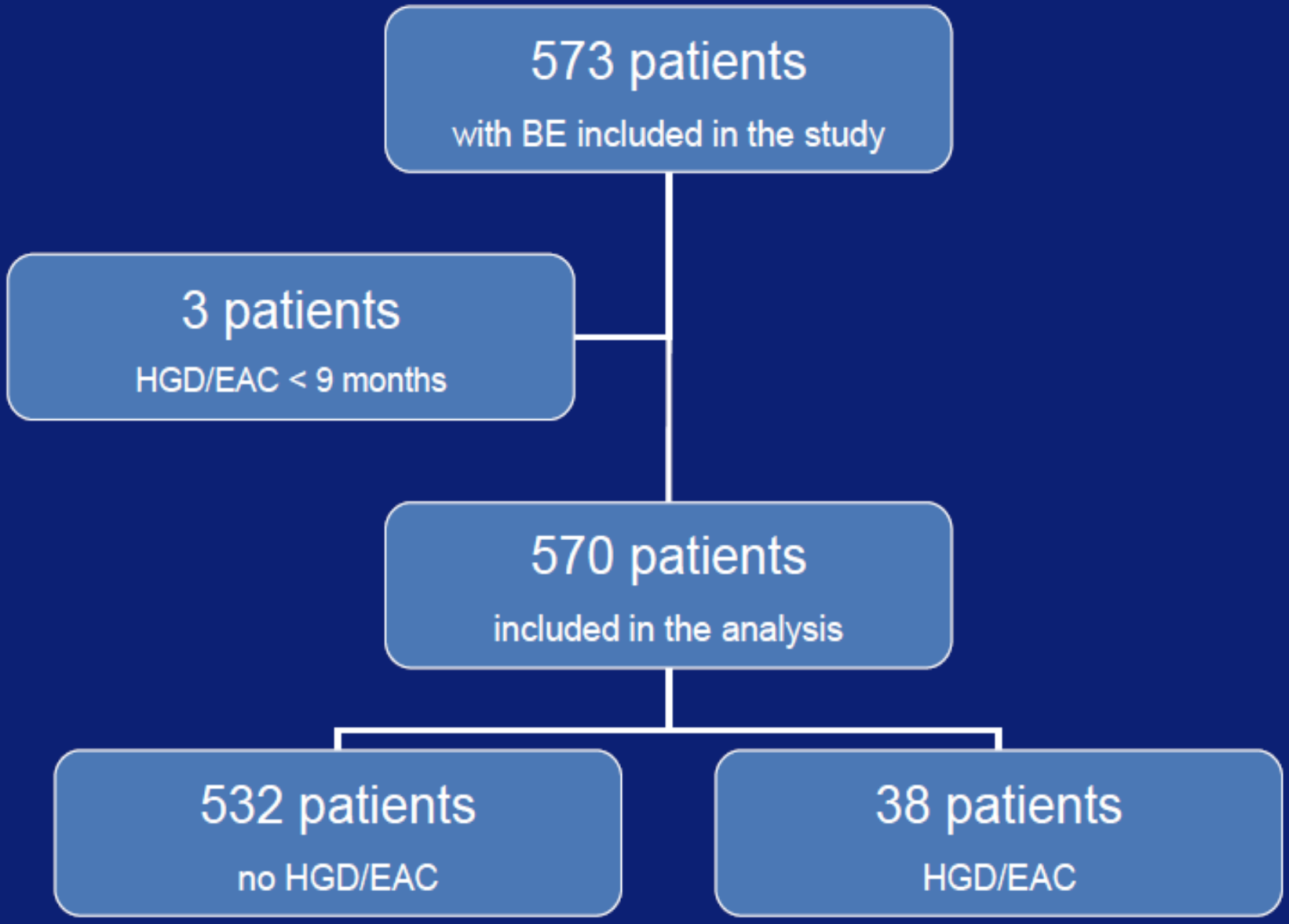


Incidence BE per 100.000 endoscopies
van Soest. Gut, 2005. **54**: 1062-1066

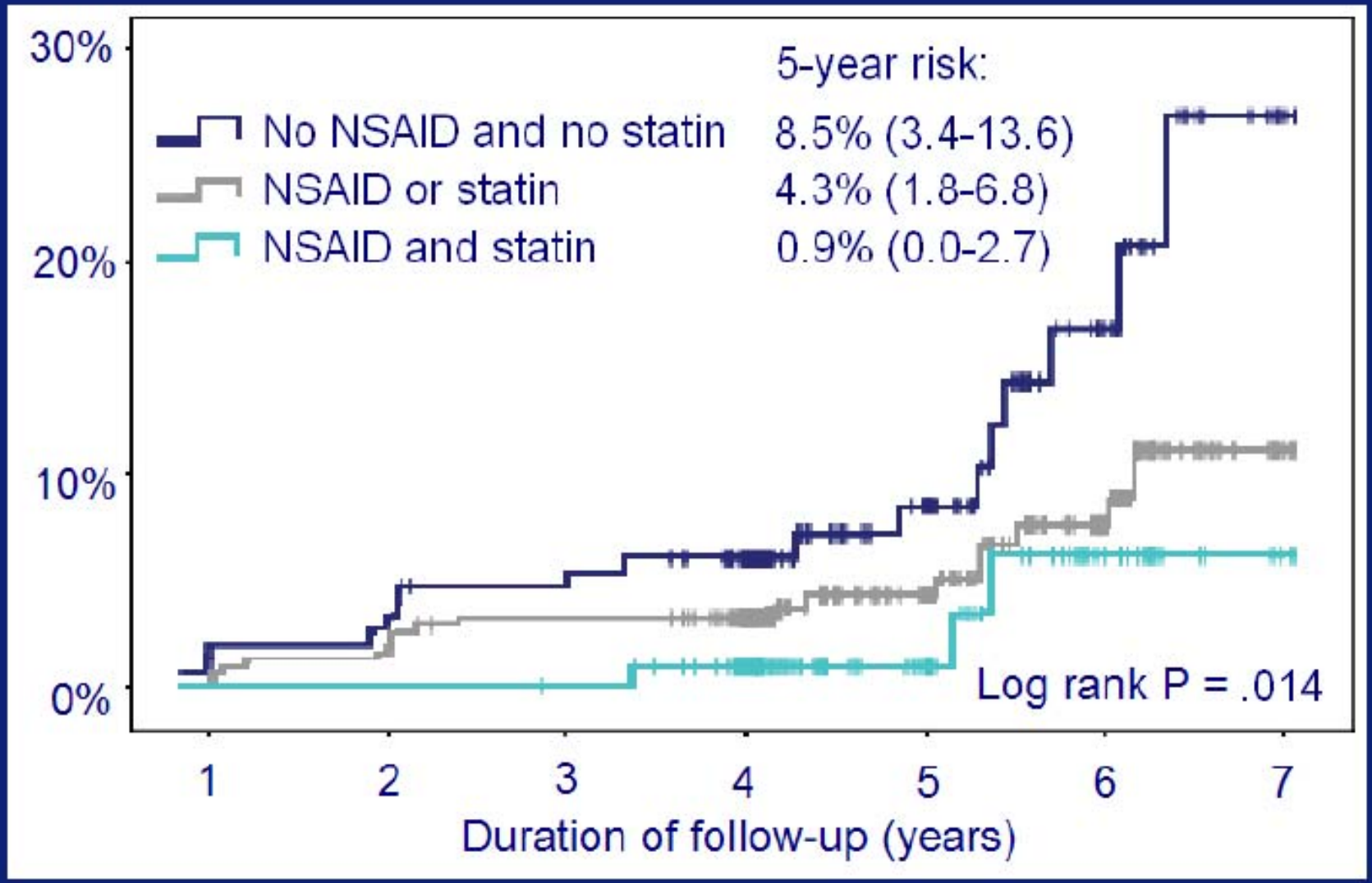


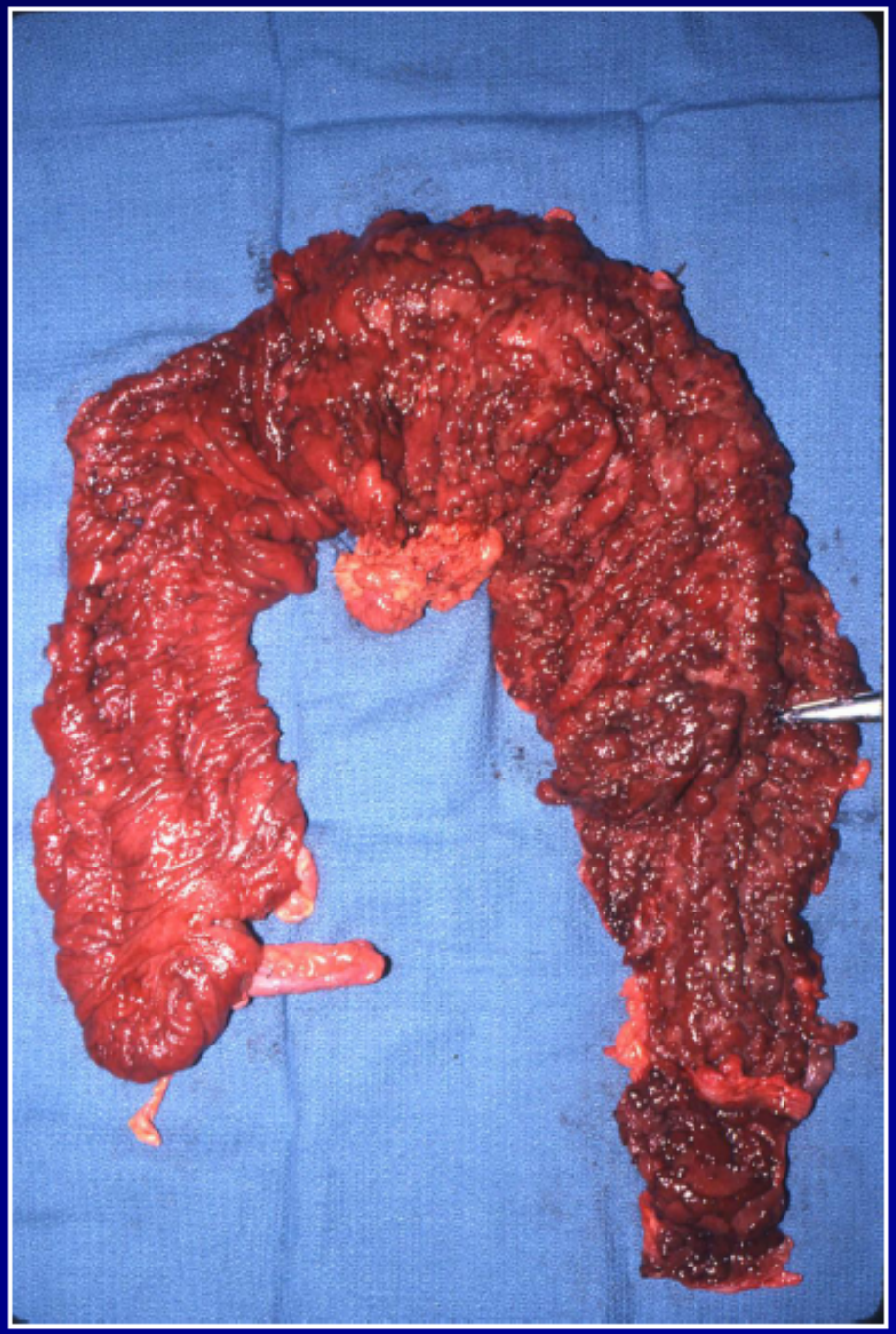
Incidence EAC per 100.000 persons
Dutch Cancer Registration

Flowchart


573 patients
with BE included in the study
3 patients
HGD/EAC < 9 months
570 patients
included in the analysis
532 patients
no HGD/EAC
38 patients
HGD/EAC

Kaplan Meier showing the cumulative incidence of HGD/EAC stratified by NSAID and statin use





Revisión sistemática del uso de corticoides IV en Colitis Ulcerosa Grave

-Entre 1974-2004, un total de 34 estudios controlados de uso corticoides iv en colitis ulcerosa grave.

-581 de 1991 pacientes (27%) han requerido colectomía por corticorefractariedad

-22 fallecimientos (1%)

-No beneficio el > dosis de 60mg metilprednisolona IV

-No ha habido mejoría de evitar colectomía en los últimos 30 años.

Turner D, et al. *Clin Gastroenterol Hepatol.* 2007; 5(1): 103-110.

Factores que predicen corticorefracteriedad en CU grave. ¿Cuanto tiempo se debe esperar?

-Considerar siguiente paso terapéutico al 3 día de corticoides

-Fracaso de los esteroides al 3 día:

fiebre persistente
diarreas persistente
sangrado en las heces
>de 6 deposiciones al día
PCR elevada

Plantearse tempranamente alternativa medica /quirúrgica

Lindgren, Eur J Gast Hep 1998; Bernal, Dig Dis Sci 2006

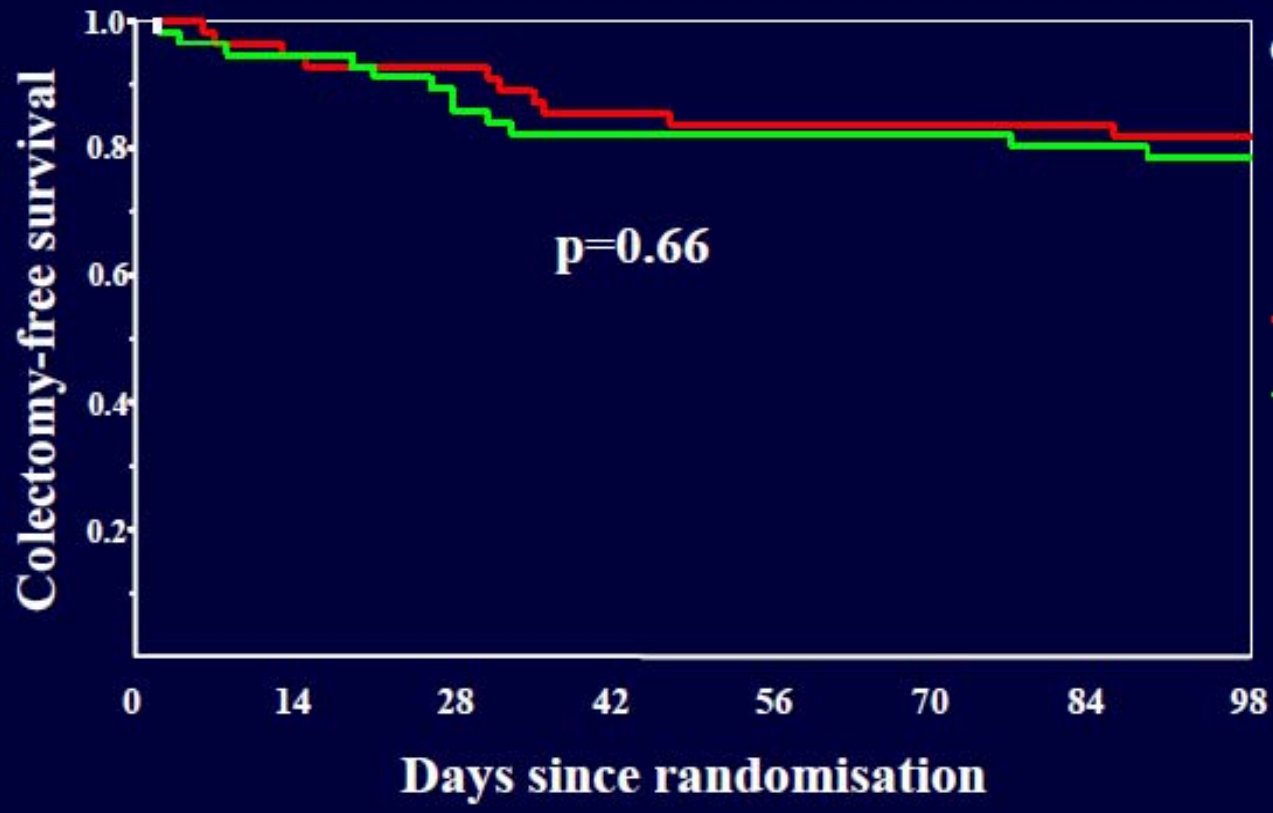
CsA vs IFX in IV Steroid-Refractory UC: The CYSIF Study

First randomized, controlled study comparing CsA to IFX in IV steroid-refractory severe acute UC

- n=111 (55 received CsA; 56 received IFX)
- Day 7 response rates:
  - CsA = 84%; IFX = 86% (*P*=0.76)
- Day 98, number of patients undergoing colectomy: CsA = 10, IFX = 13

Laharie D et al. DDW 2011; May 9, 2011;Chicago, IL. Abstract 619.

CYSIF: IFX vs. CSA Time to Colectomy



% of patients	56	53	50	46	46	46	45	41
at risk	55	52	50					

Laharie D et al. DDW 2011; May 9, 2011;Chicago, IL. Abstract 619.

Conclusión: CsA vs IFX para CU grave corticoresistente

Utilizar CsA si:

-Se requiere respuesta rápida en paciente hospitalizado

Utilizar IFX si:

-Paciente no requiere hospitalización

-Paciente no ha respondido previamente a inmuno-moduladores (6-MCP/AZA)

-Paciente presenta hipocolesterolemia

Vigilancia extrema si se utiliza CsA después de IFX y viceversa