

Functional Dyspepsia

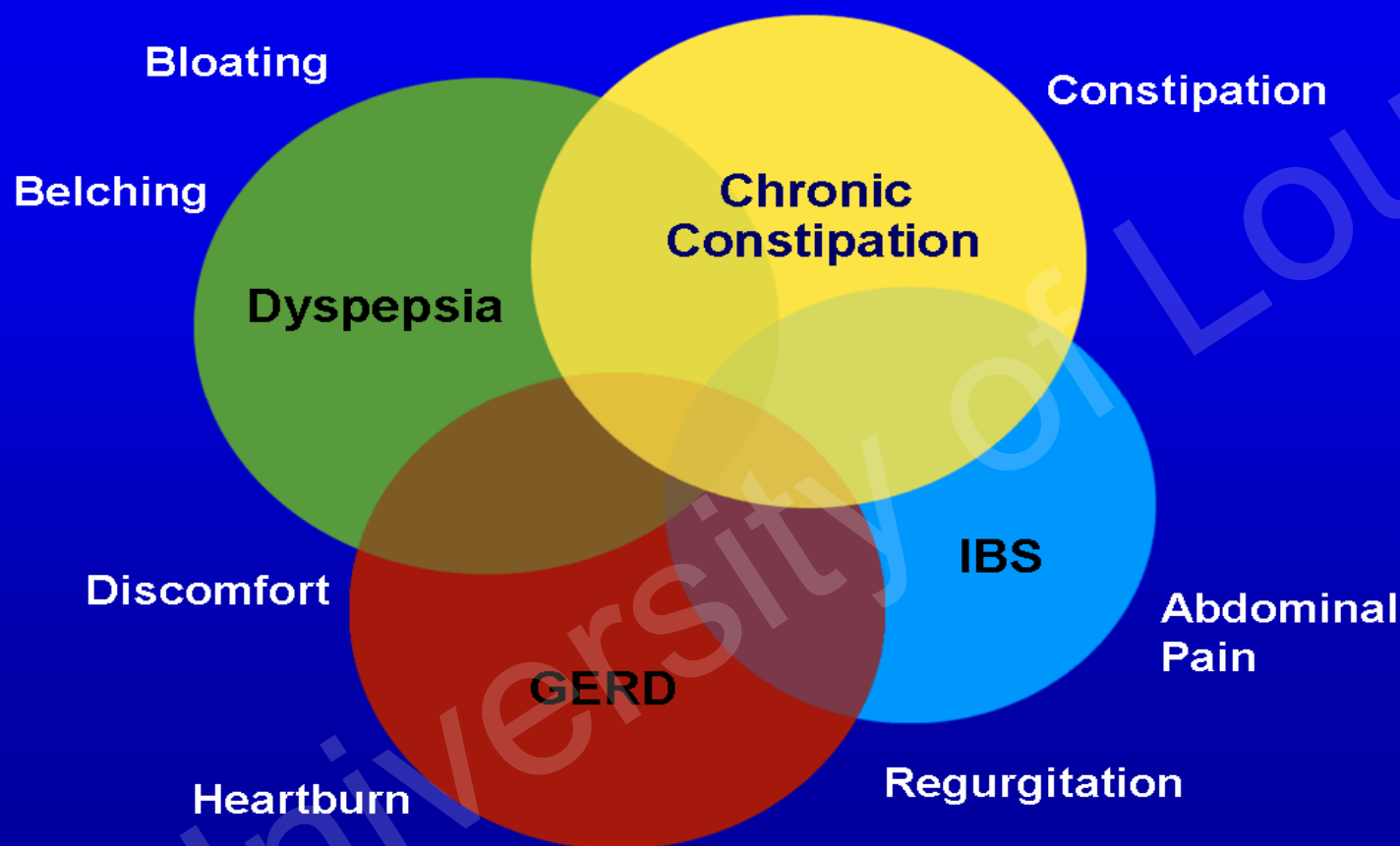
John M. Wo, M.D.

August 28, 2008

Functional Dyspepsia

- Pathophysiology
- Clinical manifestation and classification
- Treatment “strategy”
- Therapies

There Is Significant Overlap Among GI Disorders



- 29% of GERD patients have Chronic Constipation*
- Diagnoses can shift from one disorder to another over time†
- Possible common pathophysiological mechanisms‡

*Locke GR et al. *Neurogastroenterol Motil.* 2004;16:1-6.

†Corazzari E. *Best Prac Res Clin Gastroenterol.* 2004;18:613-631.

‡Talley NJ et al. *Am J Gastroenterol.* 2003;98:2454-2459.

Uninvestigated dyspepsia

vs.

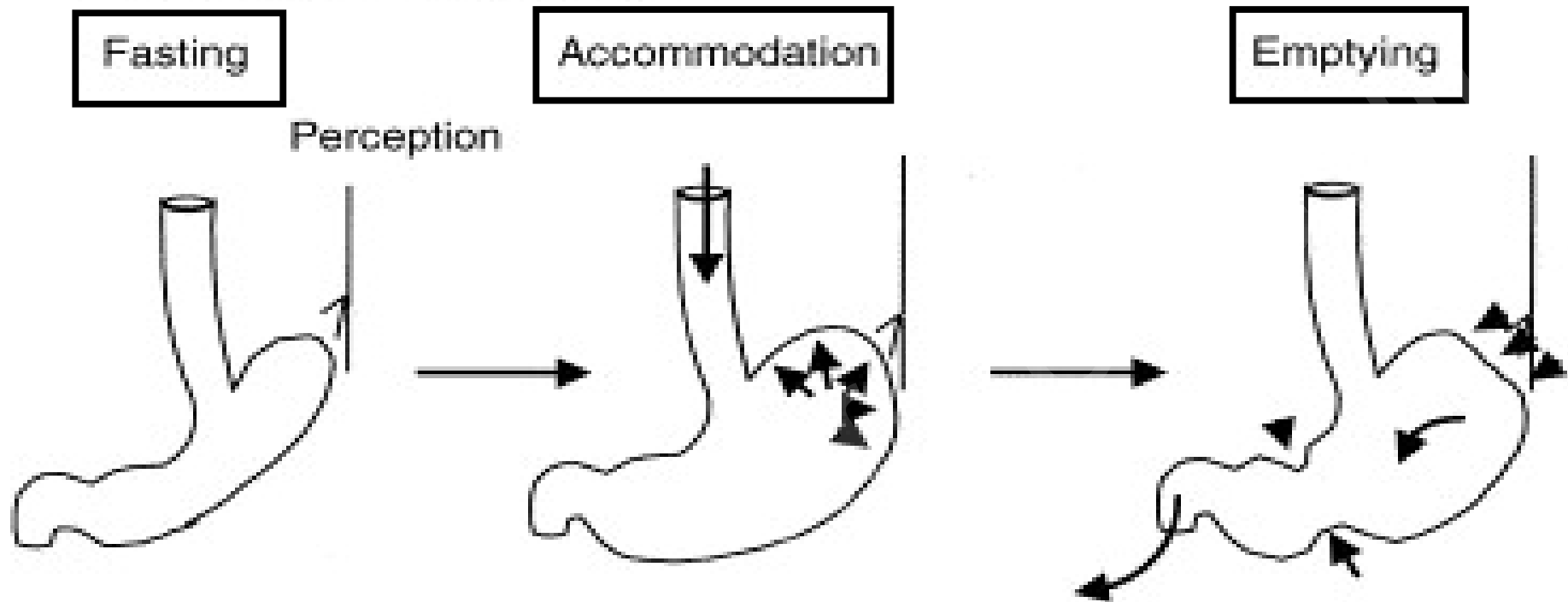
Investigated dyspepsia

**(functional, non-ulcer or
endoscopy-negative dyspepsia)**

Symptoms of Dyspepsia

- Discomfort in the upper abdomen
- Bloating
- Early satiety
- Abdominal distension
- Nausea
- Indigestion

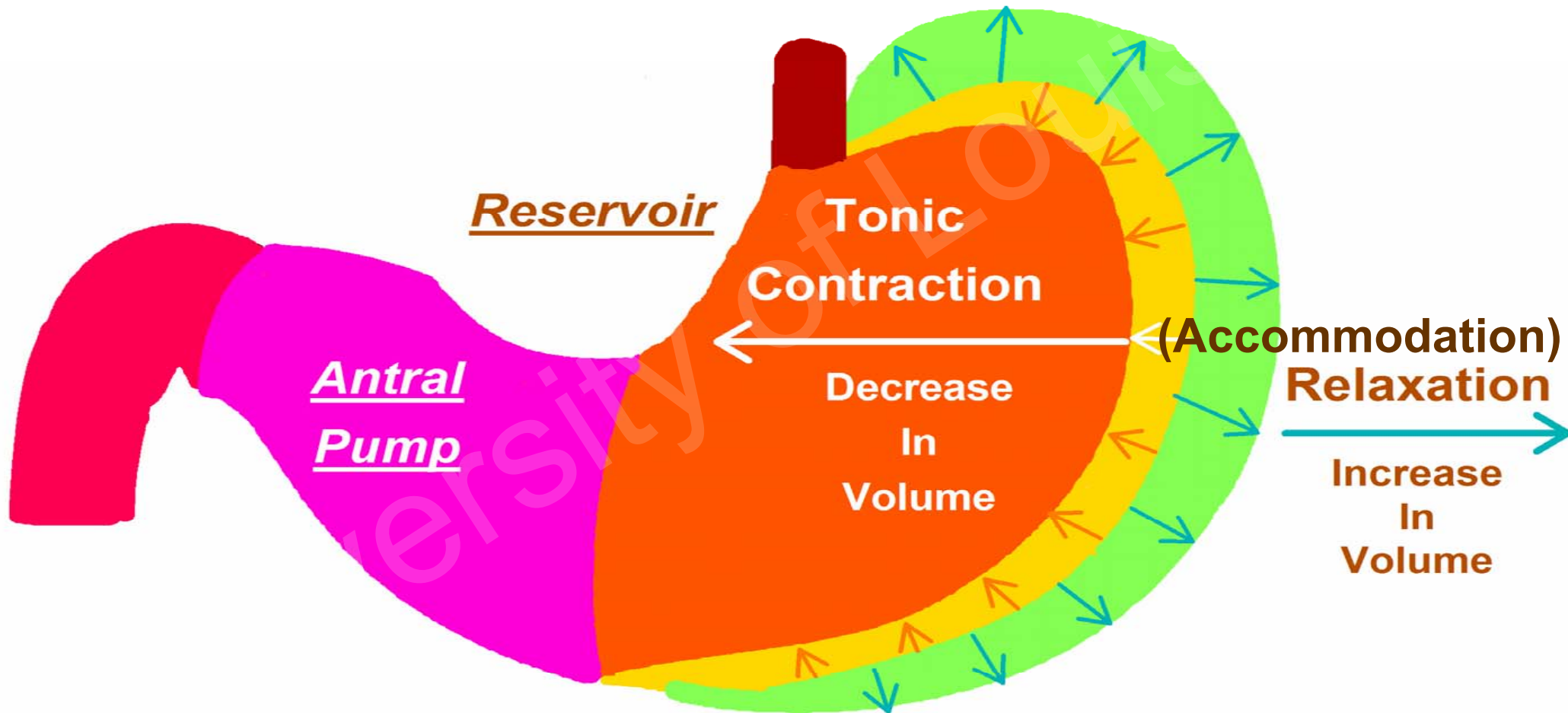
Normal gastric function:



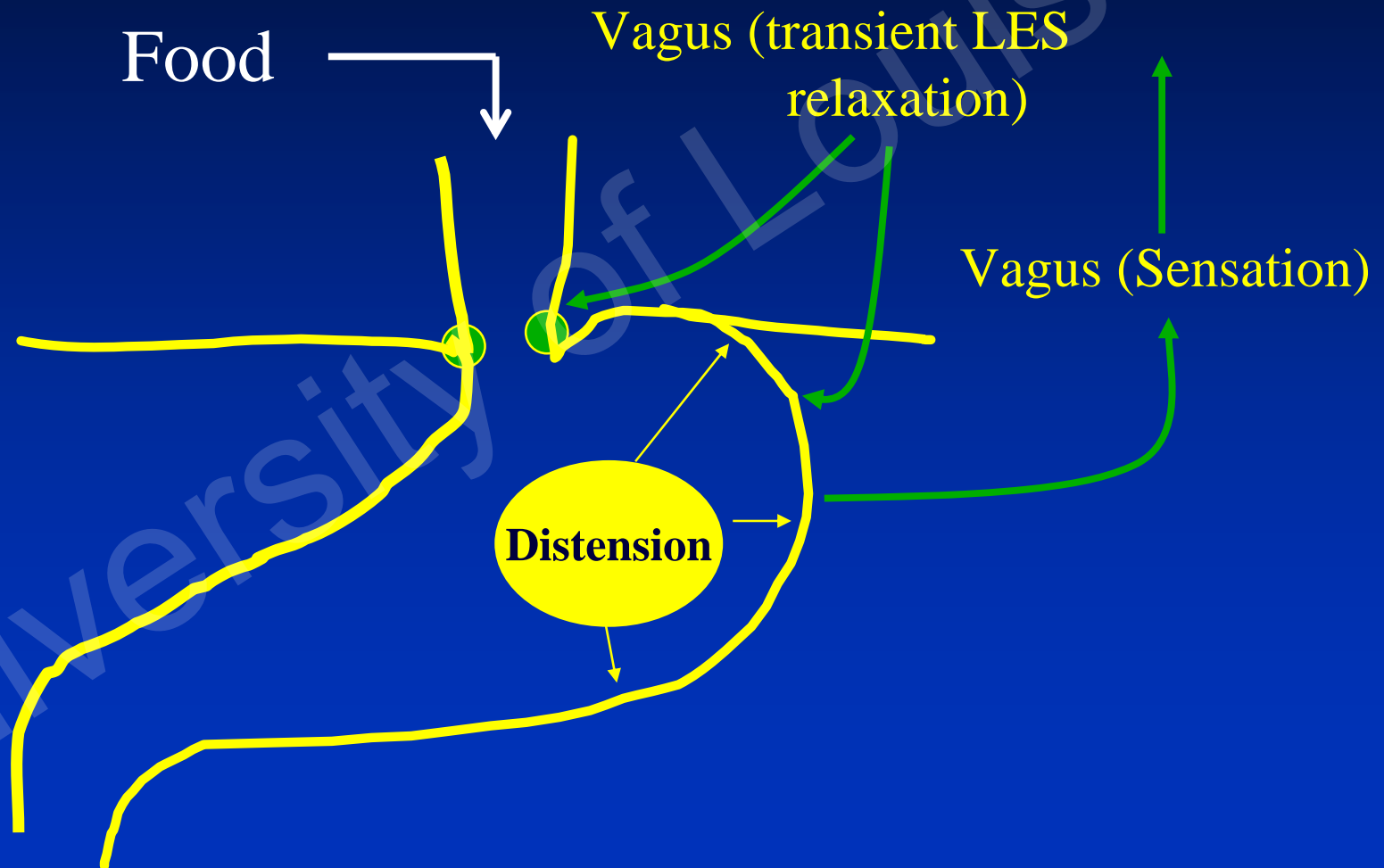
Pathophysiological abnormalities in functional dyspepsia:

- H. pylori infection
- Hypersensitivity to gastric distention
- ANS/CNS disorder
- Impaired accommodation
- Unsuppressed phasic contractile activity
- Abnormalities of gastric electrical rhythm
- Delayed emptying
- Duodenal lipid or acid hypersensitivity
- Small intestinal dysmotility

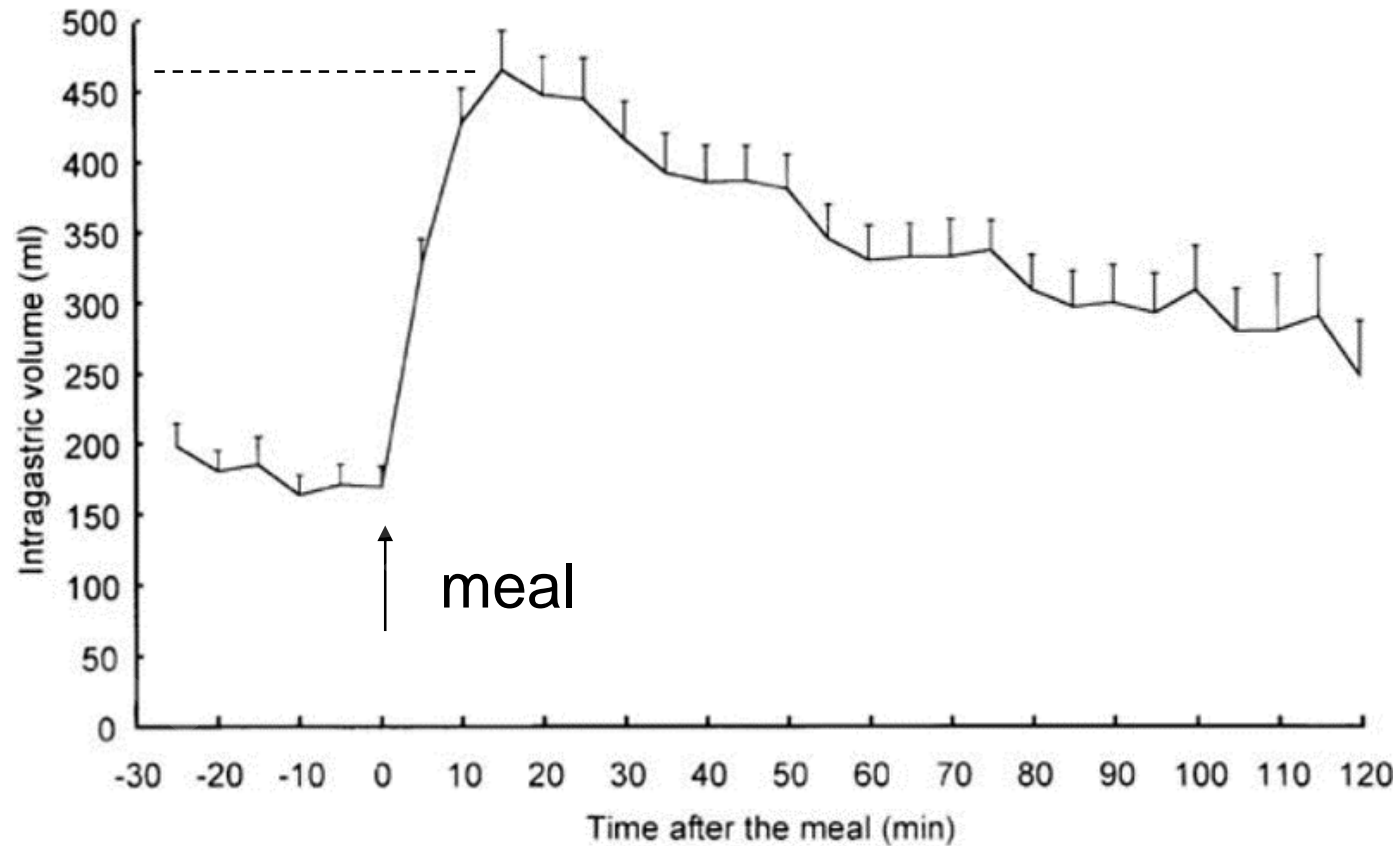
Normal Proximal and Distal Stomach Function



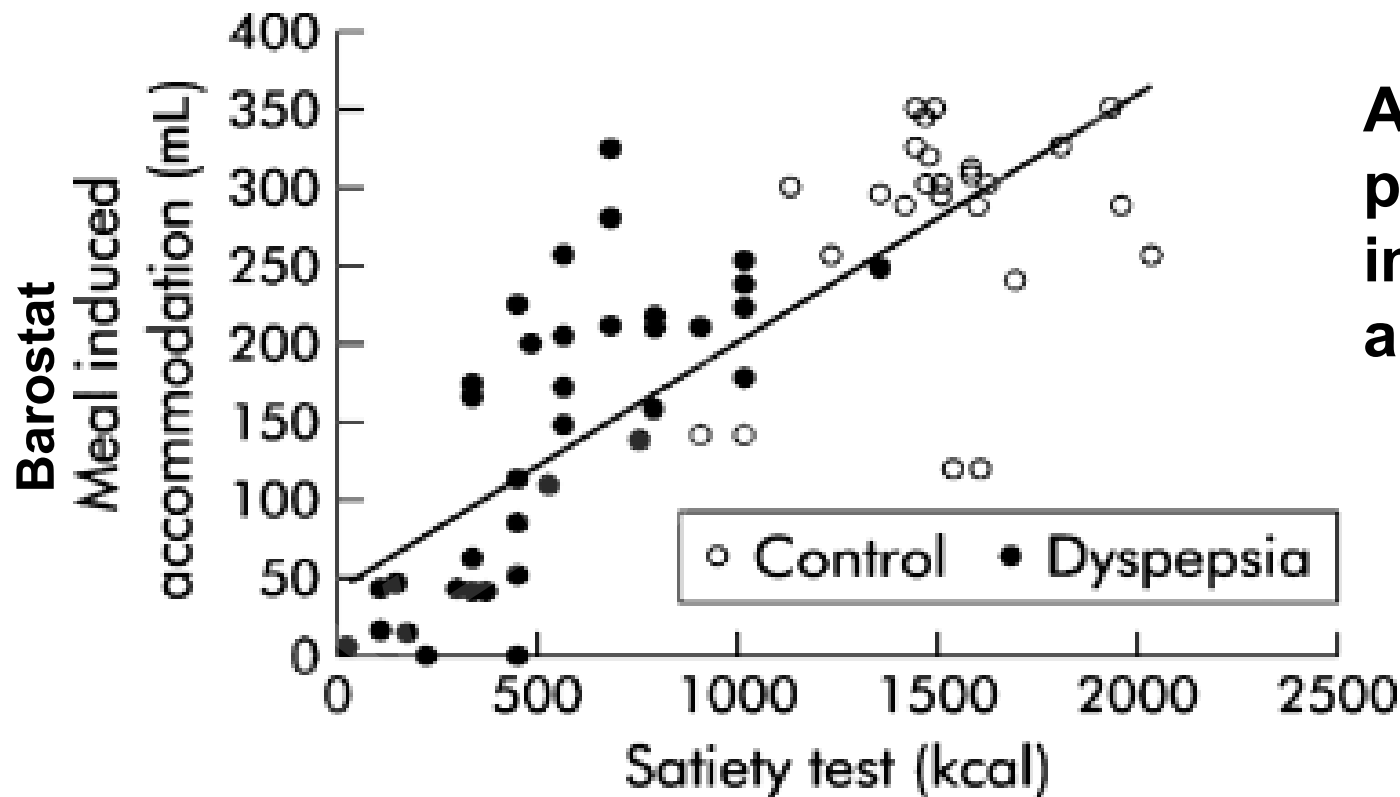
Gastric Distension and Functional Dyspepsia



Proximal Gastric Accommodation to Meals

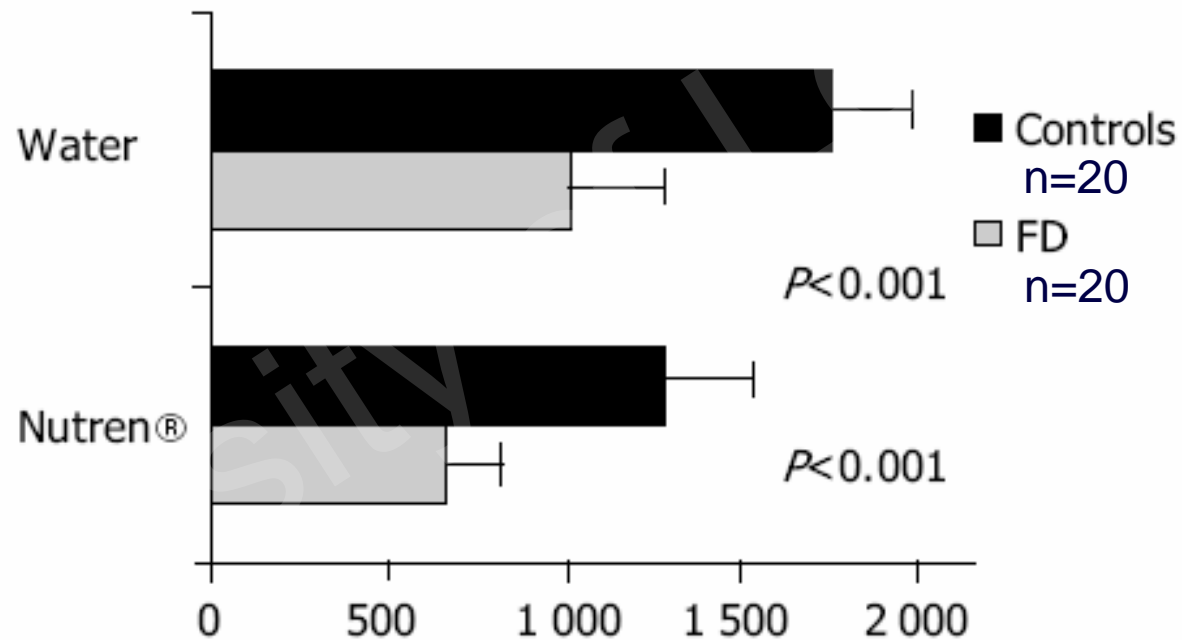


Impaired Proximal Gastric Accommodation

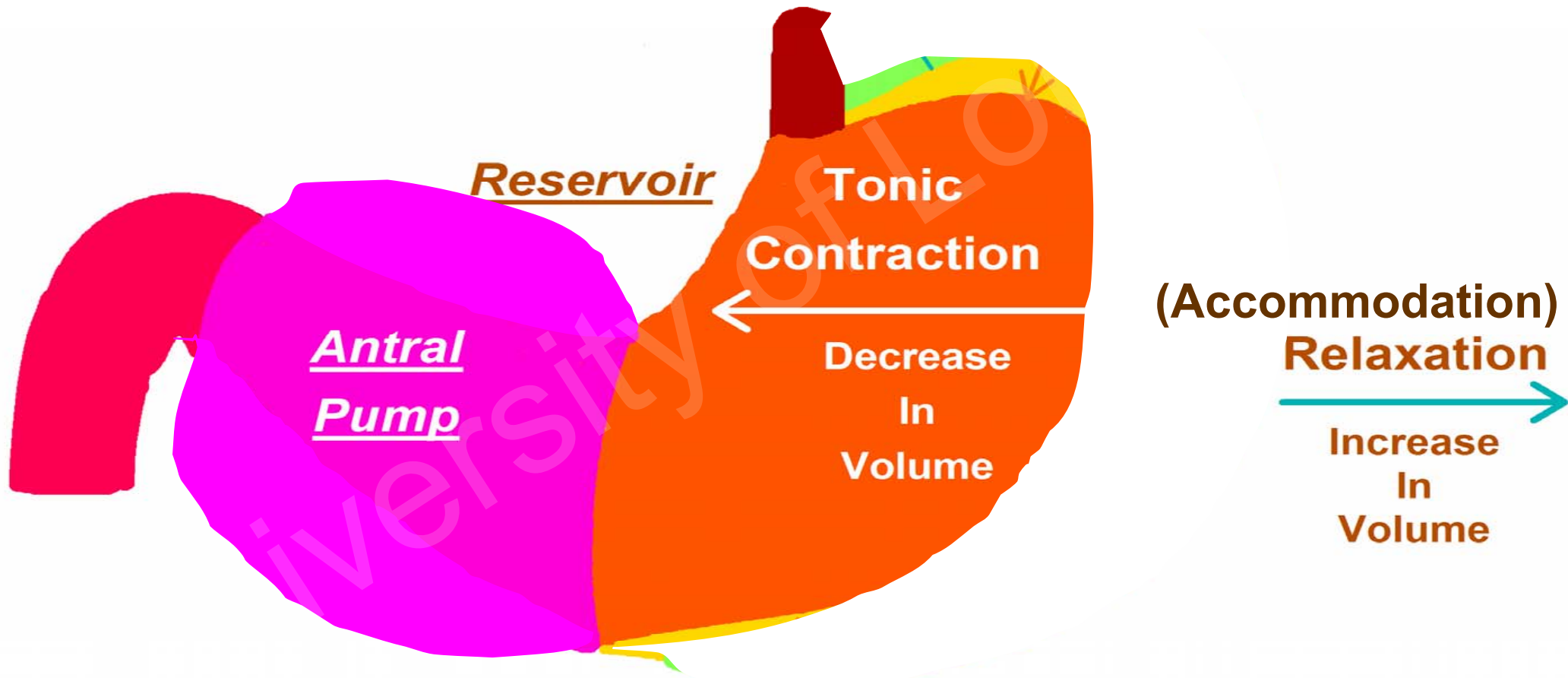


About 41% of patients have impaired gastric accommodation

Liquid Load Test for FD



Abnormal Proximal and Distal Stomach Function

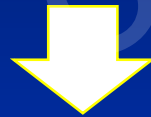


Probable Pathophysiology of Functional Dyspepsia

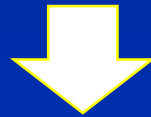
Impaired Fundic Accommodation



Rapid Proximal Gastric Emptying



Antral Distension



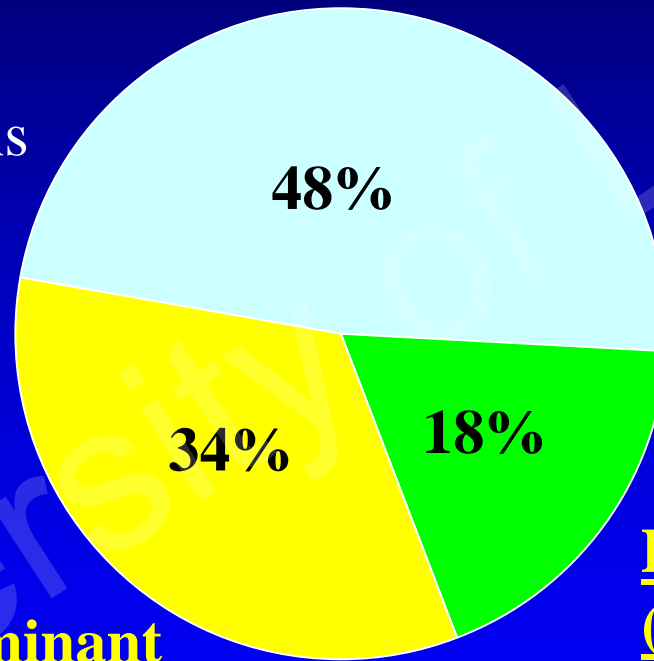
Dyspeptic Symptoms

Delayed Gastric Emptying in Functional Dyspepsia

Vomiting-Predominant

- Vomiting
- Dehydration
- Hospitalizations
- Weight loss

N=339 patients
presenting to University
of Louisville



Regurgitation-Predominant

- Refractory heartburn
- Effortless regurgitation

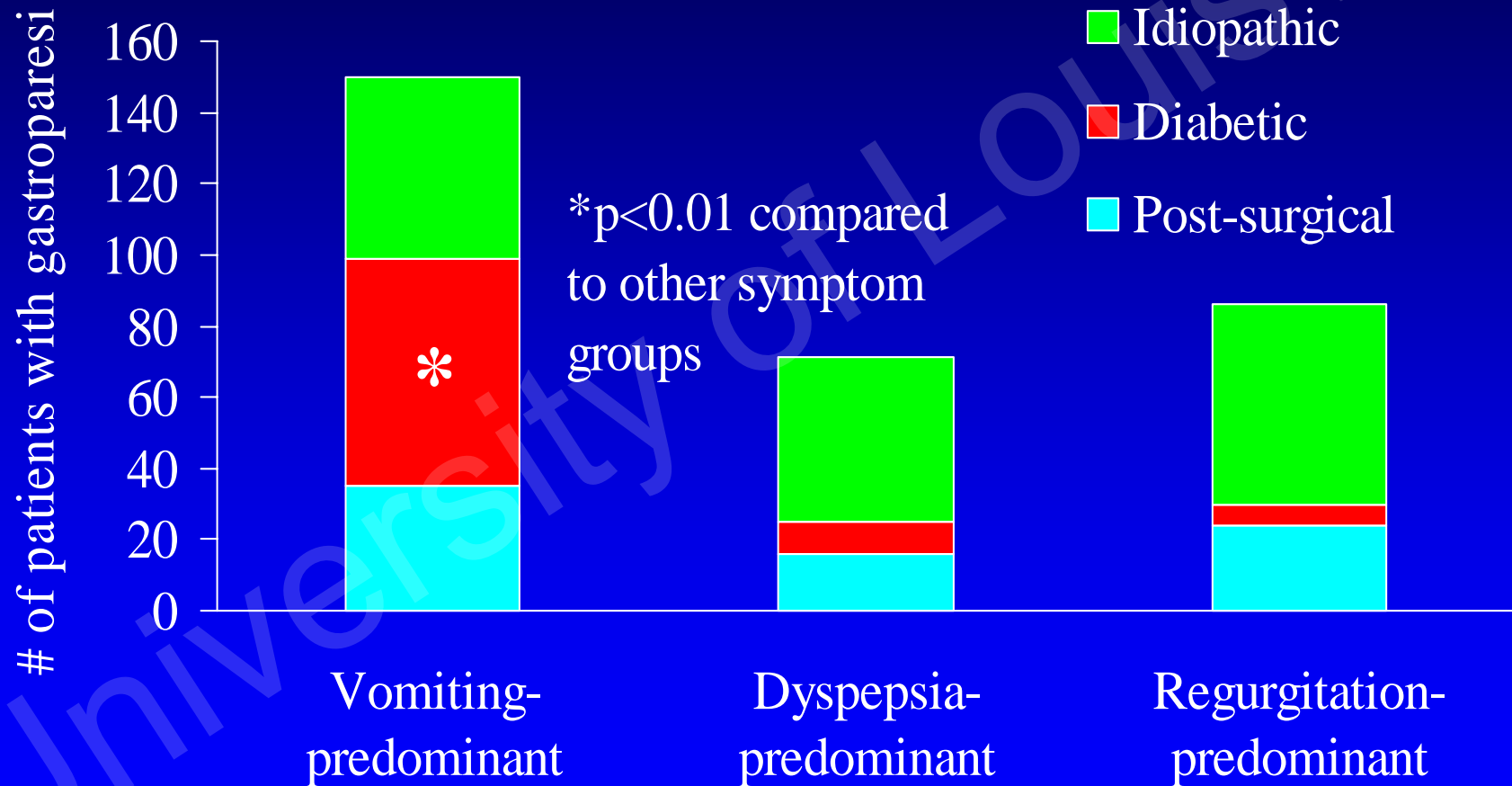
Dyspepsia-Predominant (Functional Dyspepsia)

- Epigastric pain
- Bloating
- Abdominal distension

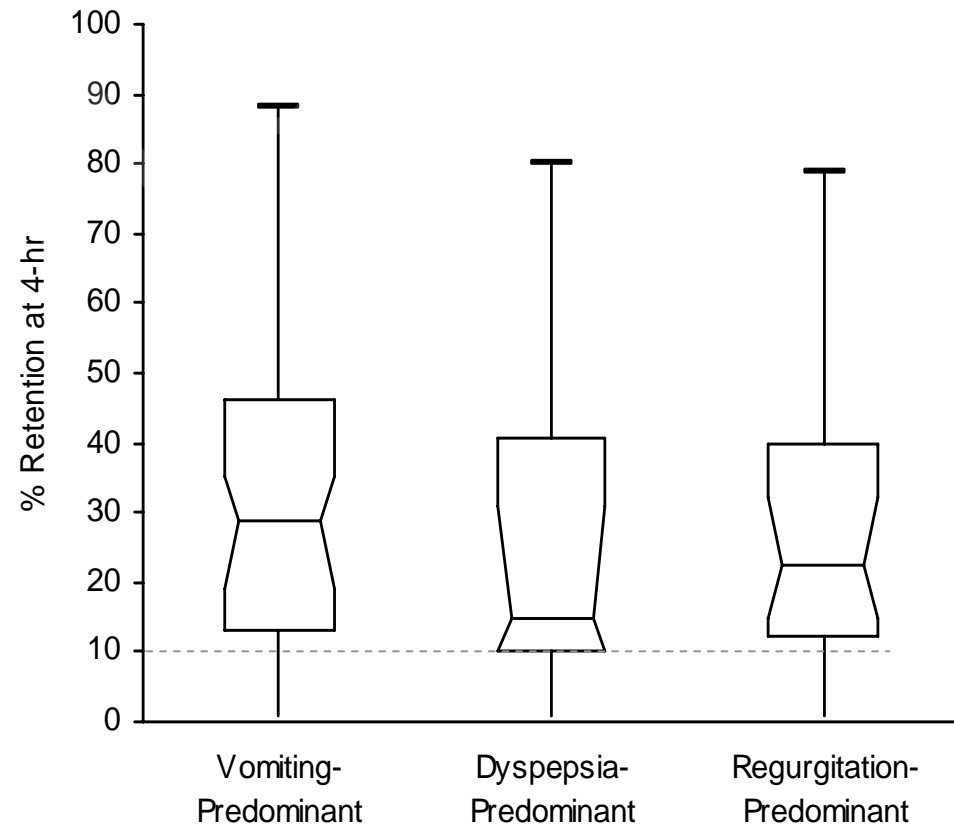
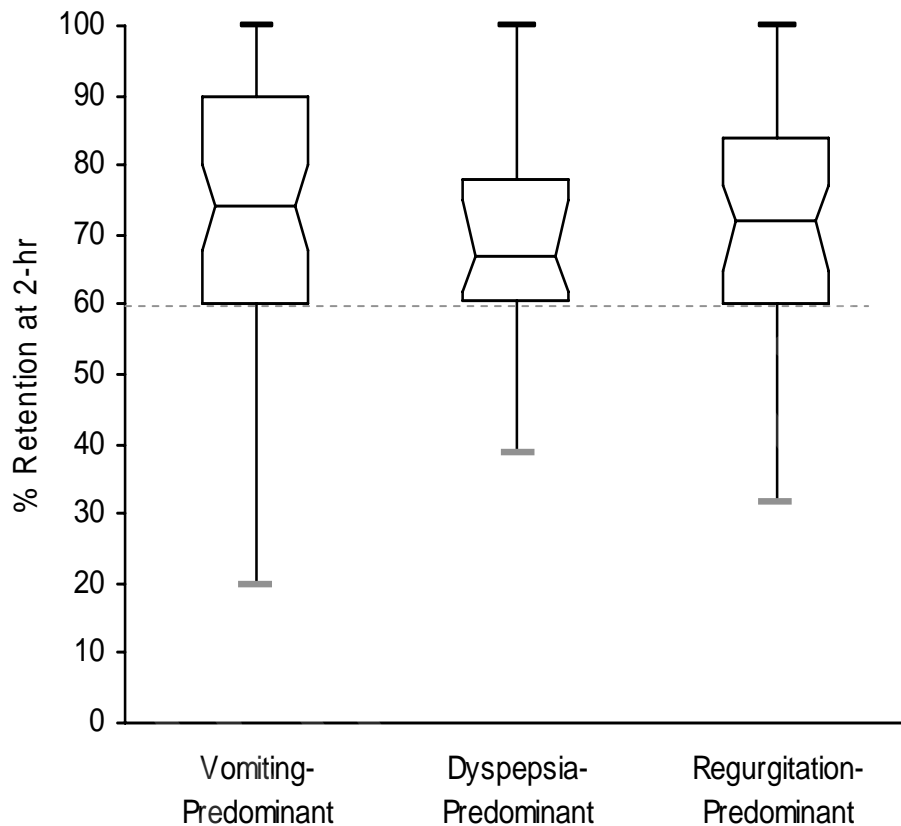
Classification of Gastroparesis Based on Predominant-Symptom Presentation

	Definitions
1. Vomiting-predominant gastroparesis	Vomiting with retching and nausea are the most bothersome symptoms
2. Dyspepsia-predominant gastroparesis	Discomfort centered in upper abdomen is the most bothersome symptom; may be characterized by upper abdominal fullness, early satiety, bloating, or nausea
3. Regurgitation-predominant gastroparesis	Effortless regurgitation of acid or undigested food or heartburn is the most bothersome symptom

Patients with Diabetic Gastroparesis Presents with Vomiting-Predominant Symptoms



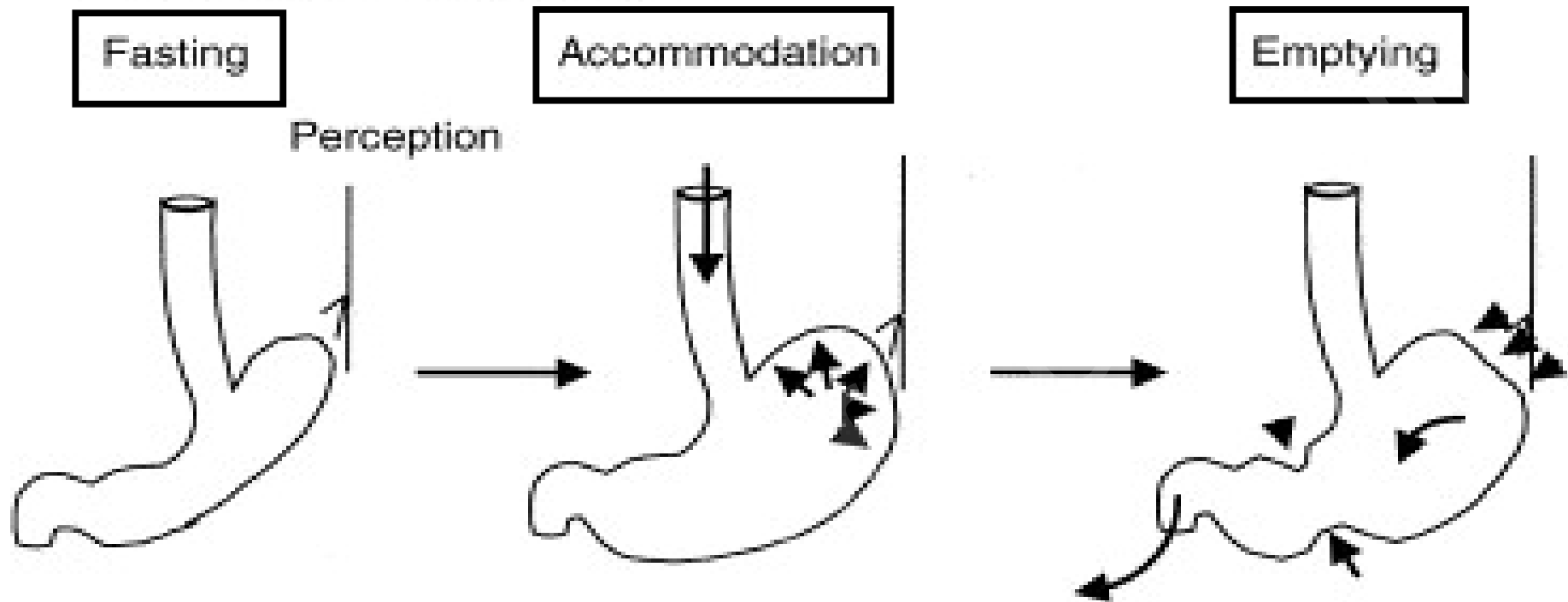
Delayed Gastric Emptying Does Not Correlate with Clinical Presentation



Delayed Gastric Emptying in Functional Dyspepsia

- Occur in 23 to 32% of patients with functional dyspepsia
- Poor correlation between gastric emptying and functional symptoms
- Delayed gastric emptying is not likely the cause of dyspepsia in most patients

Normal gastric function:



Pathophysiological abnormalities in functional dyspepsia:

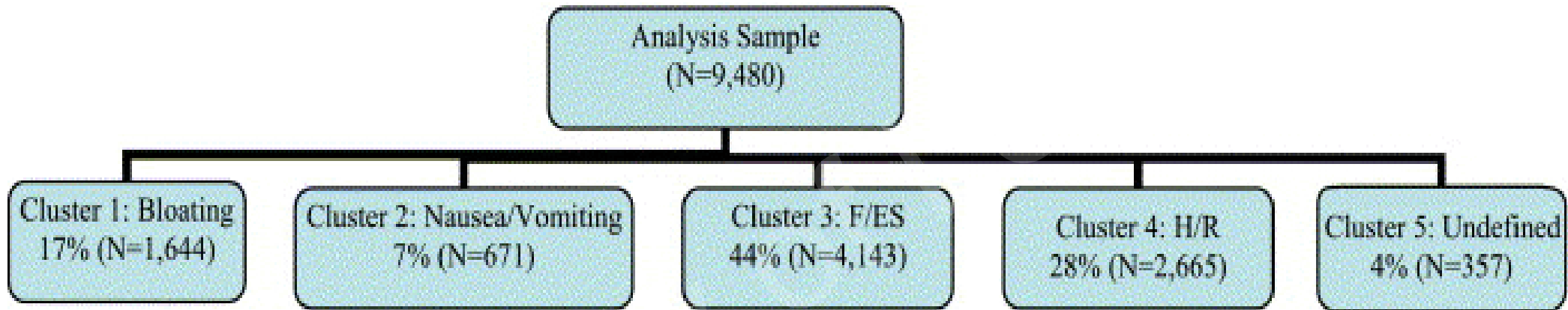
- **H. pylori** infection
- Hypersensitivity to gastric distention
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- Impaired accommodation
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- Abnormalities of gastric electrical rhythm
- Delayed emptying
- Duodenal lipid or acid hypersensitivity
- Small intestinal dysmotility

Past Classification of Functional Dyspepsia

- Ulcer-like
- Dysmotility-like
- Reflux-like
- Non-specific

But symptoms overlap and unstable over time

Symptom Clusters in Patients with Functional Dyspepsia



Abbreviations:
F/ES = Fullness/Early Satiety
H/R = Heartburn/Regurgitation

Analysis included symptomatic respondents (those reporting the specific symptom ≥ 1 time per month for the past 3 months).

Camilleri et al. Clin Gastroenterol Hepatol 2005; 3:543.
Telephone survey of 21,128 adults

New Classification for Functional Dyspepsia (Rome III)

- Postprandial Distress Syndrome

- Postprandial fullness after ordinary sized meals and/or
- Early satiety preventing finishing a regular meal
- Supportive criteria
 - Upper abdominal bloating
 - Postprandial nausea
 - Excessive belching

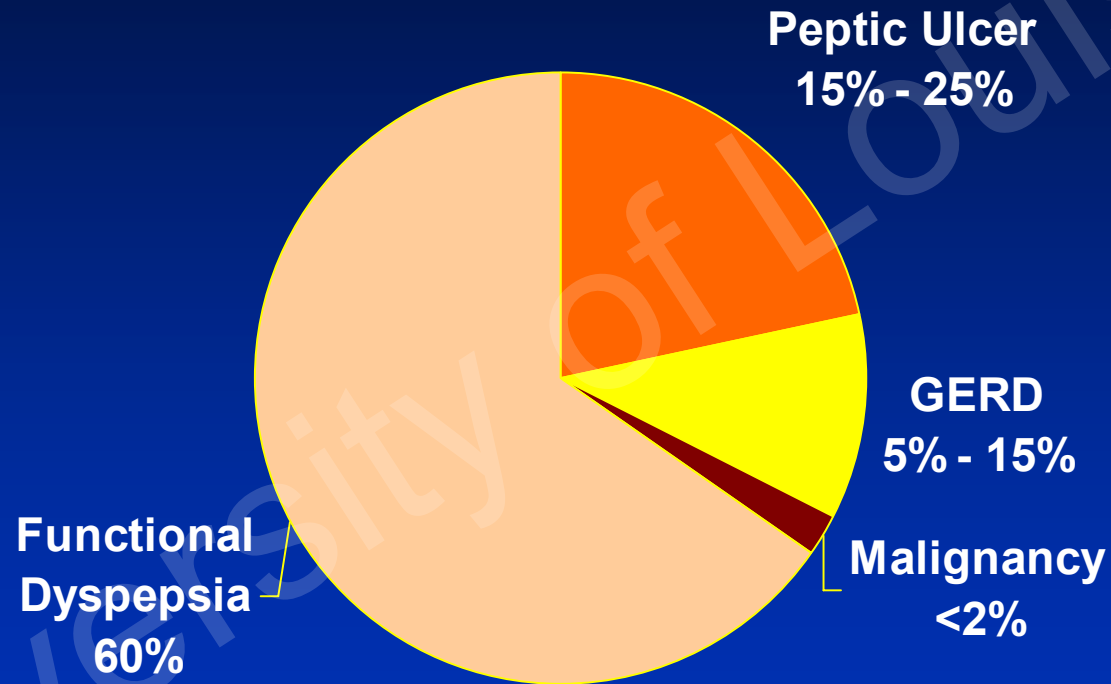
- Epigastric Pain Syndrome

- Epigastric pain or burning and
- Pain is intermittent and
- Not generalized or localized to other abdominal regions and
- Not relieved by defecation or passage of flatus and
- Not gallbladder and sphincter of Oddi disorders

Dyspepsia or Epigastric pain

TO SCOPE OR NOT TO SCOPE?

Non-Ulcer (“Functional”) Dyspepsia is Very Common



Treatment Approach to Uninvestigated Dyspepsia

Alarm Symptoms/Risk Factors

Yes

Endoscopy

No

Test for treat
strategy for
H. pylori

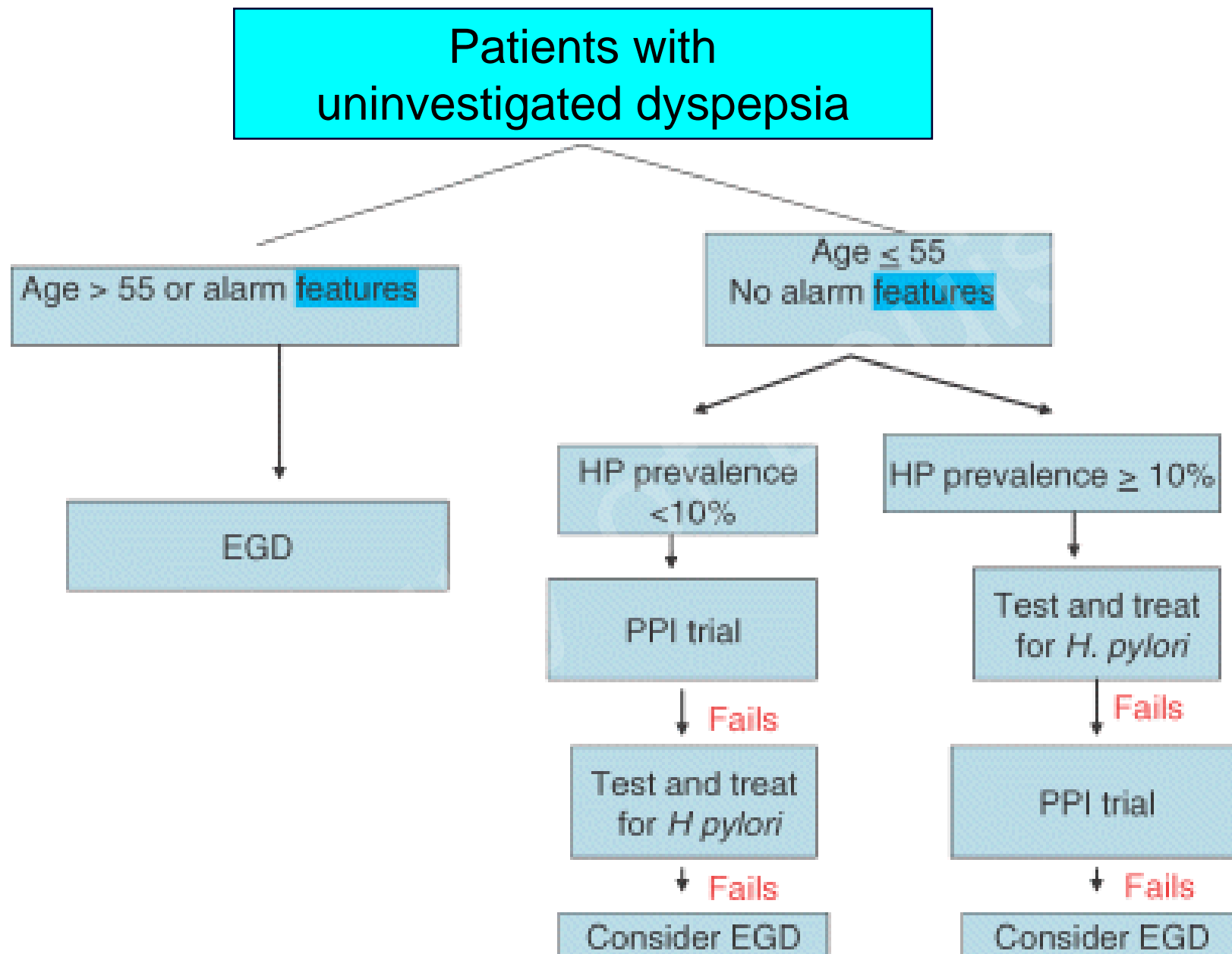
Acid-
suppression

Others

- Treat bacterial overgrowth
- Improve accommodation
 - Sildenafil (↑ NO-smooth muscle relaxation)
 - Buspirone (5-HT_{1A} agonist)
 - Sumatriptan (5-HT_{1P} agonist)
- Complimentary alternative medicine
- Prokinetics
- Psychologic intervention

Alarm Symptoms in Patients Presenting with Dyspepsia

- New onset at age >55 years
- Unexplained weight loss >10%
- Progressive dysphagia
- Gastrointestinal bleeding
- Iron deficiency anemia
- Persistent vomiting
- Previous esophagogastric cancer
- Previous documented peptic ulcer
- Family history of gastrointestinal cancer
- Lymphadenopathy or abdominal mass on exam



Test-and-Treat for *H. pylori* Strategy For Uninvestigated Dyspepsia

Accuracy of Tests for *H pylori* Infection

Parameter	Percentages	
	Sensitivity	Specificity
Urea Breath Test	94.7	95.7
Stool Antigen Test	93.1	92.8
Rapid Urease Test From Gastric Biopsy	71.1	87.6
Serum IgG Antibody	85.0	79.0

Uninvestigated Dyspepsia: 1-Year Follow-Up

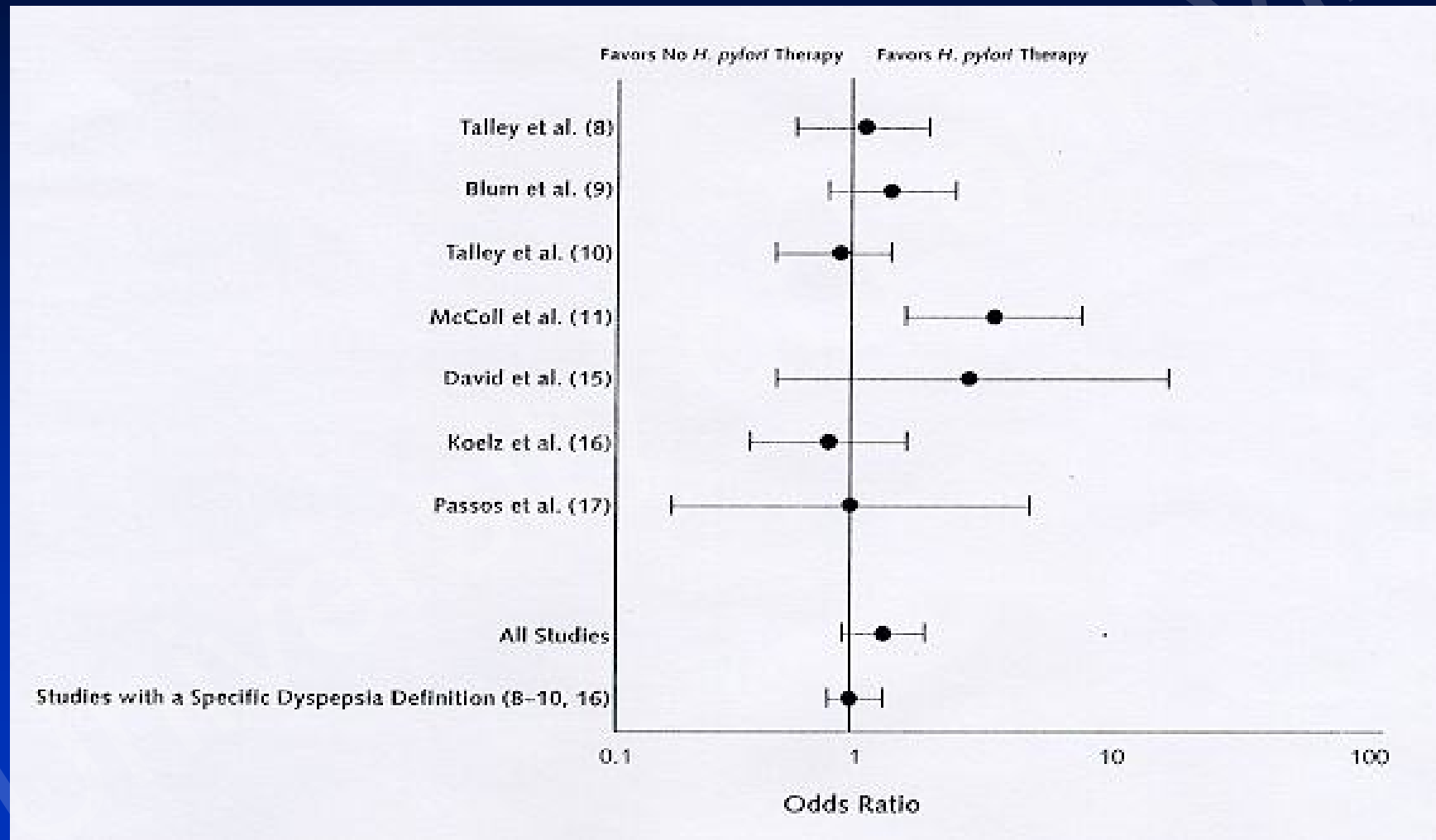
	Test-and-Treat n = 223	Endoscopy n = 224
Symptom-Free	50%	55%
Average Doctor Visits per Year	0.98	0.66
PPI Therapy	52	59
Endoscopies/Patients	0.50	1.25*
Dissatisfied With Care	12%	4%†

* $P < 0.0001$; † $P < 0.013$.

Lassen et al. *Lancet*. 2000;356:455-460.

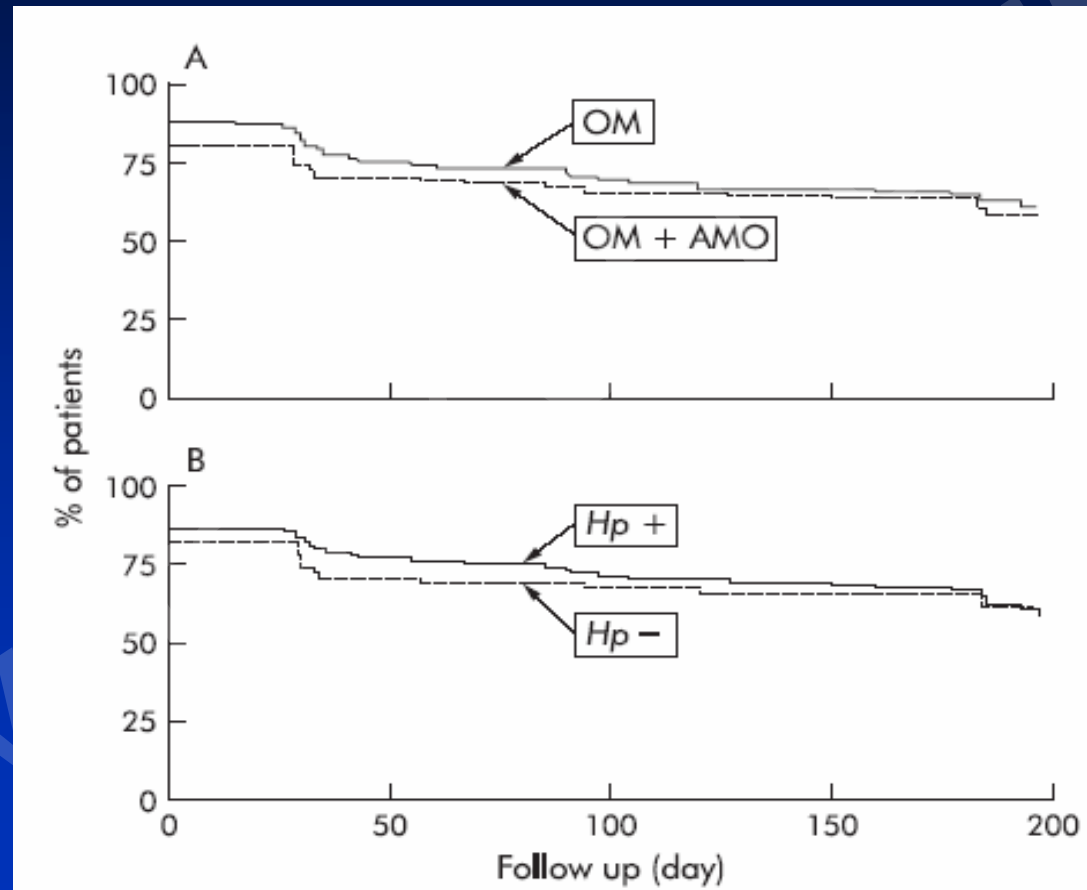
H. Pylori Treatment for Functional (Non-Ulcer) Dyspepsia

Benefit of *H. Pylori* Therapy for Functional Dyspepsia is Minimal



H. Pylori Treatment for FD

% of patients in remission

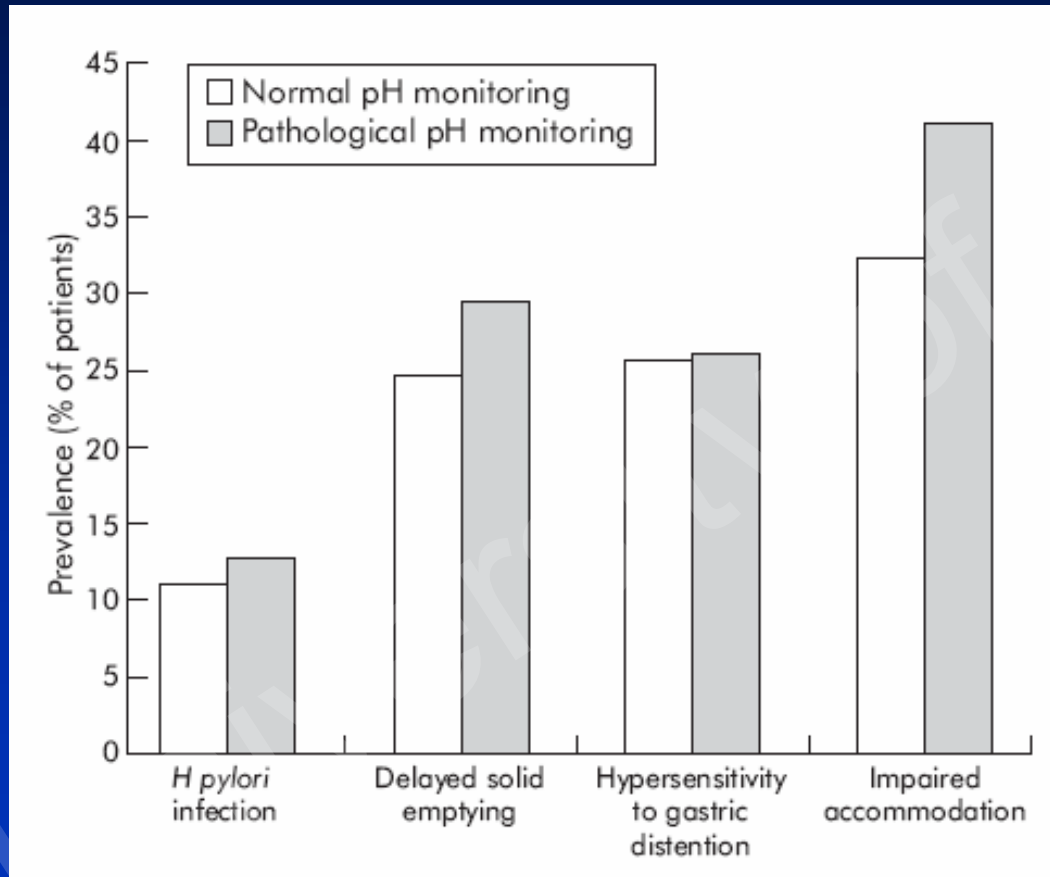


H. Pylori and Functional Dyspepsia

- No significant evidence to show:
 - H. pylori causes FD or
 - H. pylori treatment improves FD or
 - H. pylori eradication success did not correlate with treatment success

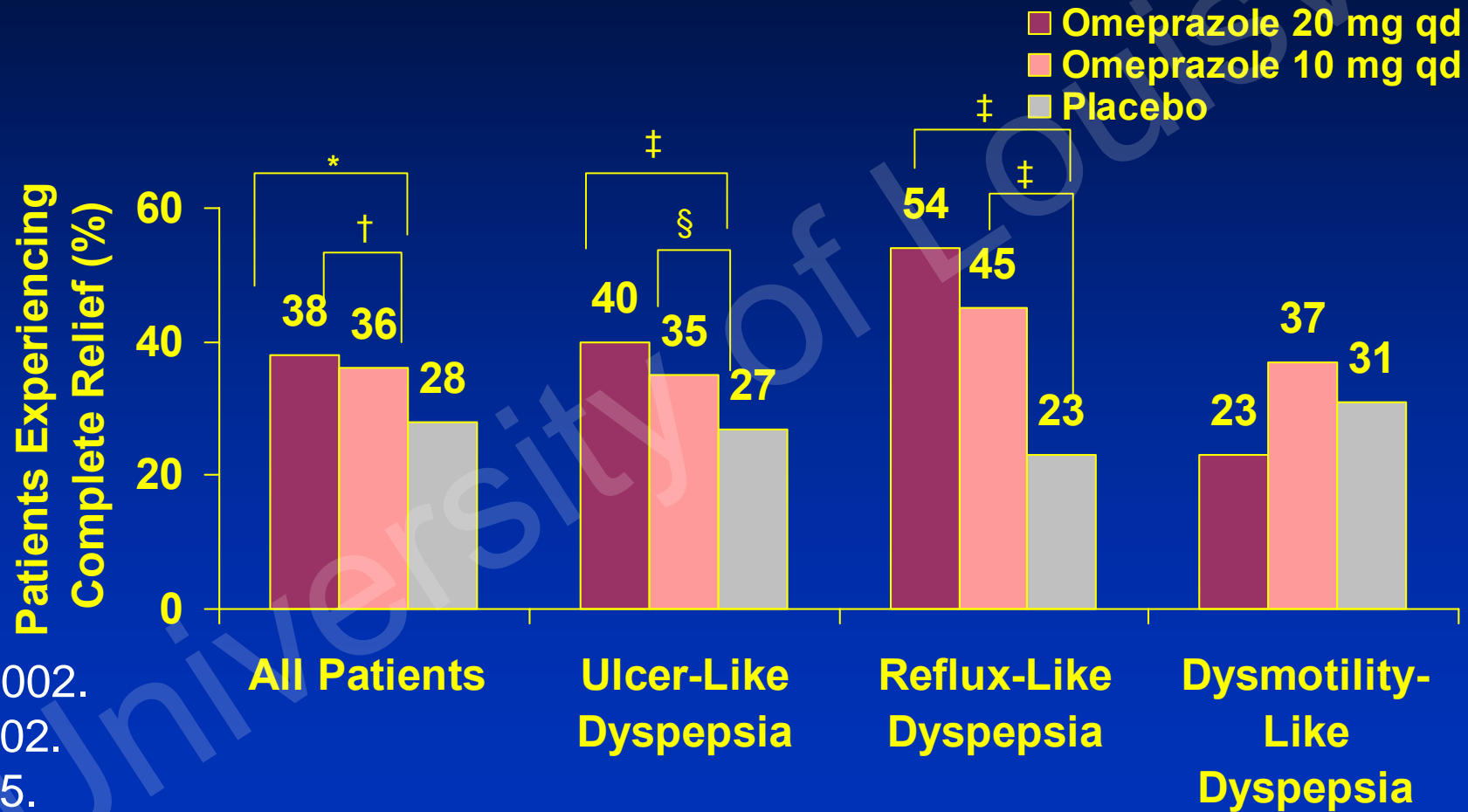
Acid Suppression Therapy for Functional Dyspepsia

Prevalence of GERD in FD



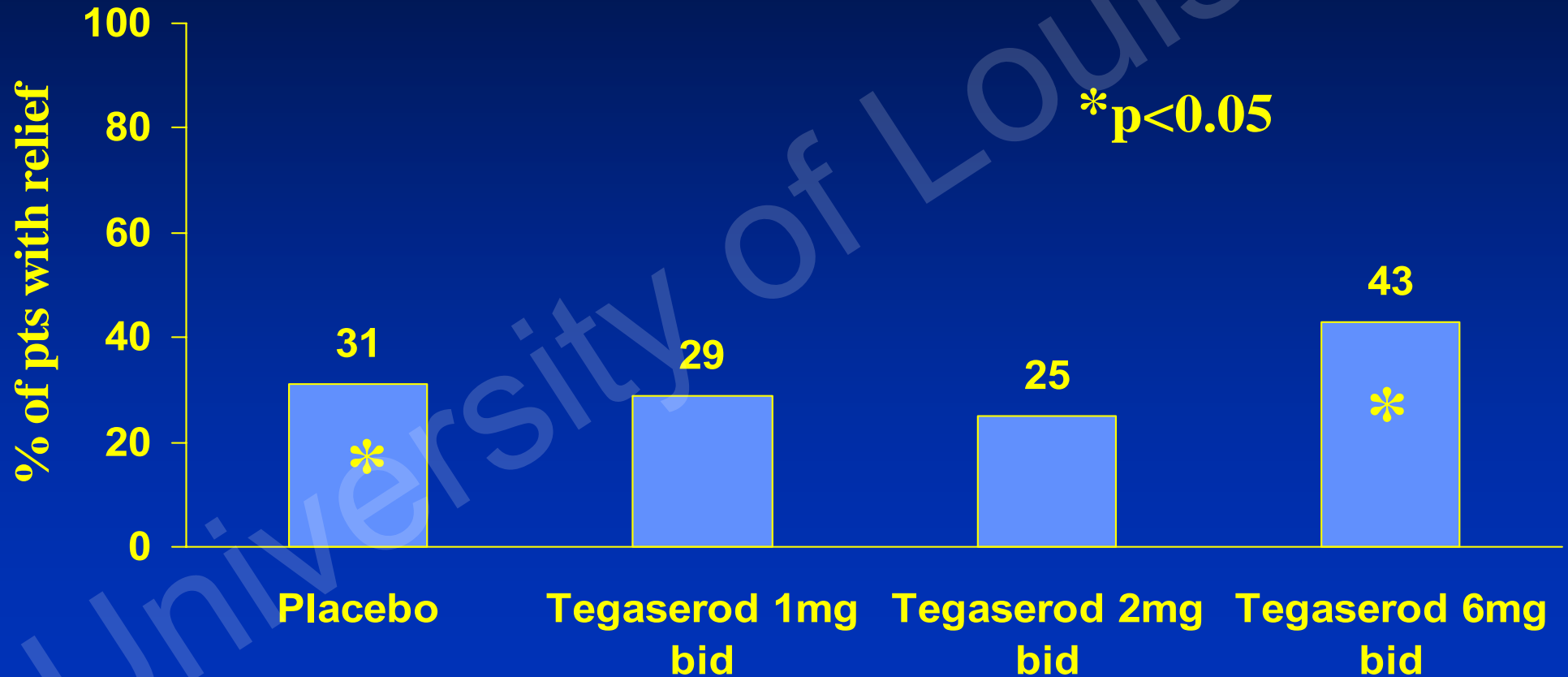
N=247 pts with FD without dominant heartburn

Acid Suppression Therapy for Functional Dyspepsia is Suboptimal



Prokinetics for Functional Dyspepsia

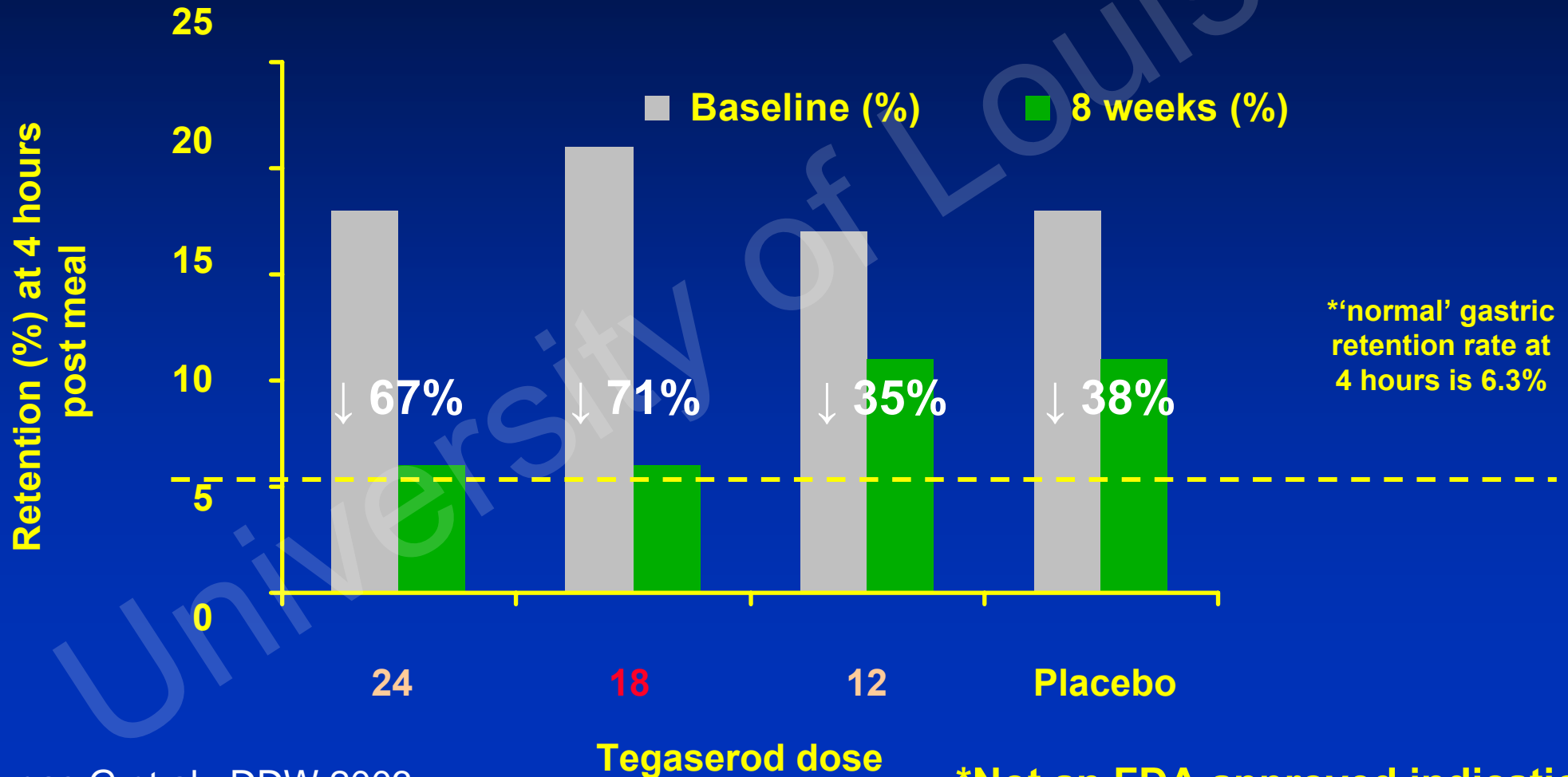
Tegaserod (*Zelnorm) for Functional Dyspepsia with Normal Gastric Emptying



Tack J et al. DDW 2002 (N=271, 71% females, normal EGD and 4-hr GET)

***Not an FDA approved indication**

Tegaserod (*Zelnorm) for Functional Dyspepsia with Delayed Gastric Emptying



Complimentary Alternative Medicine

University of Louisville

Iberis amara
(Annual Candytuft, Clown's Mustard)



STW-5 (Iberogast®)

Nine herbal extracts

- Clown's Mustard (*Iberis amara*)
- Peppermint leaves
- Caraway fruit
- Angelica root
- Milk thistle fruit
- Greater celandine
- Liquorice root
- Camomile flowers
- Lemon balm leaves



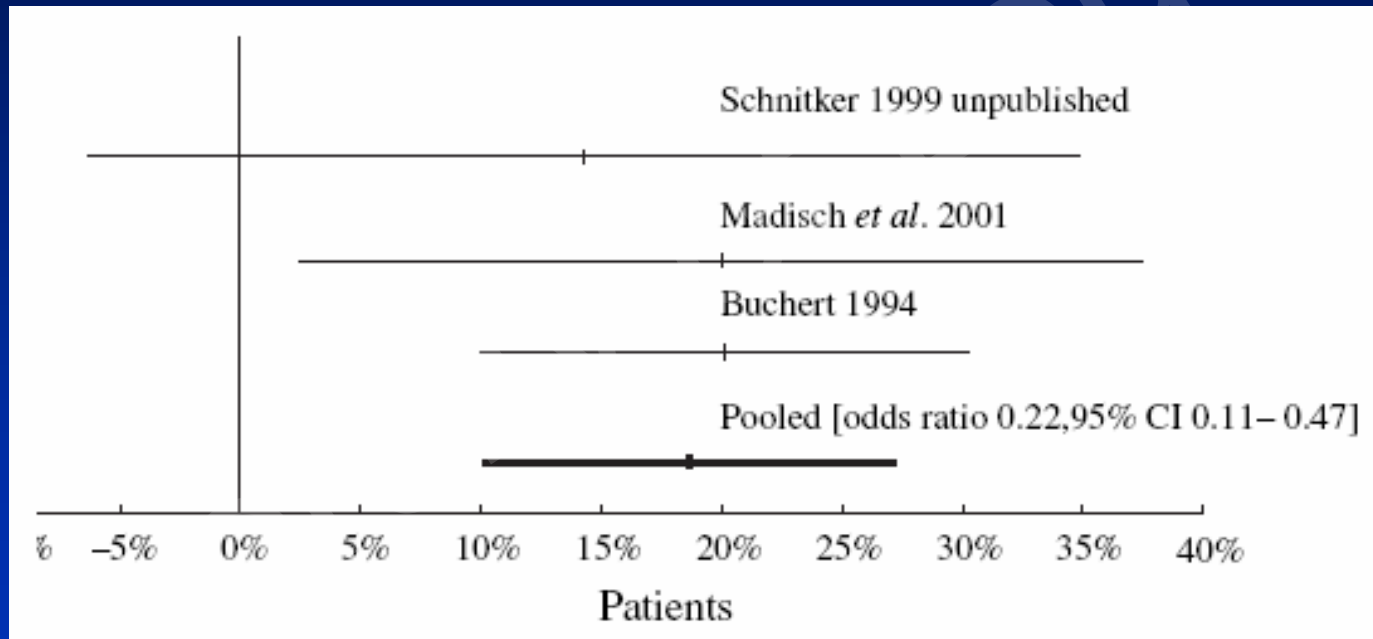
20 drops tid

~~\$49.95~~
\$29.71

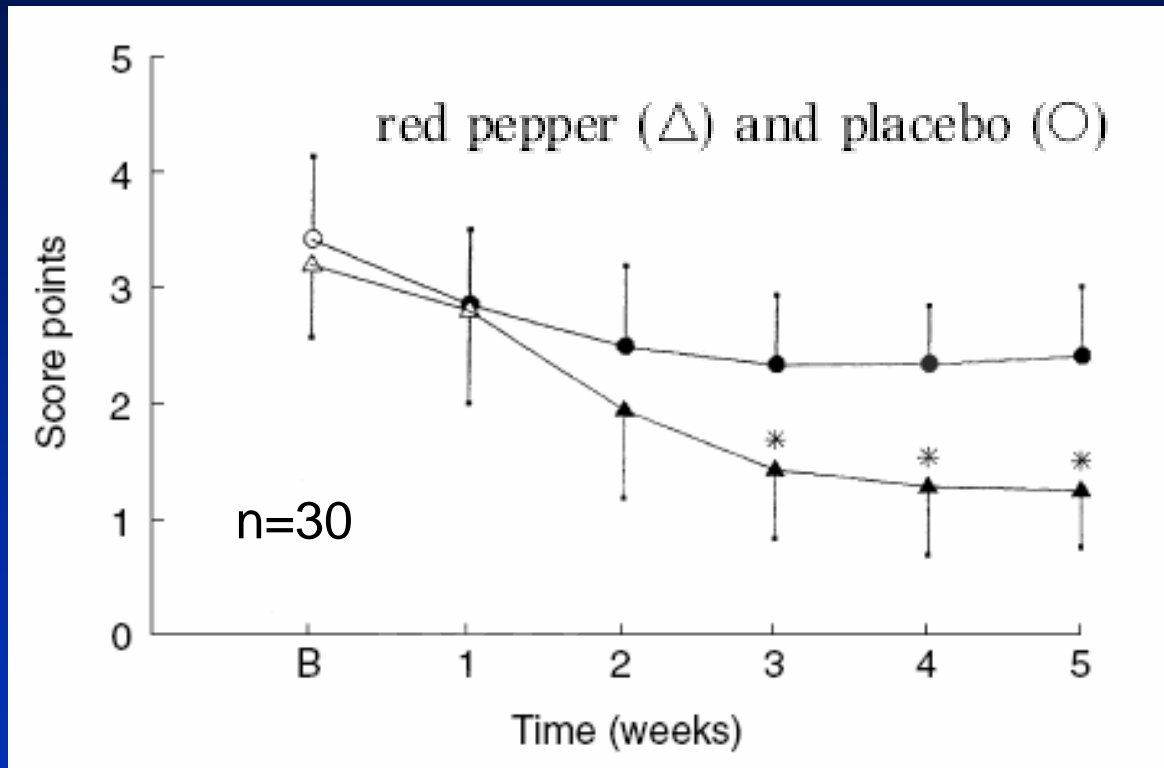
STW 5 in Guinea-Pig

- Fundus and corpus muscle strips
 - Dose-dependently relaxation of circular and longitudinal muscle
- Antral muscle strips
 - Increase contraction
- Effects resistant to tetrodotoxin, atropine, capsaicin
 - Pathways not involving nitric oxide or vagus
- STW 5 alters gastric motility in a region-specific manner, may improve:
 - Impaired fundus accommodation
 - Antral hypomotility

Phytotherapy of Functional Dyspepsia with STW 5 (Iberogast)



Red Pepper (Capsaicin) for FD



Red pepper powder
0.5 g capsules - 5 per day
vs.
Placebo (tomato powder)



Summary: Functional Dyspepsia

- “Patient needs a doctor, not an endoscopist”
- Investigated vs. Uninvestigated dyspepsia
- Differentiate postprandial distress vs. epigastric pain syndrome
- PPI OK, H. Pylori treatment not helpful in FD
- Valid role for CAM