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University Medical Center Rotterdam



Long-term PPI treatment; efficacy and side effects

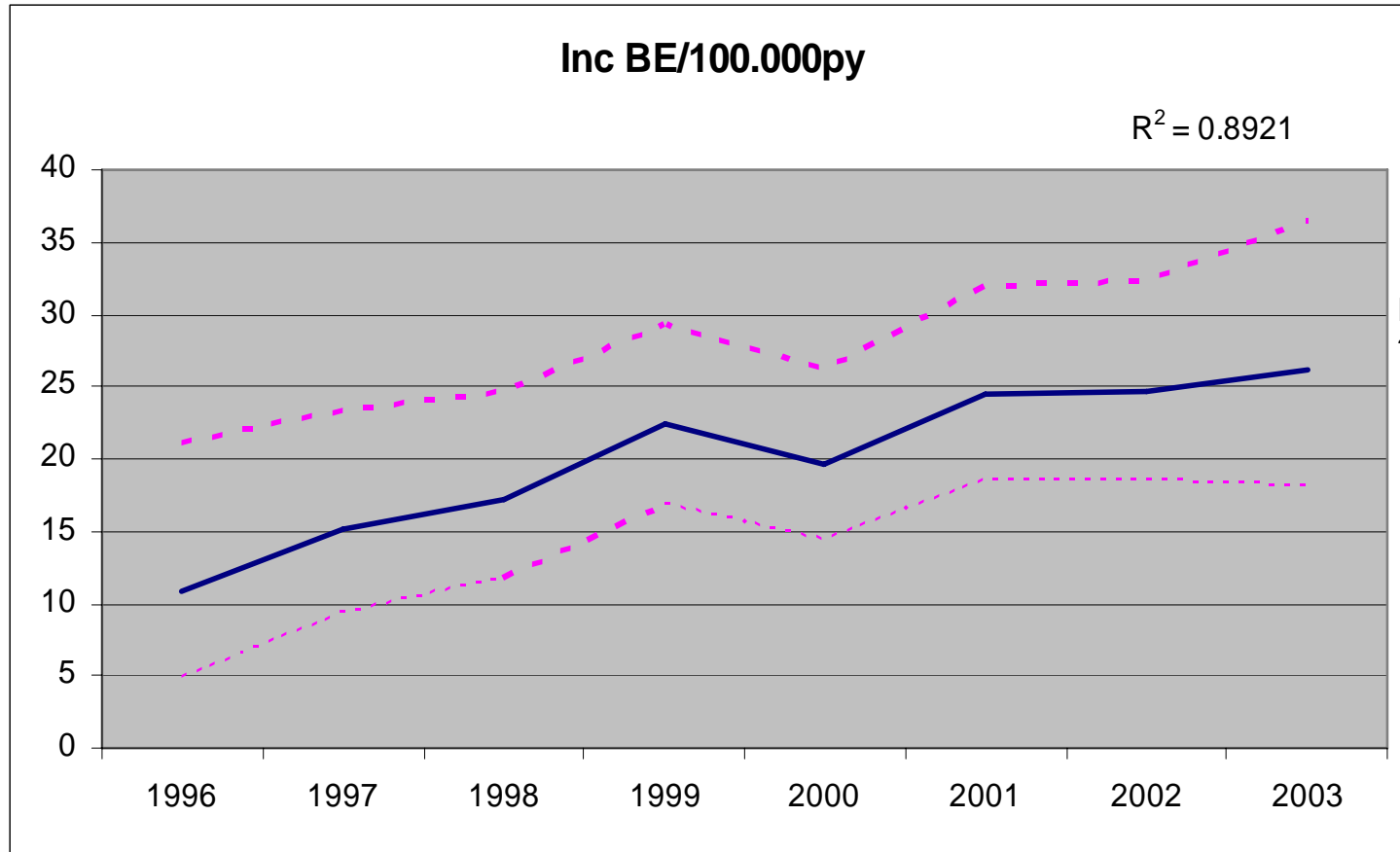
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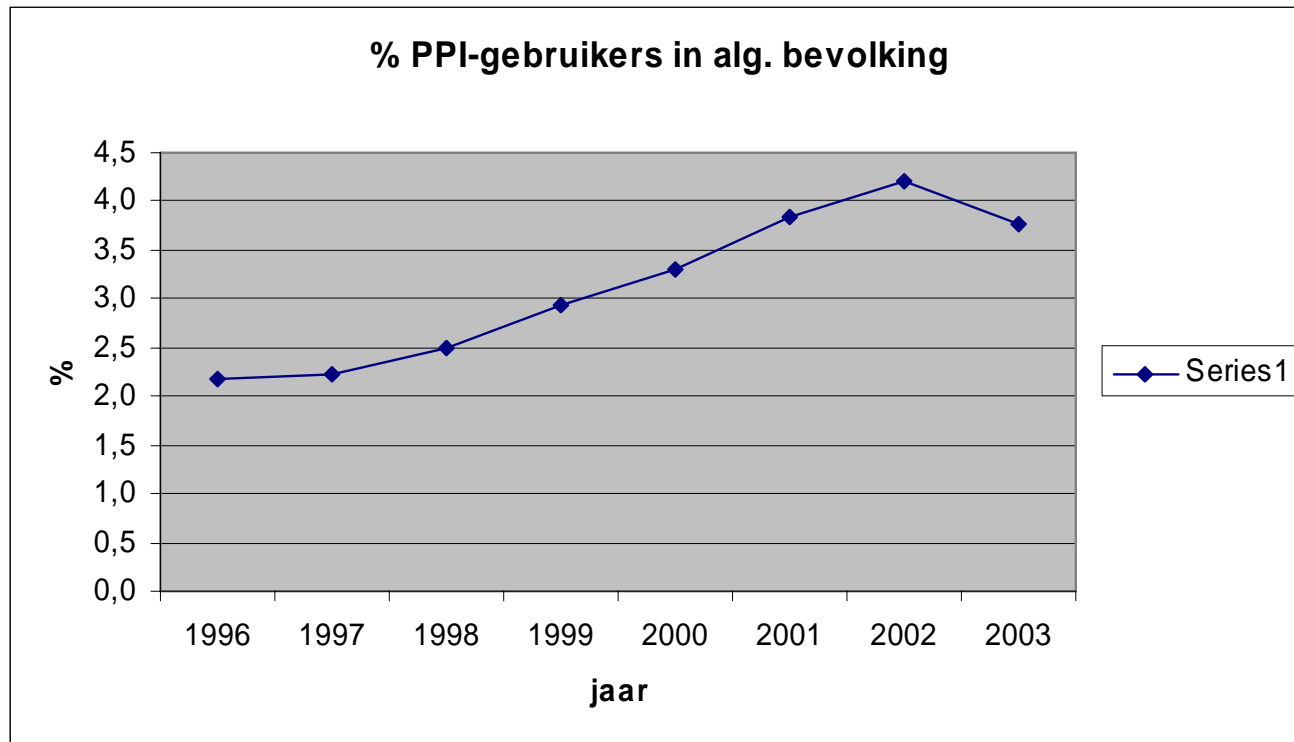
Rotterdam, the Netherlands

Incidence of Barrett's esophagus is increasing in the Netherlands



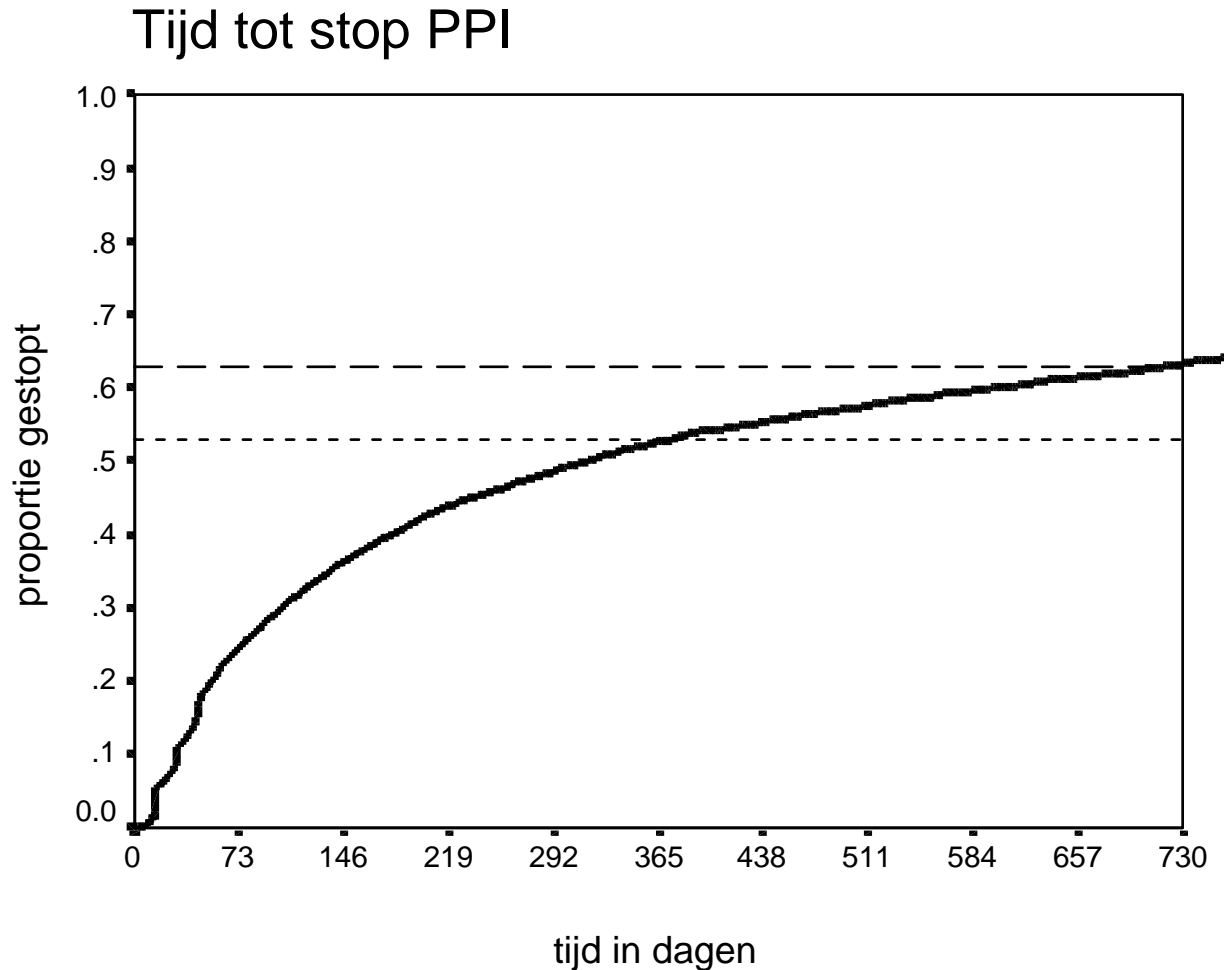
Based on Erasmus Primary Care Cohort, N = 500.000
van Soest et al. Gut 2005

Use of PPI's in a Dutch primary care population



*Based on Erasmus Primary Care Cohort, N = 500.000
van Soest et al. In preparation*

Duration of PPI use in a Dutch primary care population



Based on Erasmus Primary Care Cohort, N = 500.000
van Soest et al. In preparation

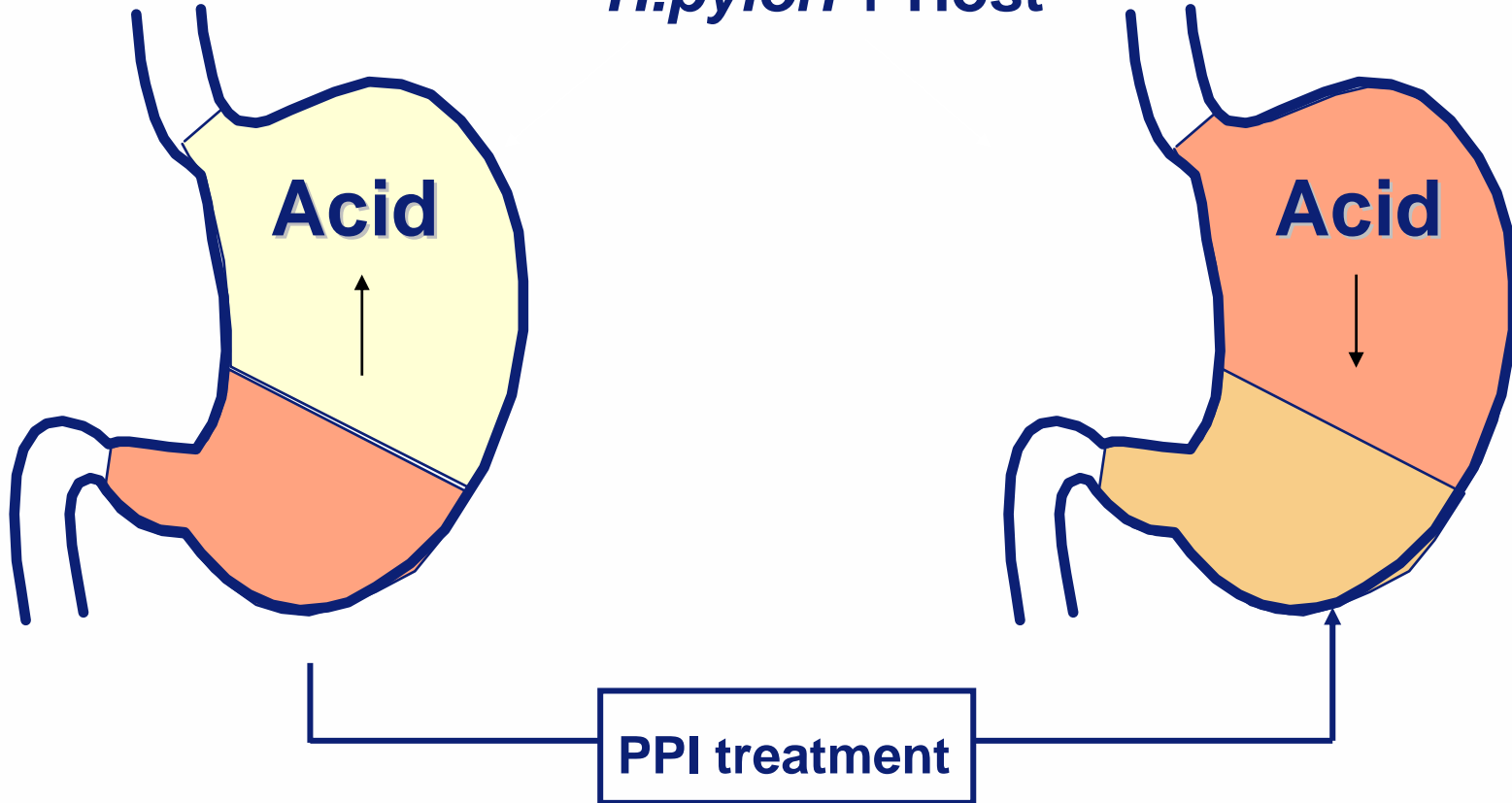
Efficacy and safety of long-term PPI treatment

Topics of discussion

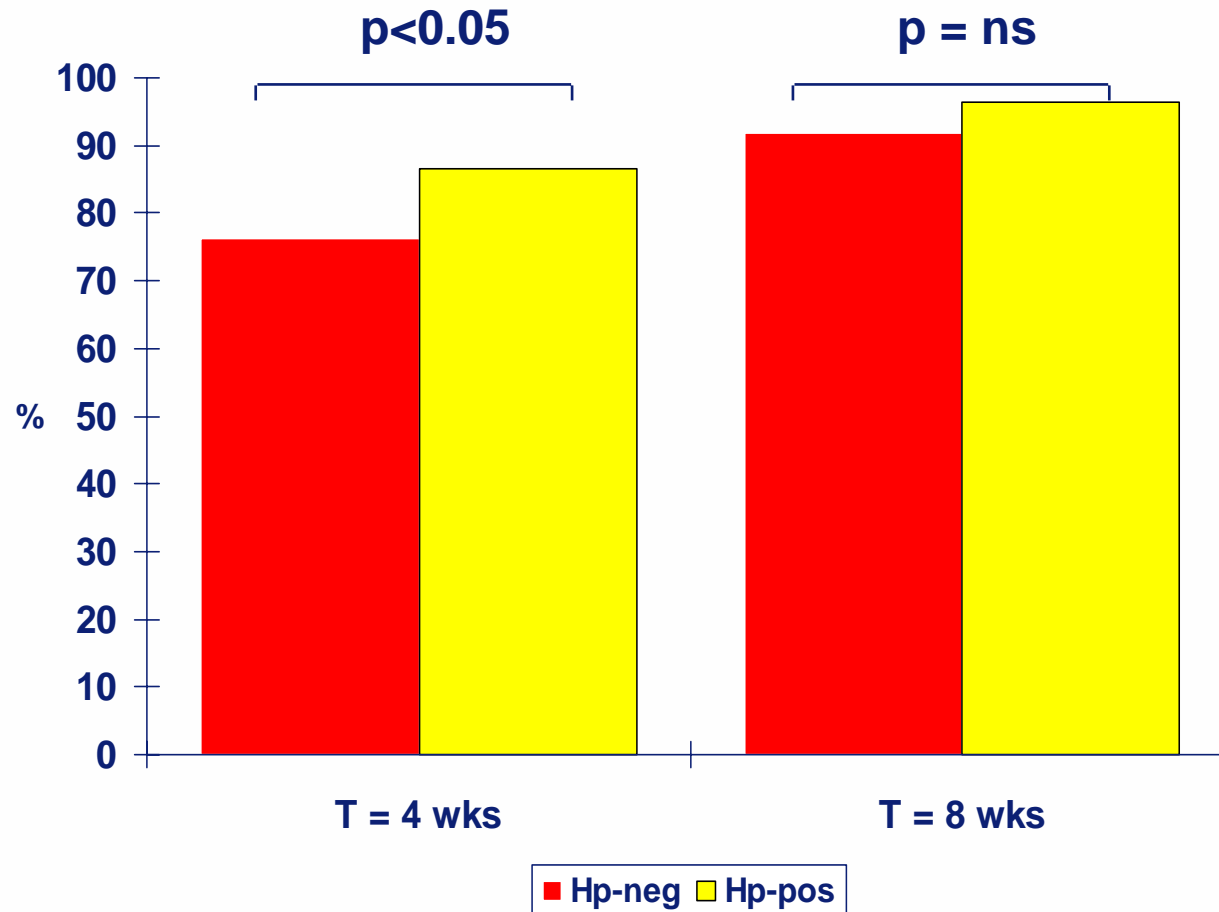
- **Pattern of *H. pylori* gastritis**
- **Development of atrophic gastritis**
- **Serum gastrin**
- **Serum vitamin B12**
- **Level of acid suppression**
- **Acid rebound**
- **Gastric polyp formation**

Acid secretion and *H.pylori* colonization interact

H.pylori + Host



Healing rates for *H. pylori*-negative and -positive patients with erosive esophagitis treated with 40 mg pantoprazole od



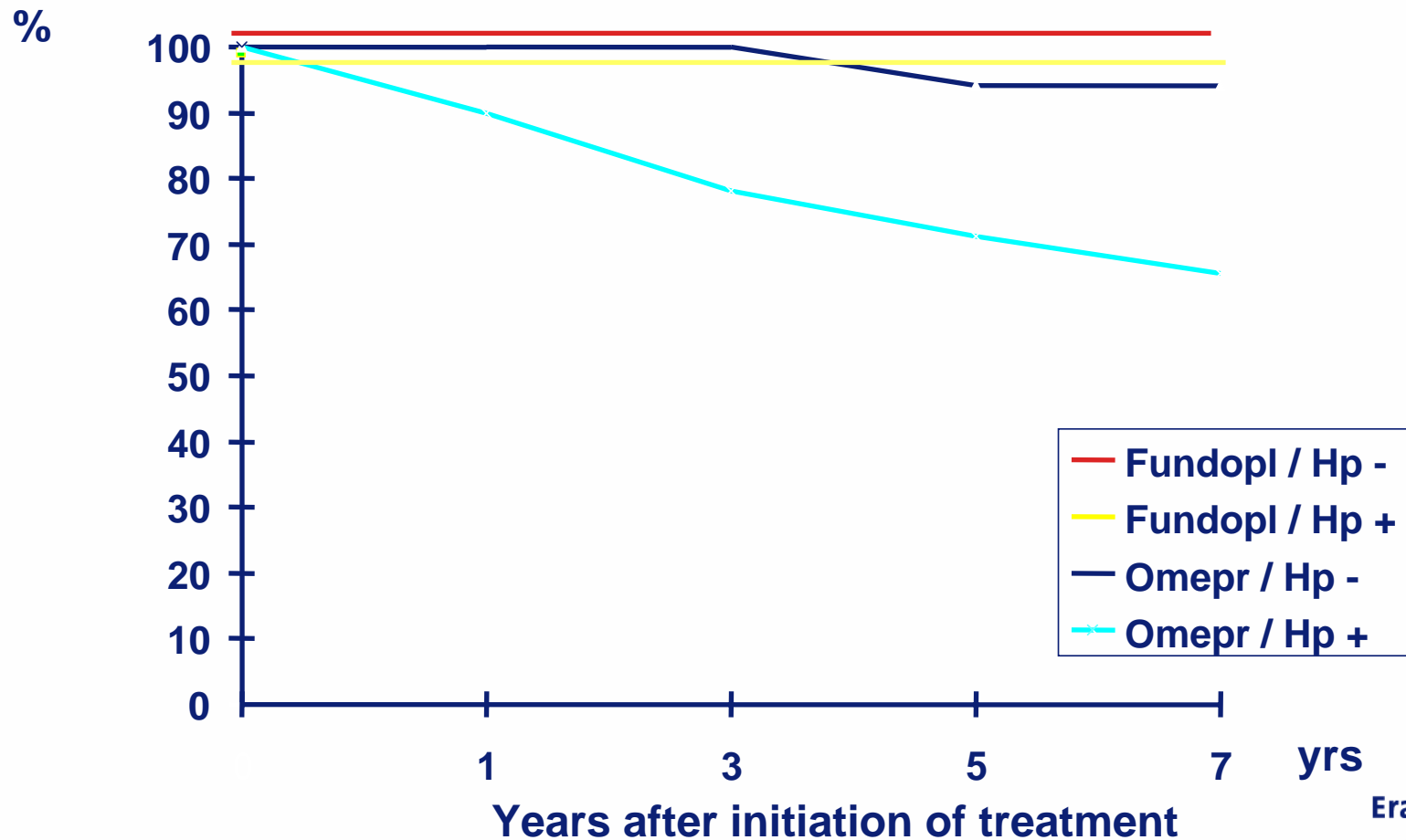
PPI maintenance remains effective for long-term treatment of GERD

Prospective follow-up of 230 patients with severe reflux esophagitis treated with omeprazole up to 11 years *

	<i>H.pylori</i> -positive	<i>H.pylori</i> -negative	p
Relapse rate (1 / x yrs)	8.5	10	NS
Median relapse severity [#]	2	2	NS
Mean omeprazole dose (mg)	28	27	NS

* 1490 patient years follow-up, [#]Savary Miller endoscopy scores

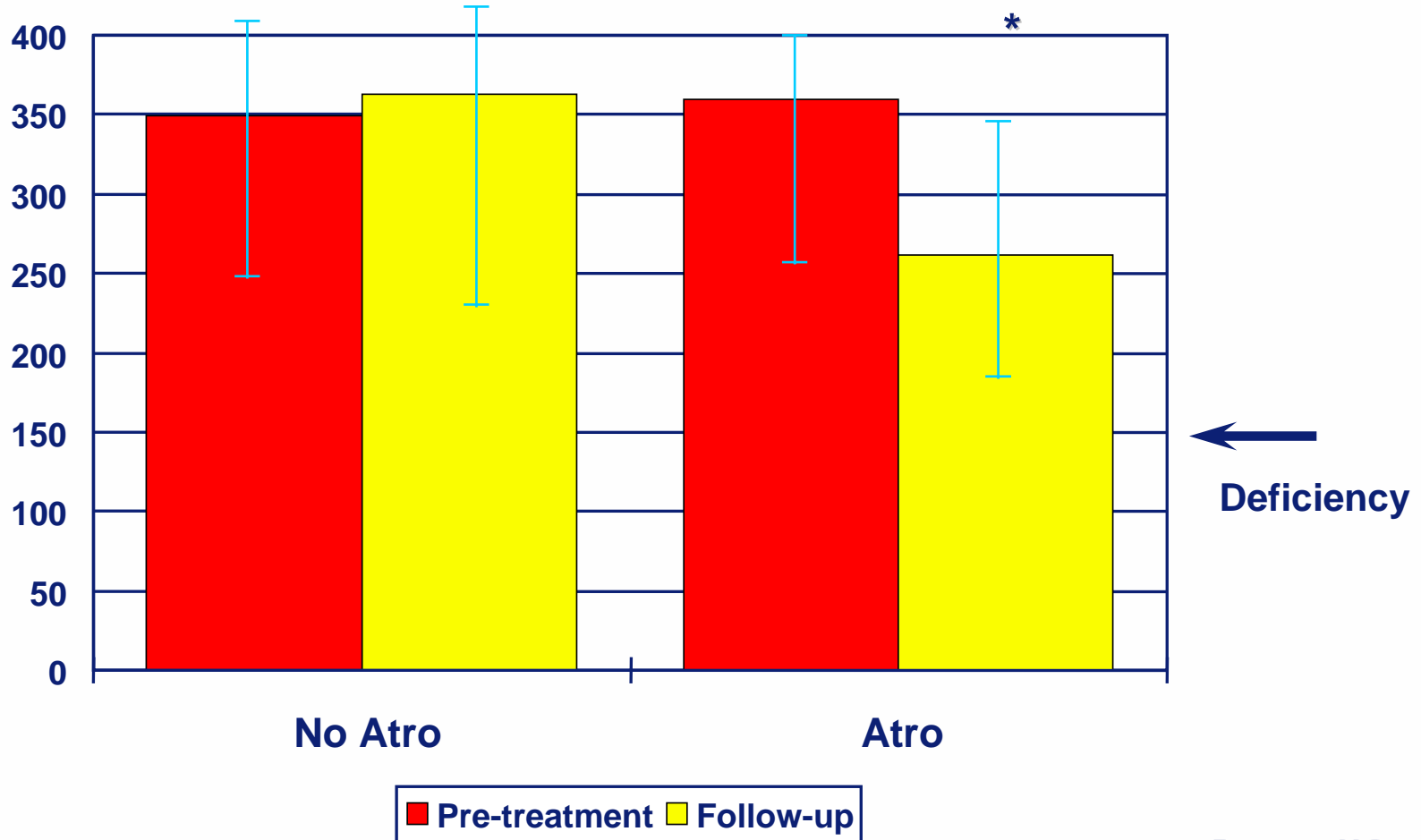
Kaplan Meier curves for the probability of survival without atrophic gastritis



Development of moderate to severe atrophic corpus gastritis in *H.pylori*-positive GORD patients

Study	Fundoplication	Omeprazole	Follow-up	p
Lundell et al.	2 / 44 (4%)	7 / 39 (18%)	3 yr	0.15
Kuipers et al	0 / 31 (0%)	11 / 59 (18%)	5 yr	0.01

Serum vitamin B12 levels in *H. pylori* infected GERD-patients treated with omeprazole



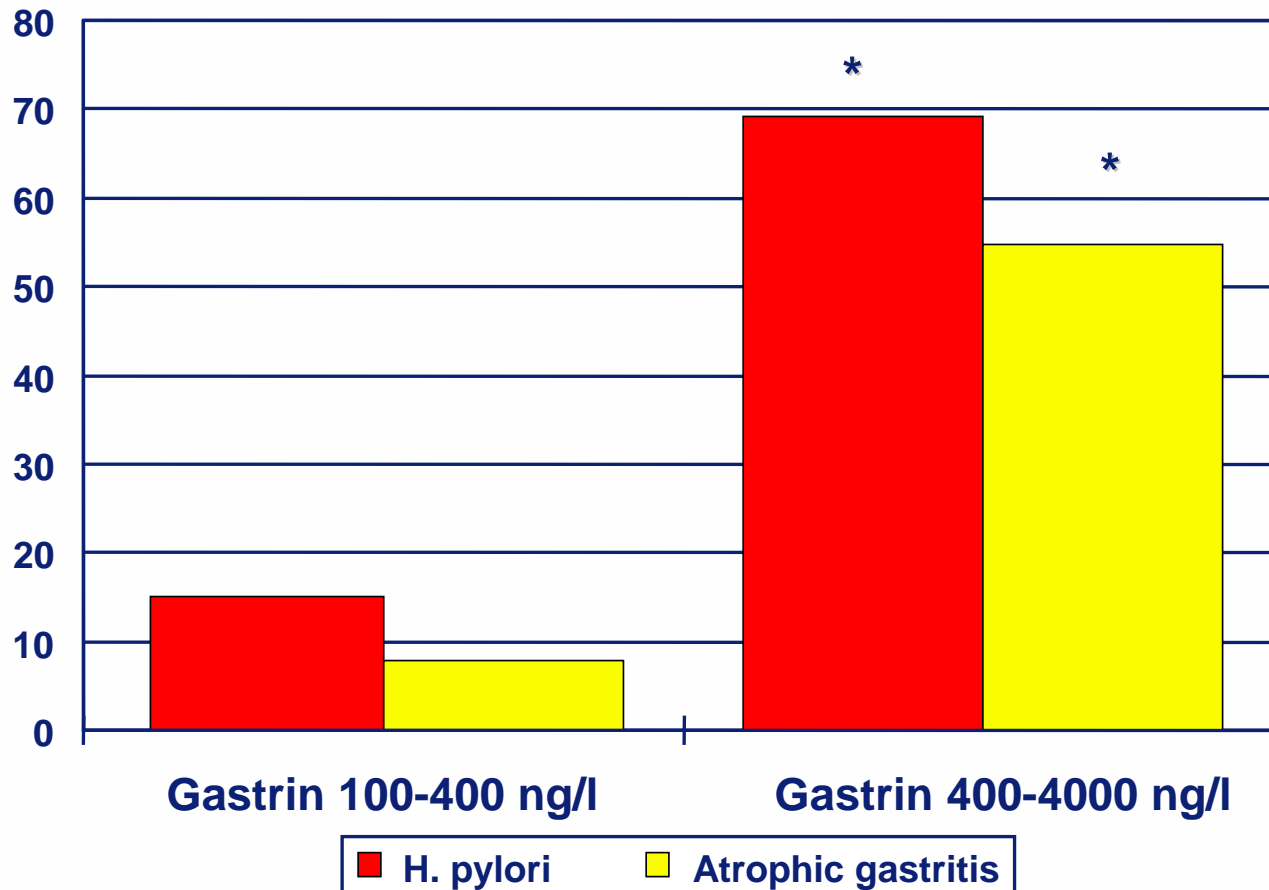
* p<0.05

Schenk et al. APT 1996; 10: 541

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GERD patients treated with omeprazole: Prevalence of *H. pylori* infection and atrophic gastritis according to serum gastrin levels



* p<0.05

Schenk et al. APT 1998; 12: 605

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Study design



baseline

12

24

months

Endoscopy



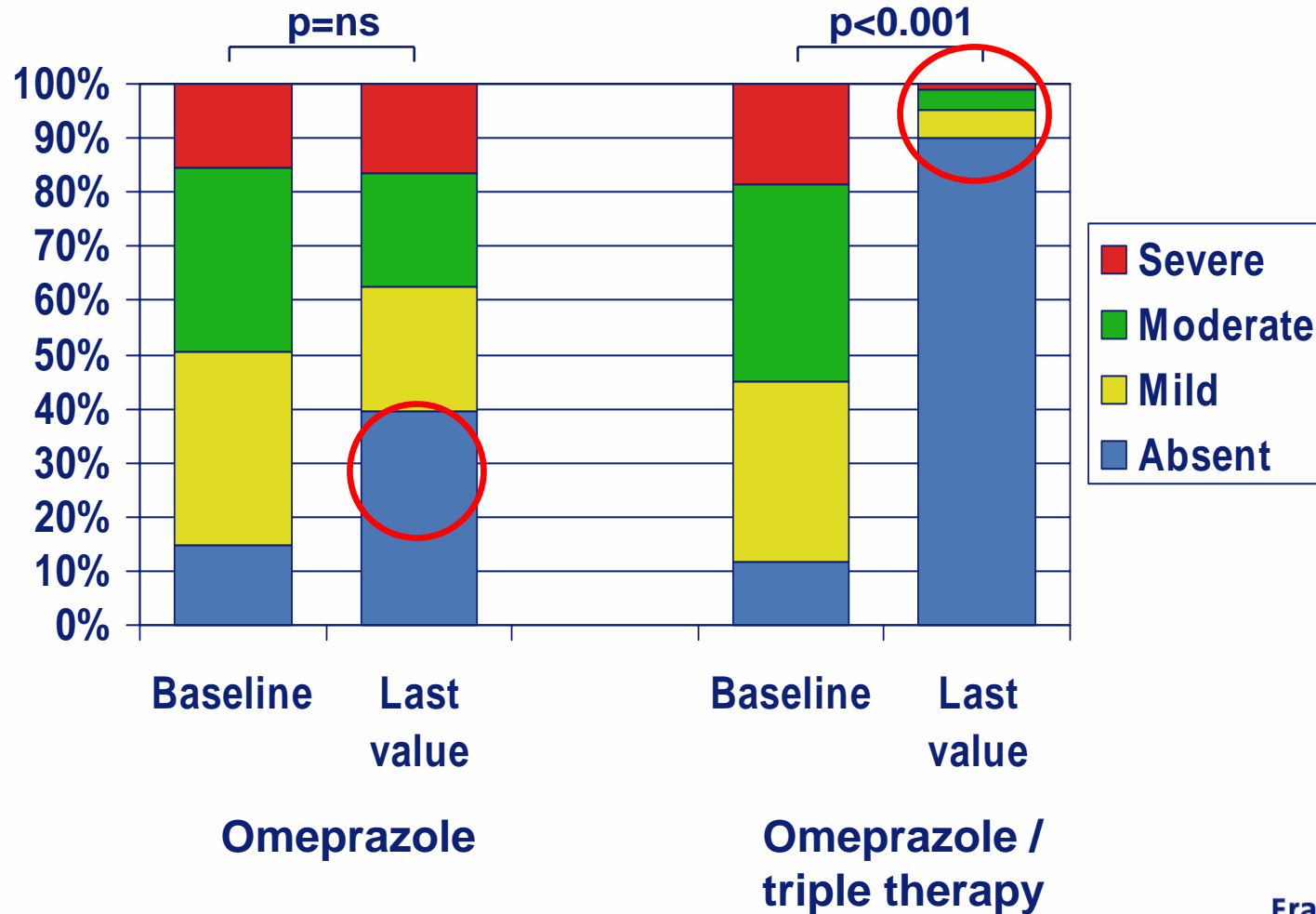
Biopsy sampling



Symptom score

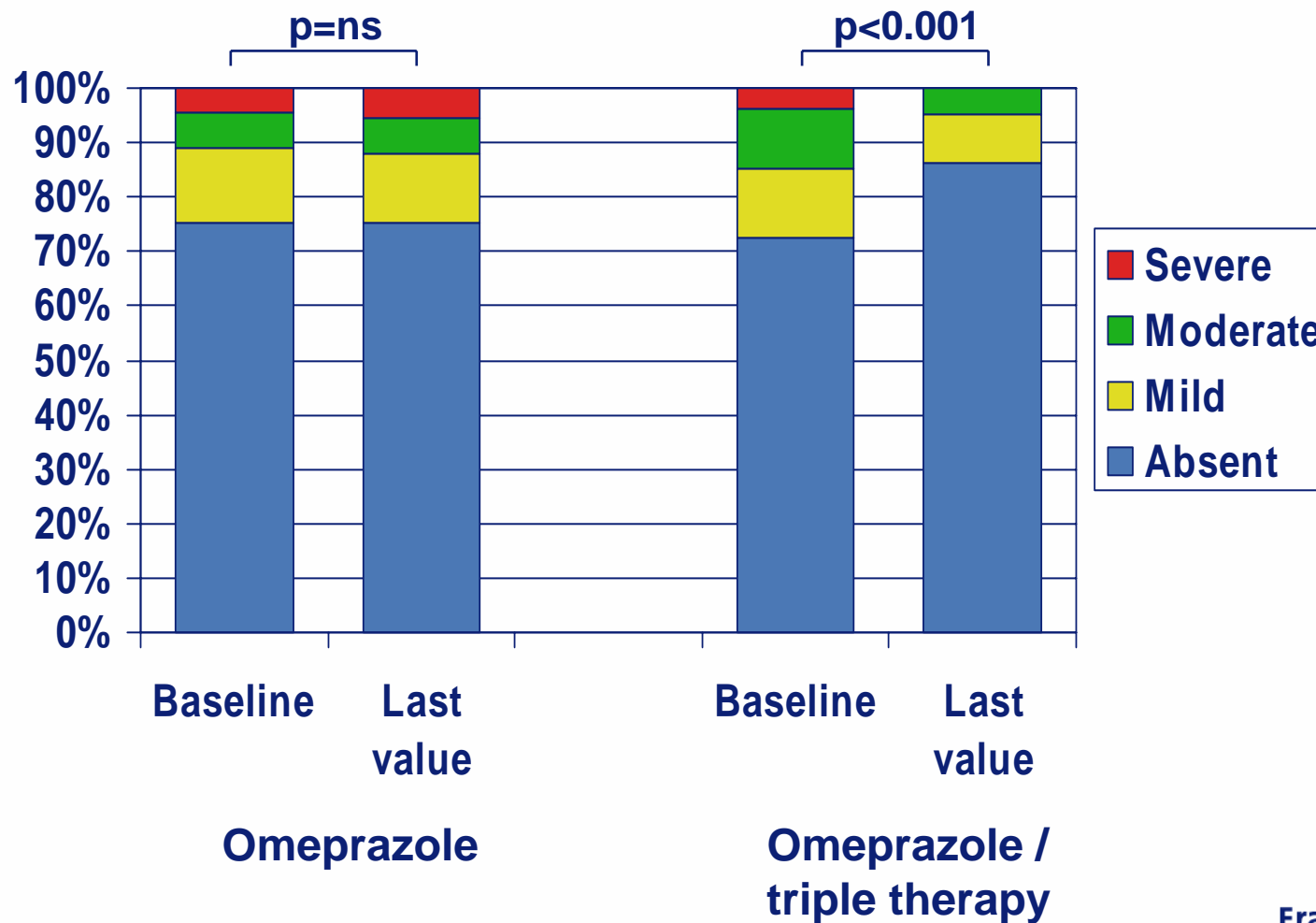


Corpus gastritis activity scores at baseline and last follow-up visit



Treatment comparisons: $p < 0.001$ ITT analysis

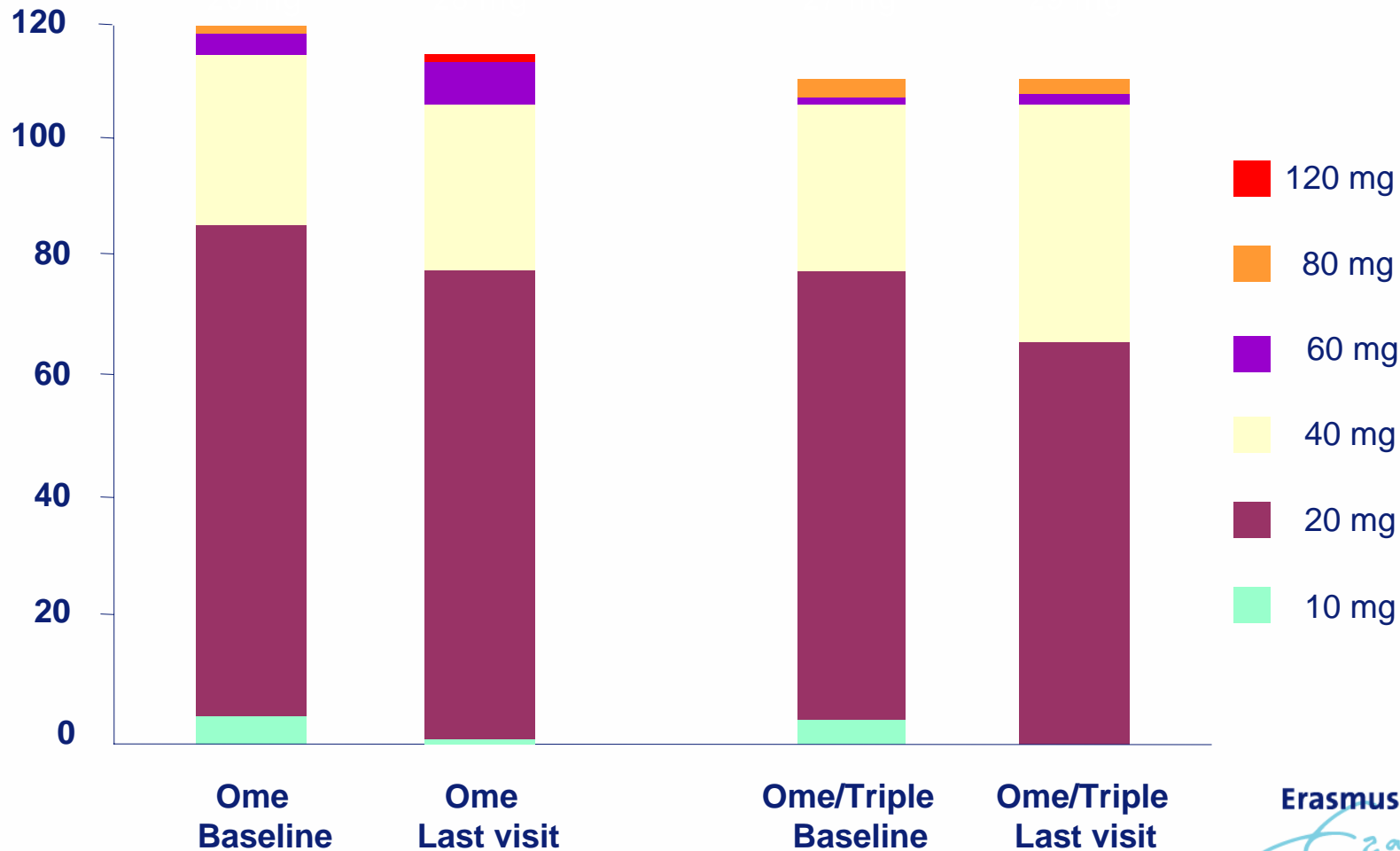
Corpus atrophy scores at baseline and last follow-up visit



Treatment comparisons: $p < 0.001$

Omeprazole dose at baseline and last visit

No of patients

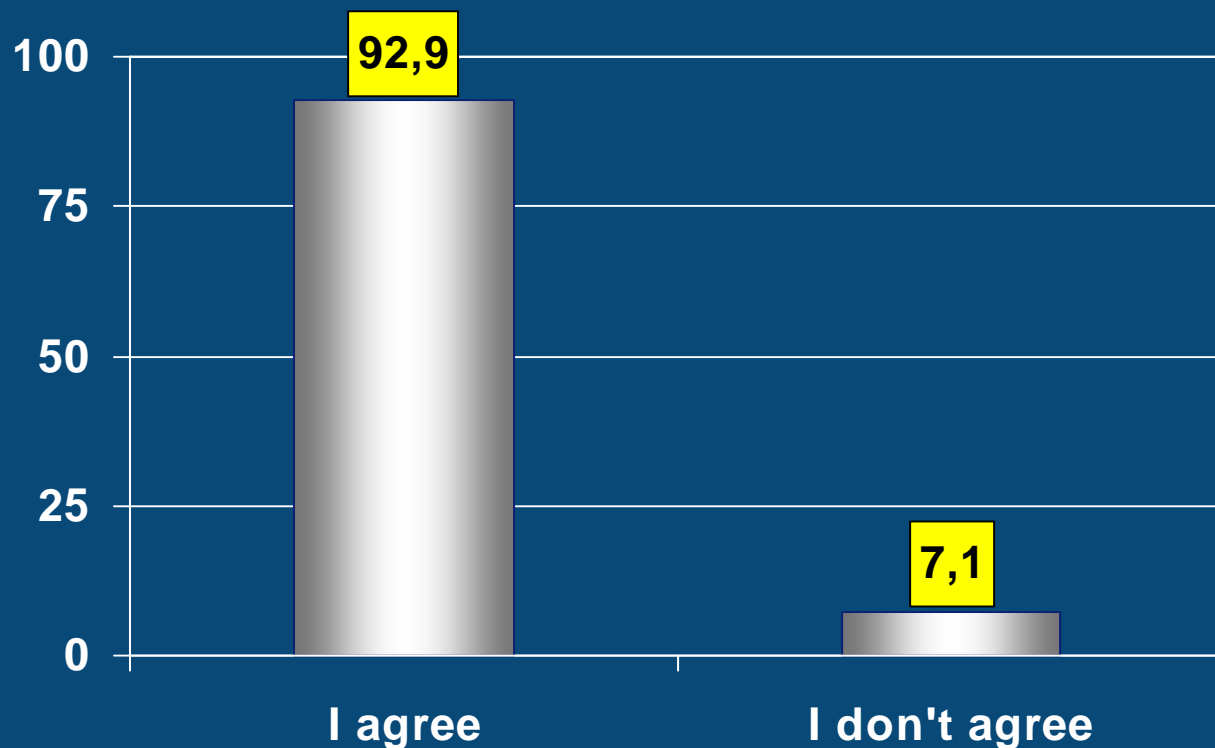


Maastricht consensus meeting on management of *H. pylori* infection

H. pylori and drug use; PPIs

Question: Is there enough evidence that profound acid suppression affects *H. pylori* gastritis? If so, what are the interactions that are considered definite and probable?

Statement:
Profound acid suppression affects the pattern and distribution of gastritis favoring corpus dominant gastritis. It may accelerate the process of loss of specialized glands leading to atrophic gastritis.

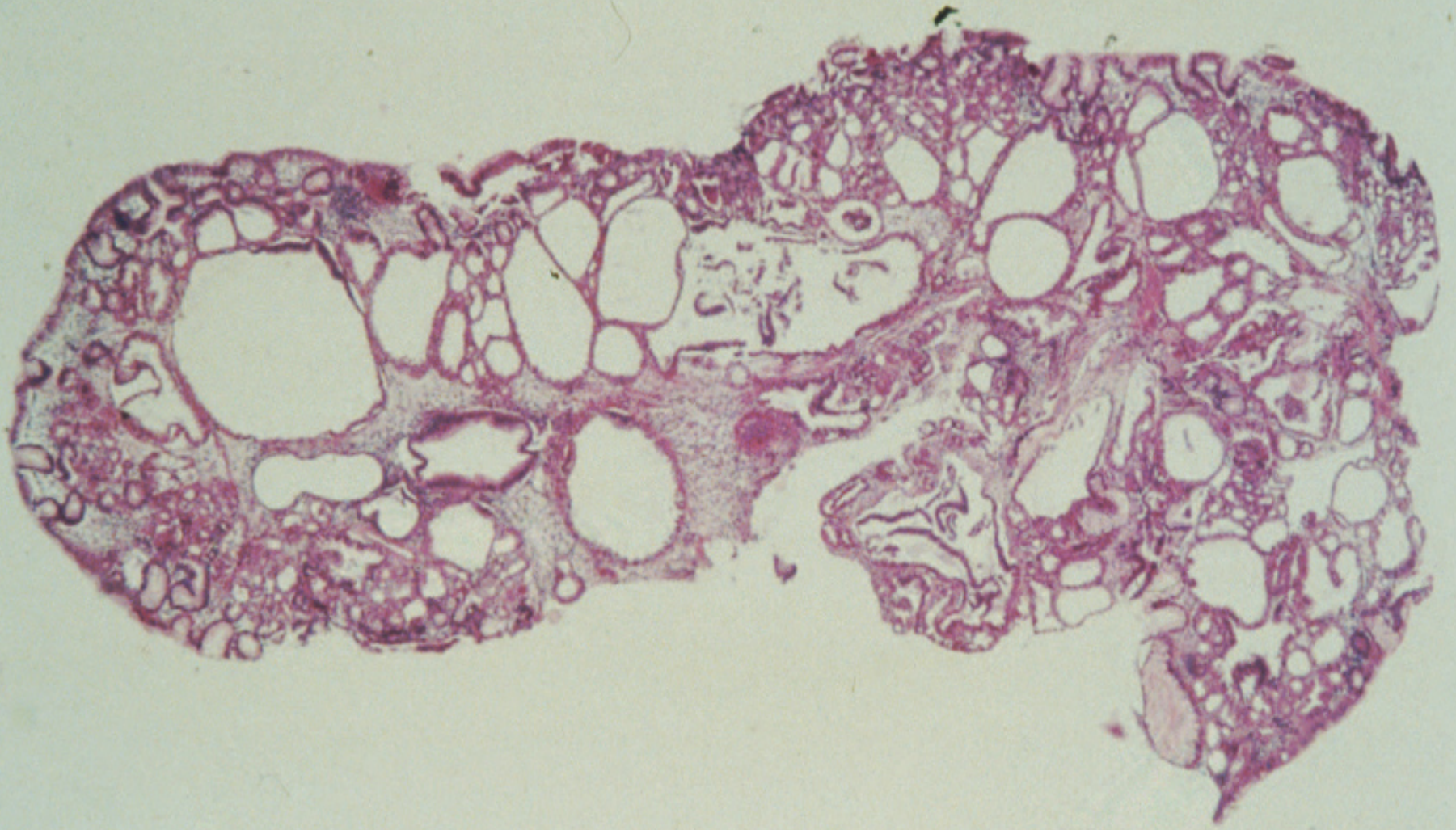


Values in percentages

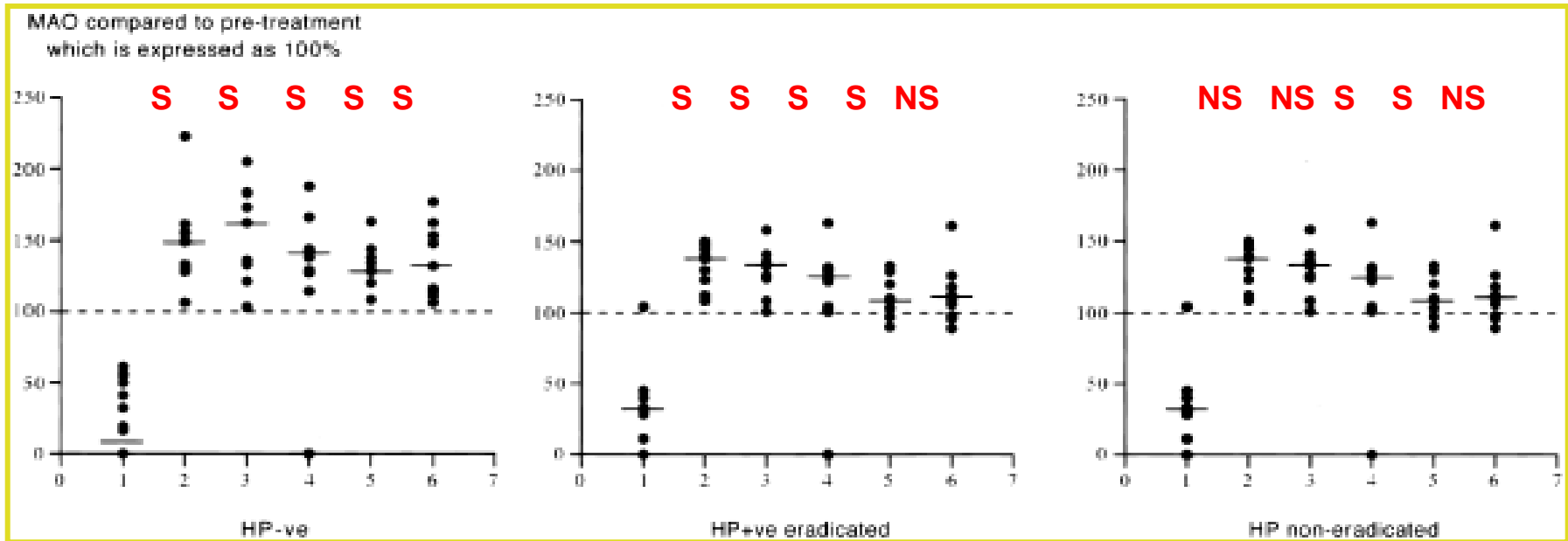


Development of fundic gland polyps during PPI maintenance therapy

Number of GERD-patients	166
Followed for mean (SD)	55 (\pm 31) months
Patients (n) with polyps	at baseline: 0 at follow-up: 30 (18%)
Mean interval between start therapy and diagnosis of polyp	45 (12-108) months



Rebound of maximal pentagastrin-stimulated acid secretion in *H. pylori*-negatives after omeprazole treatment



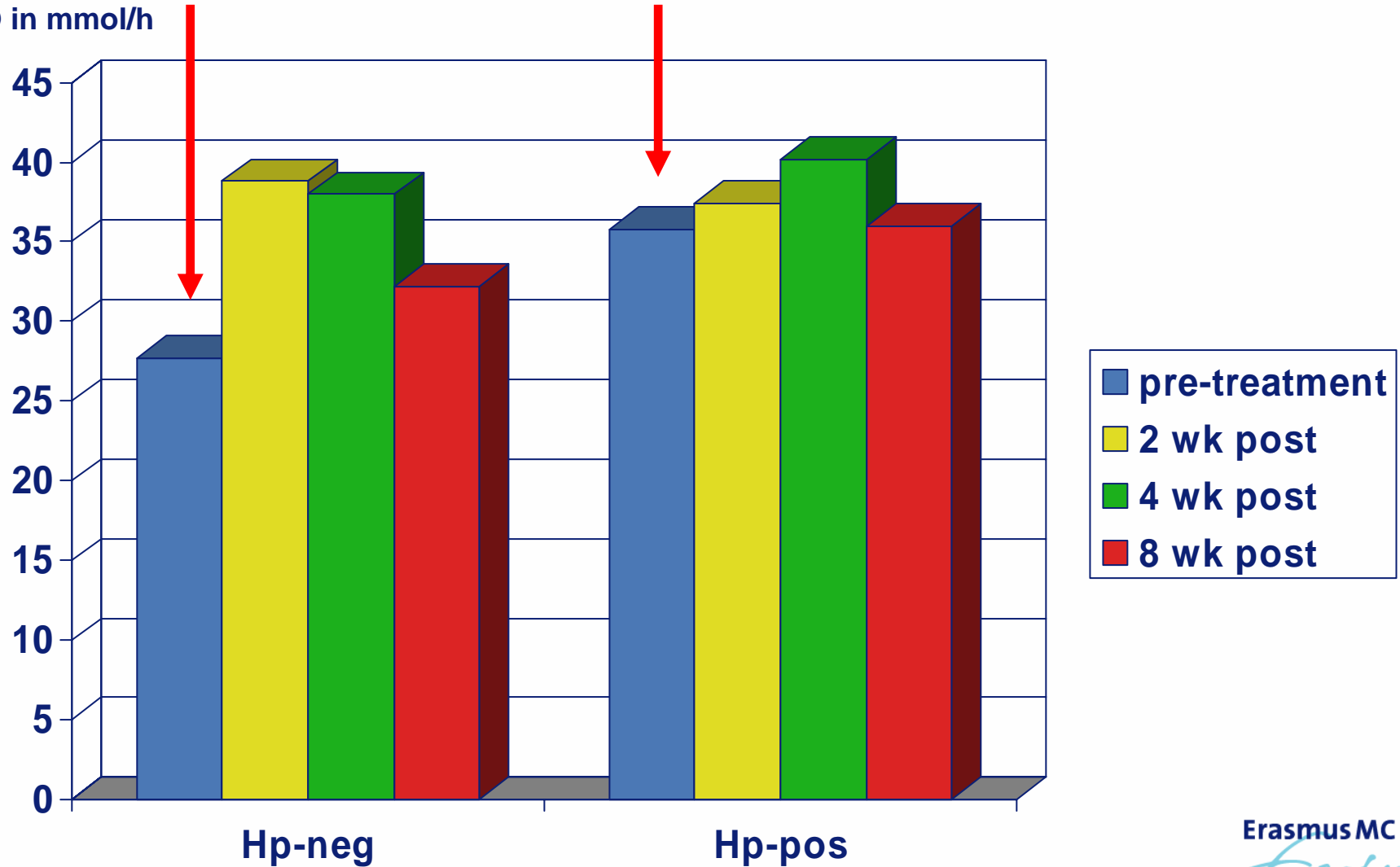
Maximal pentagastrin stimulated acid secretion at 7, 14, 28, 42 and 56 days after omeprazole treatment (40 mg/day 56 days) compared to pre-treatment (100%)

Gillen et al, Gastroenterology, 2004

- Statistical methods?
- More P values (45) than patients (32)
- Expression of data as percentages

Acid rebound after withdrawal of PPI therapy?

MAO in mmol/h



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PPI treatment does not lead to rebound acid secretion

	<i>Day 0</i>	<i>Day 16</i>	<i>P*</i>
<i>Median pH - 24h</i>	1.7	1.7	0.87
<i>Median pH - day</i>	1.5	1.6	0.92
<i>Median pH - night</i>	2.3	1.9	0.50
<i>% pH <4 – 24h</i>	87.2	86.0	0.73
<i>% pH <4 – day</i>	92.6	85.5	0.18
<i>% pH <4 - night</i>	72.4	91.4	0.61

** Wilcoxon signed rank test*

Relative risks for community-acquired pneumonia by exposure to gastric acid-suppressive therapy

			<i>Acid-suppressive drugs</i>		
	<i>Total</i>	<i>No Acid suppressive drugs</i>	<i>H2-receptor Antagonists</i>	<i>PPI's</i>	<i>Overall</i>
<i>No. of patients</i>	364 683	345 224	10 177	12 337	19 459*
<i>Person-years</i>	977 893	970 331	2351	5191	7562*
<i>No. of cases of pneumonia</i>	5551	5366	54	131	185
<i>Unadjusted relative risk (95% CI)</i>		1.00	4.24 (3.18-5.43)	4.63 (3.84-5.43)	4.47 (3.82-5.12)

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Conclusions

- PPIs are very effective in the establishment of maintained symptomatic and endoscopic remission of GERD
- Side effects with respect to function and morphology of the gastric mucosa are common
- *H. pylori* eradication can partially prevent and reverse these effects, without impairing PPI therapy for GERD