

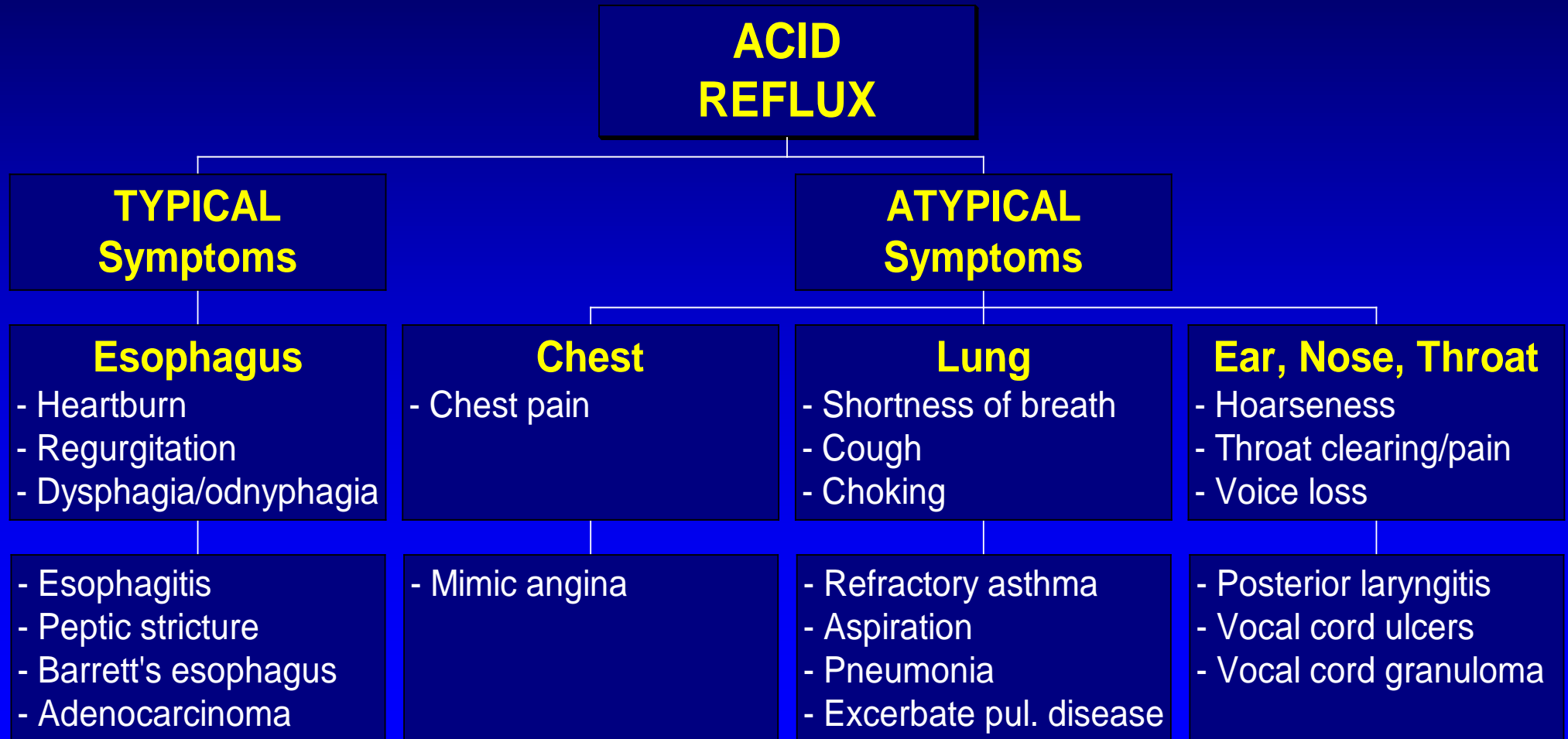
Chronic Cough and Laryngopharyngeal Reflux

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Acid Reflux is More Than Just Heartburn



Typical vs. Atypical GERD

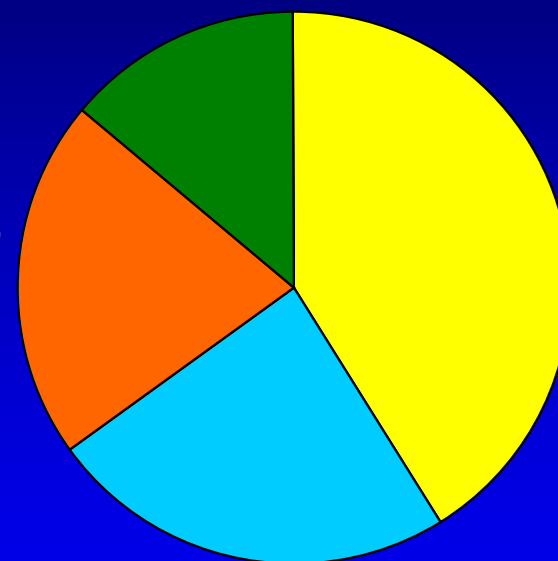
	<u>Typical</u>	<u>Atypical</u>
Symptoms	consistent	variable
Esophagitis/Barrett's	common	uncommon
Causes	reflux	reflux + multifactorial
Treatment response	rapid	variable
Therapy	step-therapy	more aggressive + longer duration

Causes of Chronic Cough

Other
14%

Postnasal
drip
41%

GERD
21%



Asthma
24%

102 patients with
chronic cough

Other causes

- Chronic bronchitis (5%)
- Bronchiectasis (4%)
- Drug induced
- Pulmonary tumors
- Restrictive lung disease
- Postviral
- Aspiration
- Psychogenic

GERD-Related Chronic Cough

- Most patients with GERD-related chronic cough have “silent reflux” without heartburn or regurgitation²³
- Character and timing of cough do not reliably distinguish GERD from other causes²⁰

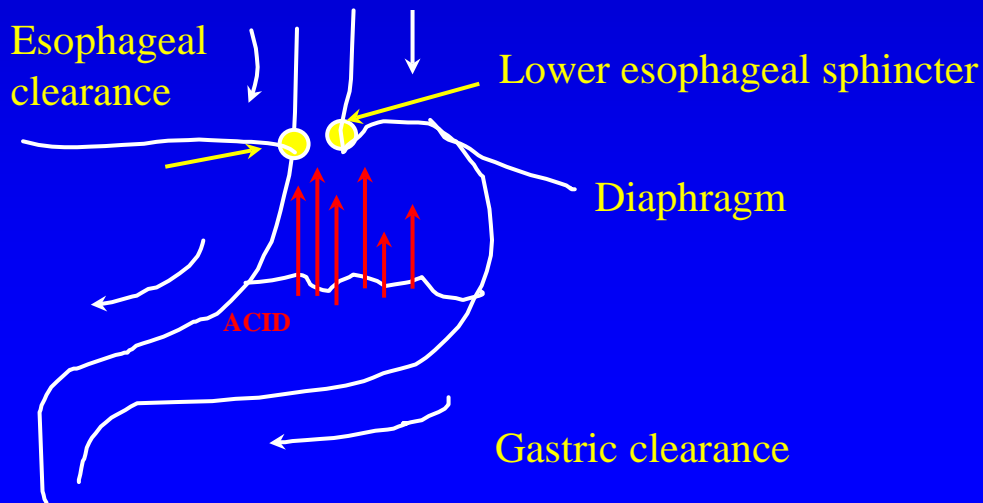
²³Irwin RS et al. Chest 1993;104:1511-7.

²⁰Mello et al. Arch Intern Med 1996;156:997-1003.

Pathophysiology

Protective Mechanisms and Etiology

Gastroesophageal Factors



UES Factors

UES
Neural reflexes

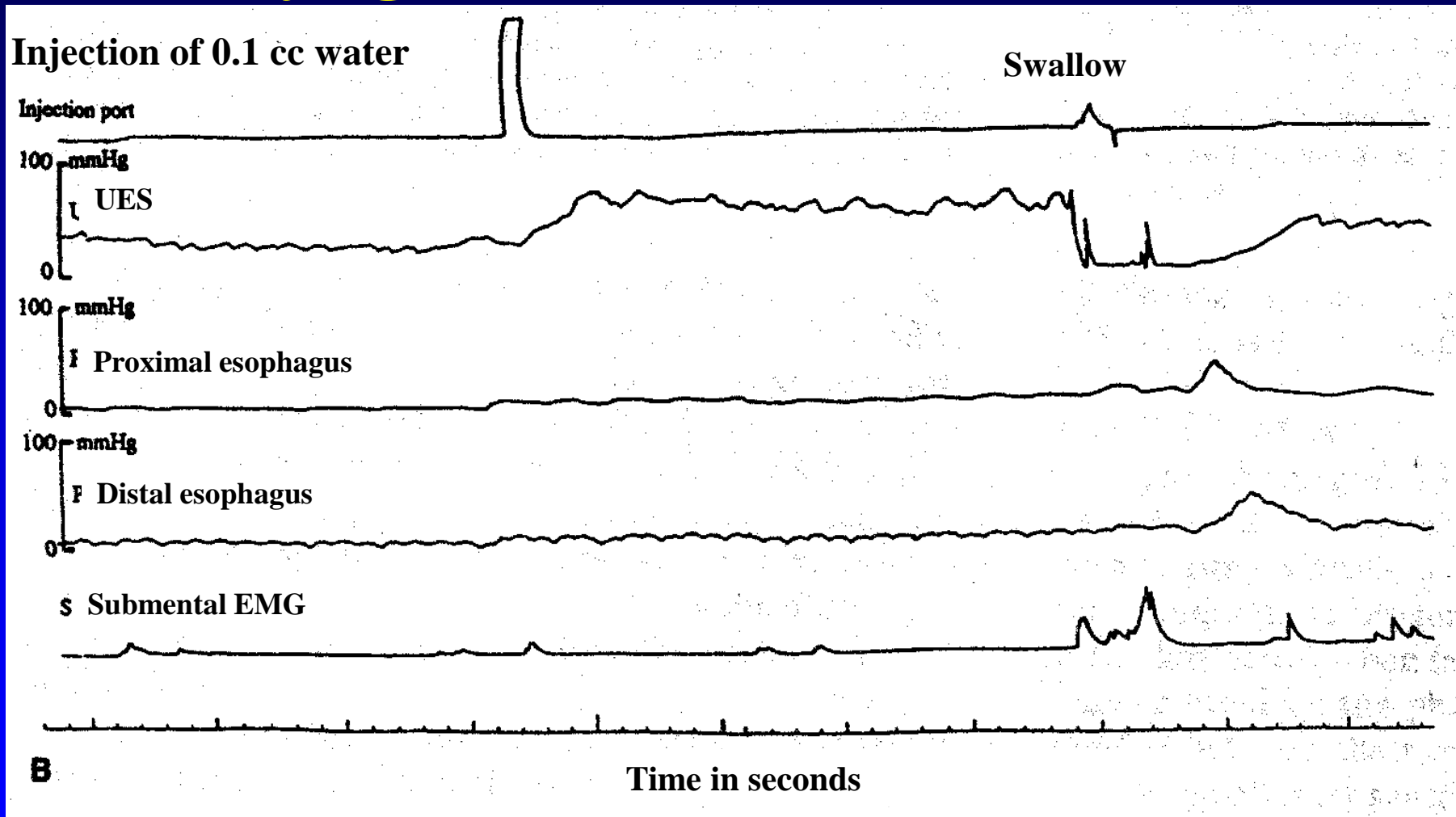
Supraesophageal Factors

Pharyngeal clearance
Neural reflexes
Mucosal resistance
Hyposensitivity
Sinusitis
Allergies
Voice abuse
Environmental
Airway hyperactivity
Aspiration

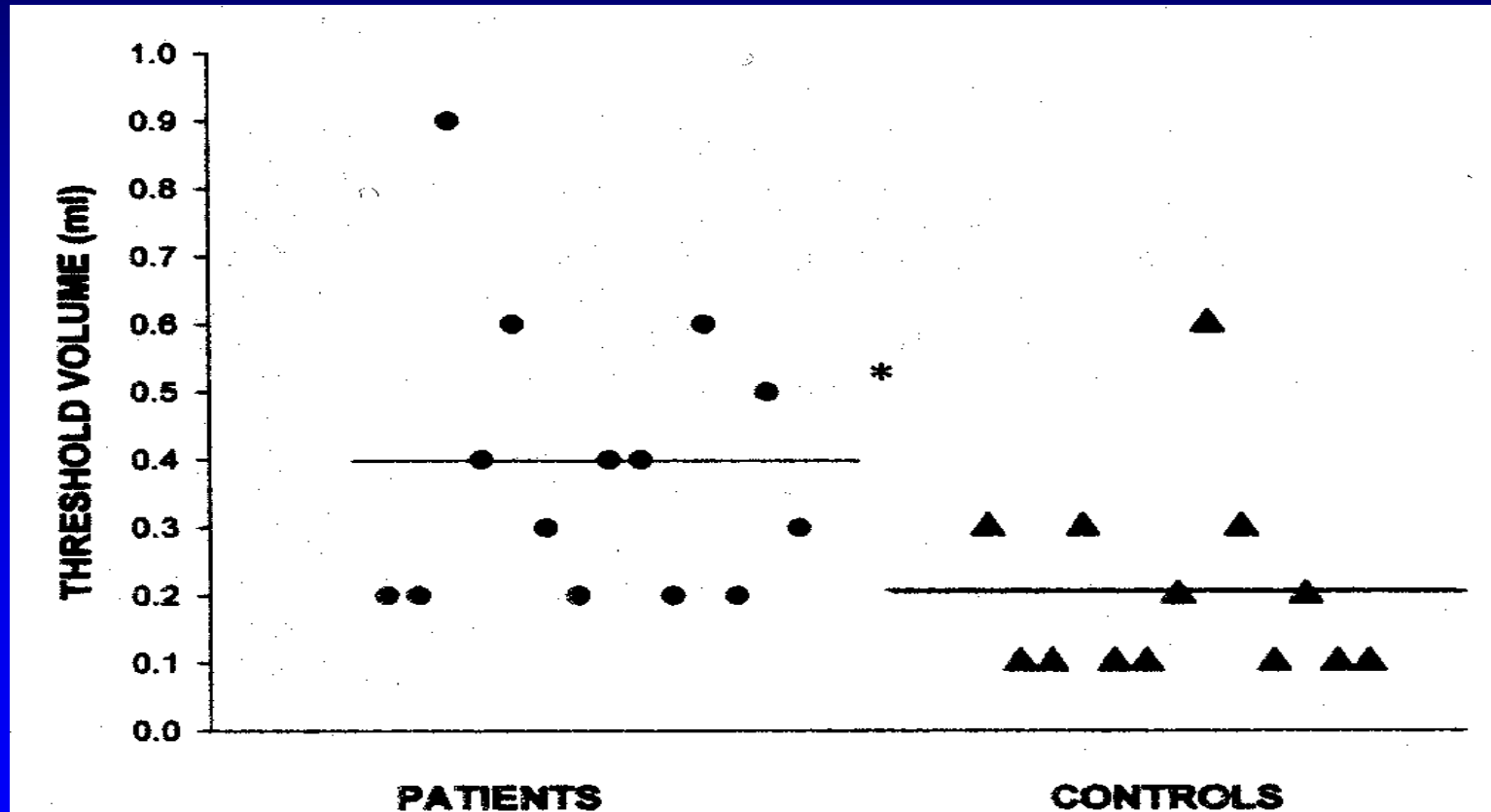
Upper Esophageal Sphincter (UES)

- UES is composed of striated muscles
- Not affected by traditional acid reflux factors
- Affected by many neuro-pathways

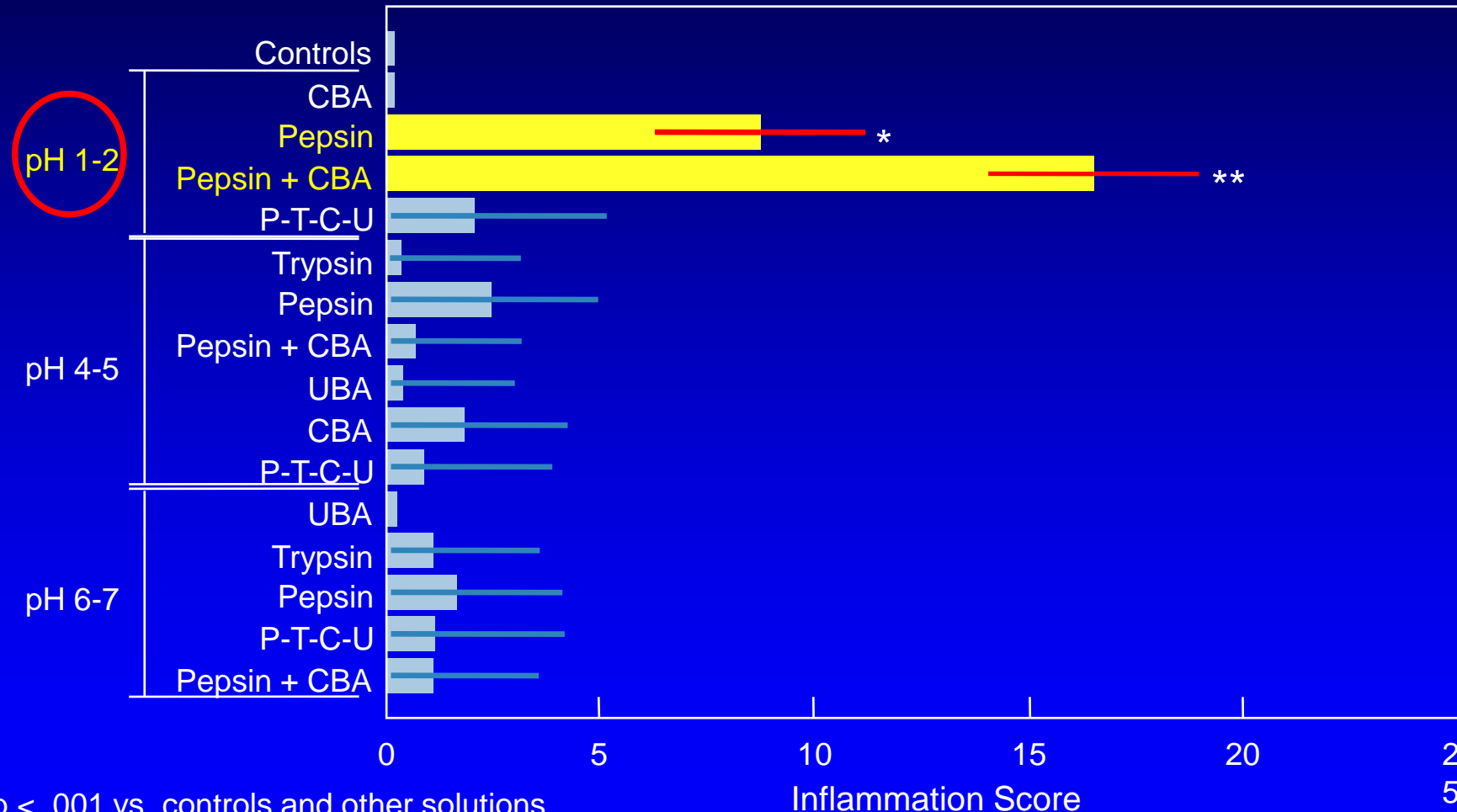
Protective Mechanisms for LPR: Pharyngo-UES Contractile Reflex



Threshold for Triggering Pharyngo-UES Contractile Reflex



Dog Model of LPR



* p < .001 vs. controls and other solutions
 **p < .001 vs. pepsin (pH 1.5)

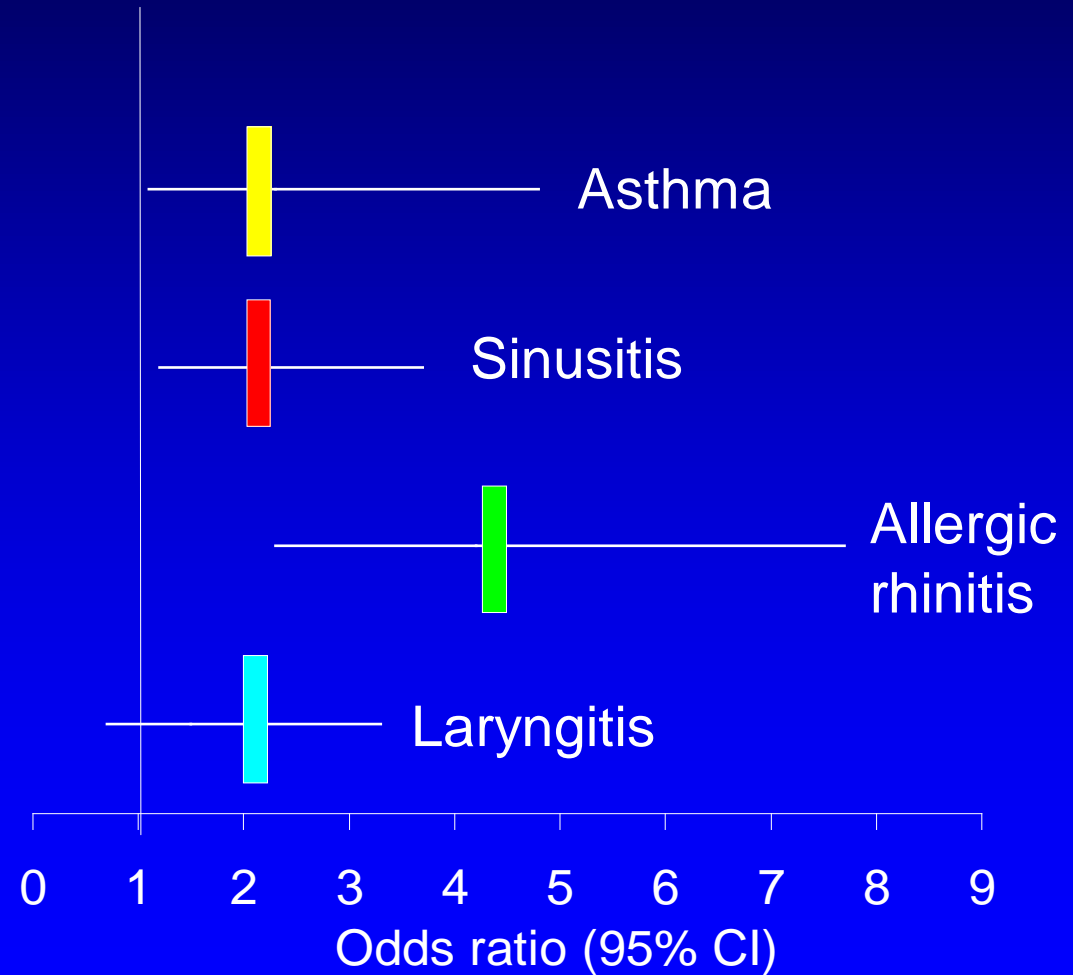
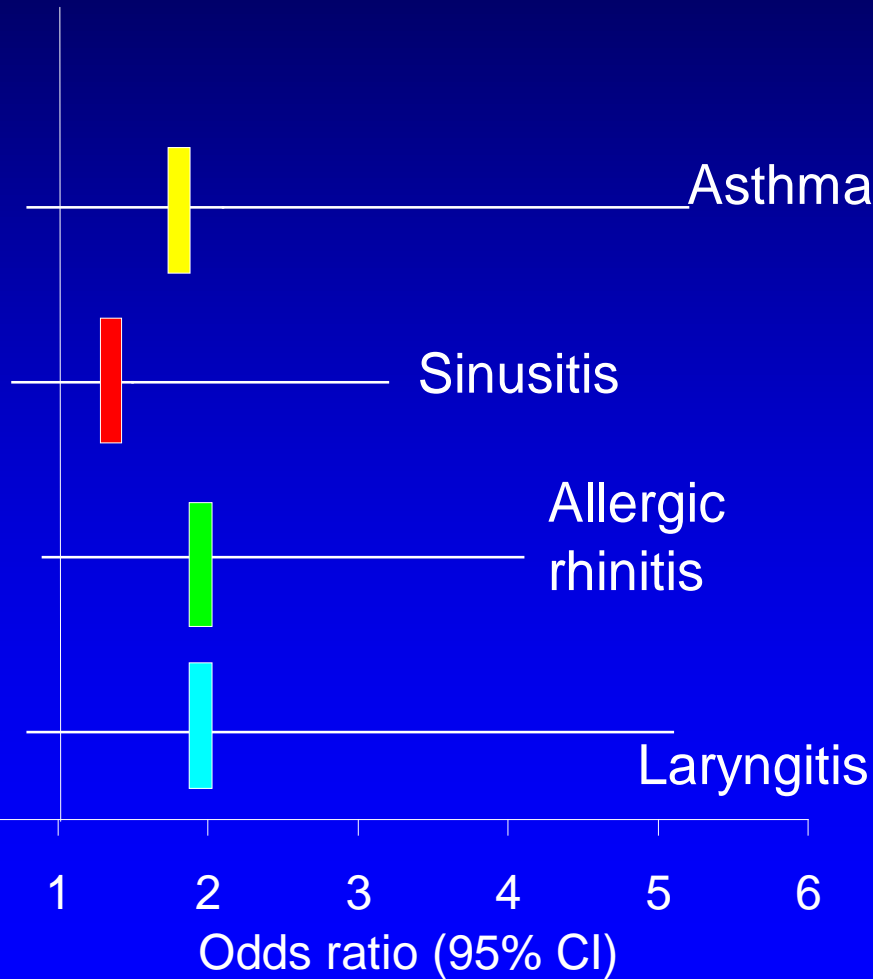
Causes of LPR are Multifactorial

- GI
 - Gastroesophageal reflux, impaired esophageal peristalsis, gastroparesis
- ENT
 - Voice abuse, vocal dysfunction, vocal granuloma, laryngeal carcinoma, sinusitis, post nasal drip
- Others
 - Impaired reflex, impaired sensation, irritants, allergy, psychological

Diagnosis Associated with LPR

Untreated LPR subjects (n=49) vs. normal volunteers (n=119)

Treated LPR subjects (n=118) vs. normal volunteers (n=119)



Symptoms and Management

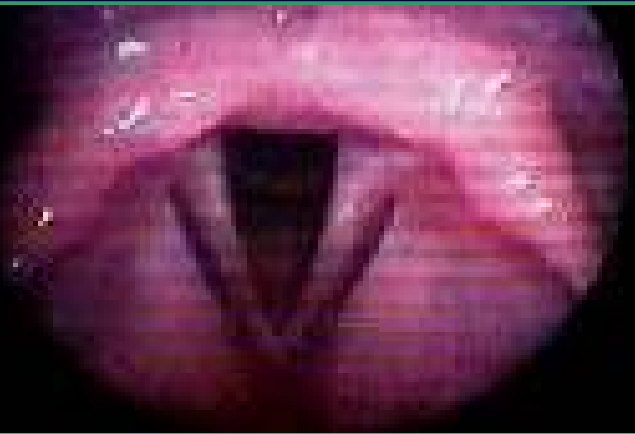
Typical Profile of Patients with GERD-Related Chronic Cough

- No exposure to environmental irritants
- Non-smoker
- Not on angiotensin-converting enzyme inhibitor
- Normal or stable chest X-ray
- Nocturnal cough
- Asthma, post-nasal drip have been excluded

Symptoms of LPR are not Specific

- Hoarseness
- Globus
- Sore throat
- Throat clearing
- Excessive throat mucus
- Cough
- Throat burning/pain
- Voice weakness
- Cervical dysphagia
- Heartburn (6-50%)

Laryngeal Signs of LPR



Normal Laryngeal Tissue



True Vocal Fold Erythema



Bilateral True Vocal Fold Nodules



Reinke's Edema

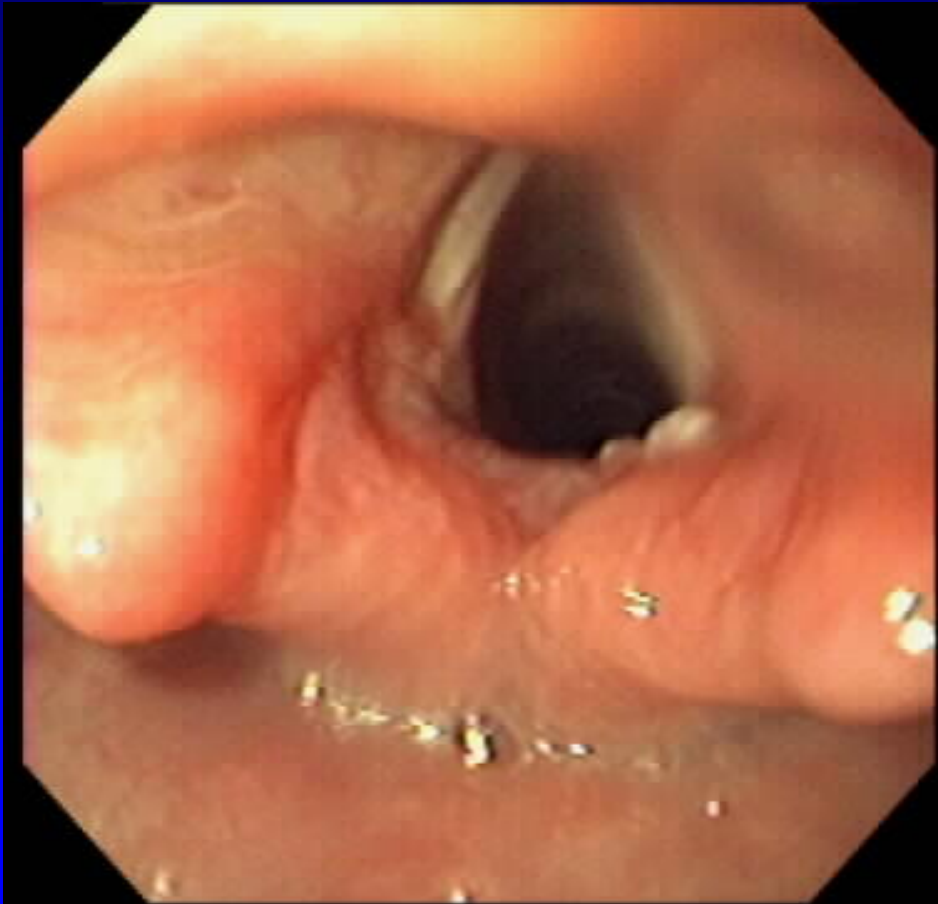


Arytenoid Medial Wall Edema



Posterior Pharyngeal Wall Cobblestoning

Vocal Cord Granuloma



Laryngoscopic Exam in Normal Volunteers

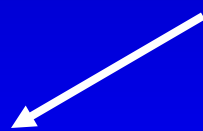
<u>ENT Findings</u>	<u>Prevalence</u>
Interarytenoid bar	35/50 (70%)
Arytenoid medial wall erythema	20/50 (40%)
Posterior pharyngeal wall cobblestoning	10/50 (20%)
Arytenoid medial wall granularity	7/50 (14%)
True vocal cord erythema	5/50 (10%)



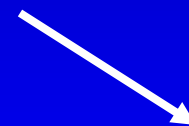
**Empiric
Antireflux
Therapy**



**Patients with
Suspected GERD**



**Upper
Endoscopy**



**Ambulatory
pH testing**

Empiric Antireflux Therapy for Chronic Cough

- Empiric trial of antireflux therapy is indicated if
 - Patient meets clinical profile of GERD-related chronic cough, or
- Twice-daily PPI is reasonable
- Response to empiric PPI is 50-70%
- Failure of empiric trial does not rule out GERD

Empiric Antireflux Therapy for LPR

- Approximately 60% response rate for empiric high dose PPI for 3-4 months
- No reliable indicators to predict response
 - demographics, presence of heartburn, laryngeal exam, +pH test

Diagnostic Testing for GERD*

	Sensitivity (%)	Specificity (%)
Empiric Trial With a PPI	70-80	60-85
Endoscopy	40-70	90-95
Esophageal pH Monitoring	70-90	80-95
Barium Swallow	30-35	60-75
Esophageal Manometry	15-30	20-40

*Depends on clinical suspicion

Upper Endoscopy in Patients with Chronic Cough

- Only 16% of patients with chronic cough had mucosal complications of GERD on endoscopy
- Given its low yield, endoscopy is not recommended as part of the initial workup

Ambulatory pH Monitoring in Patients with Chronic Cough

- Results of ambulatory pH testing do not predict response to PPI therapy²⁵
- It is difficult to prove a causal relationship between acid reflux and chronic cough
- Given these limitations, pH testing should be reserved for non-responders to empiric PPI therapy²⁶

²⁵Baldi F et al. World J Gastroenterol 2006;12:82-8.

²⁶Fass et al. Aliment Pharmacol Ther. 2004;20(Suppl. 9):26-38.

Different Types of Ambulatory Monitoring for GERD



**Transnasal probe
(pH-impedance, 24-hr)**

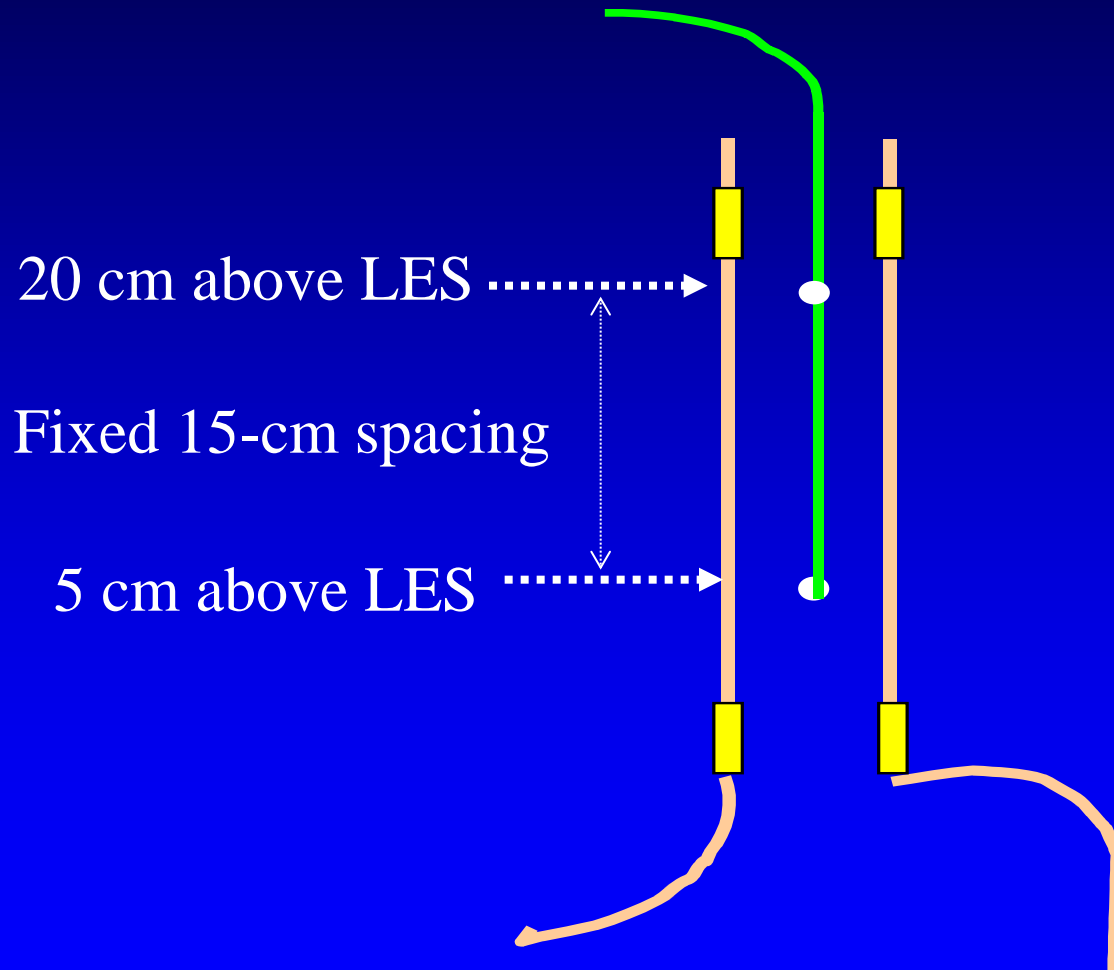


**Bravo Wireless Telemetry
(pH only, 48-hr or 96 hr)**

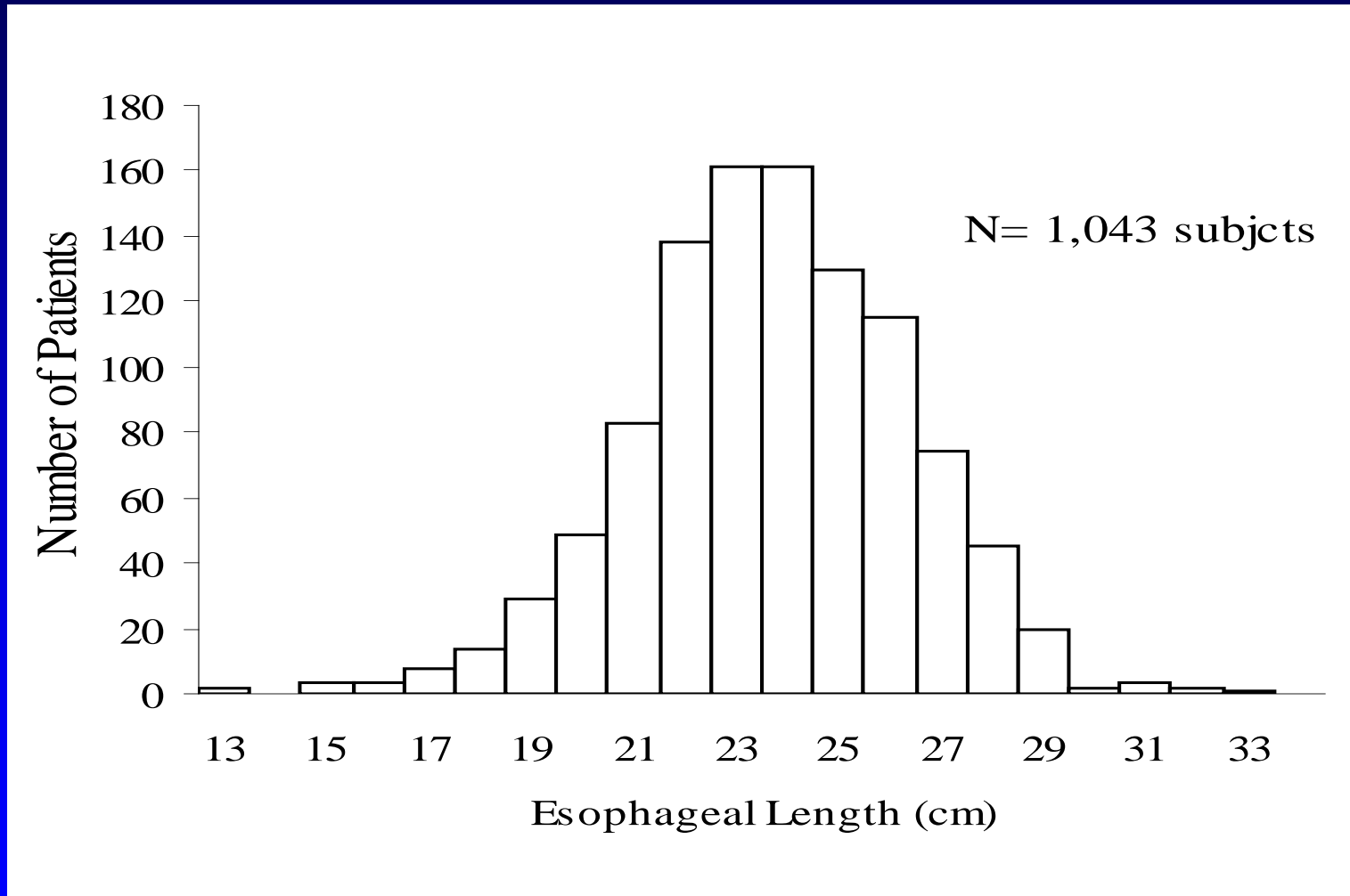


**Restech Aerosol Probe
(pH, 24-hr)**

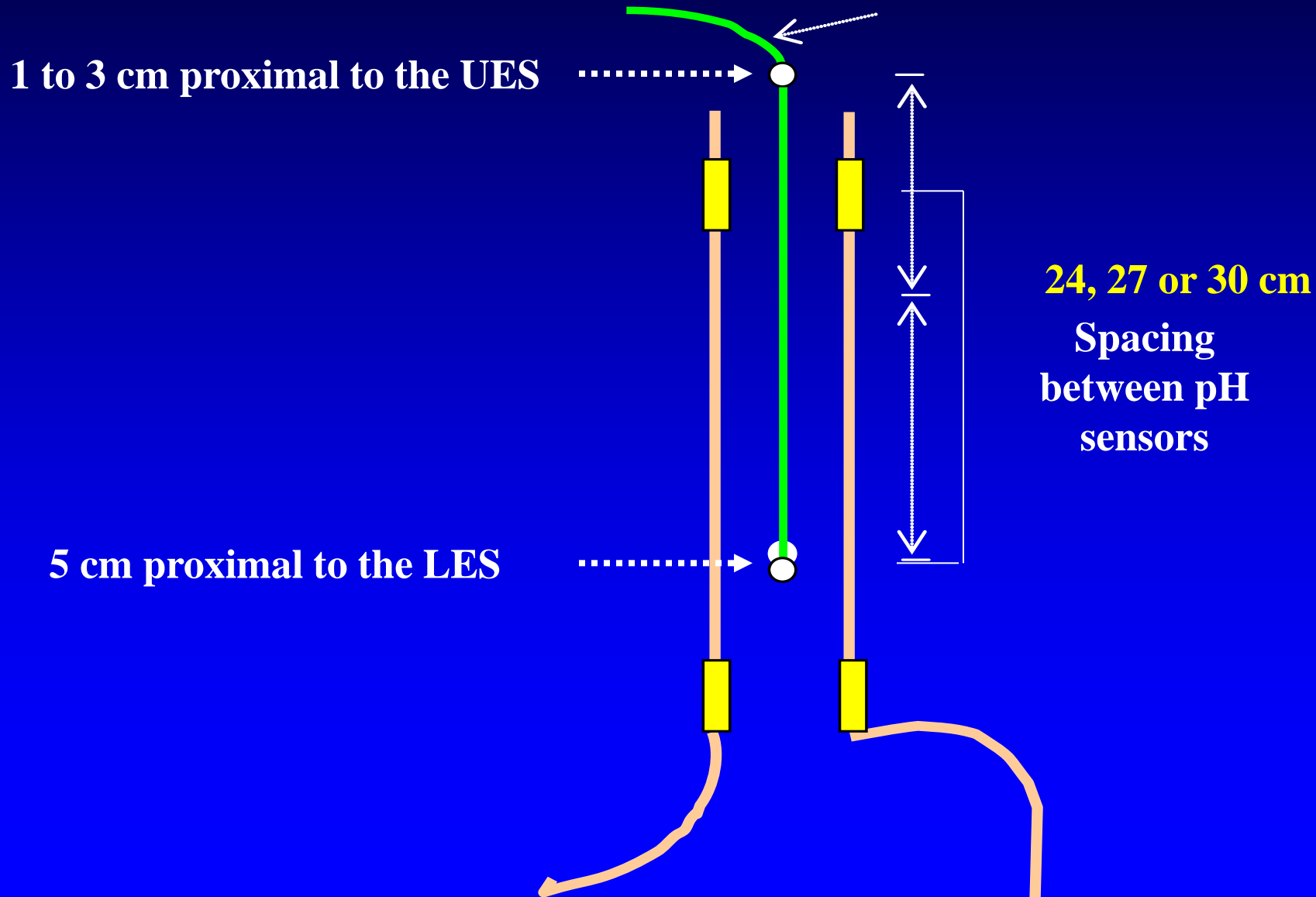
Traditional Ambulatory pH Monitoring: Proximal and Distal Esophagus



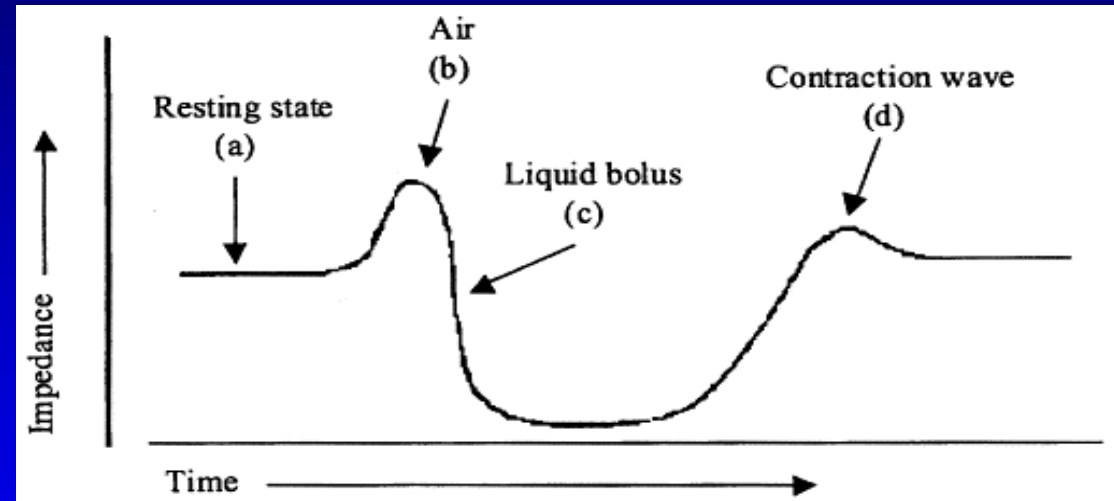
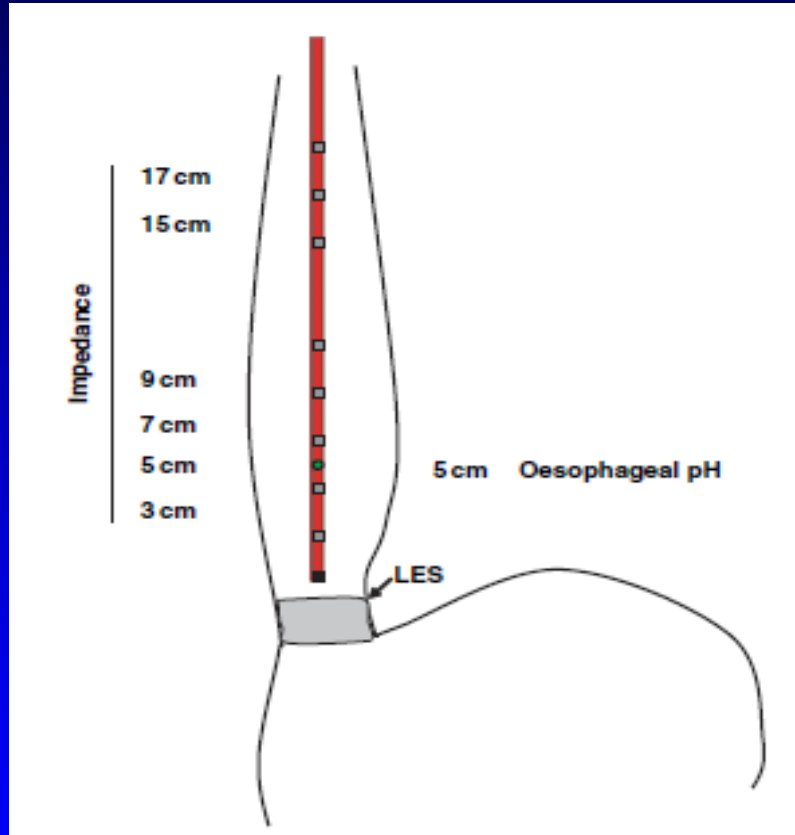
Esophageal Length Varies Among Individuals



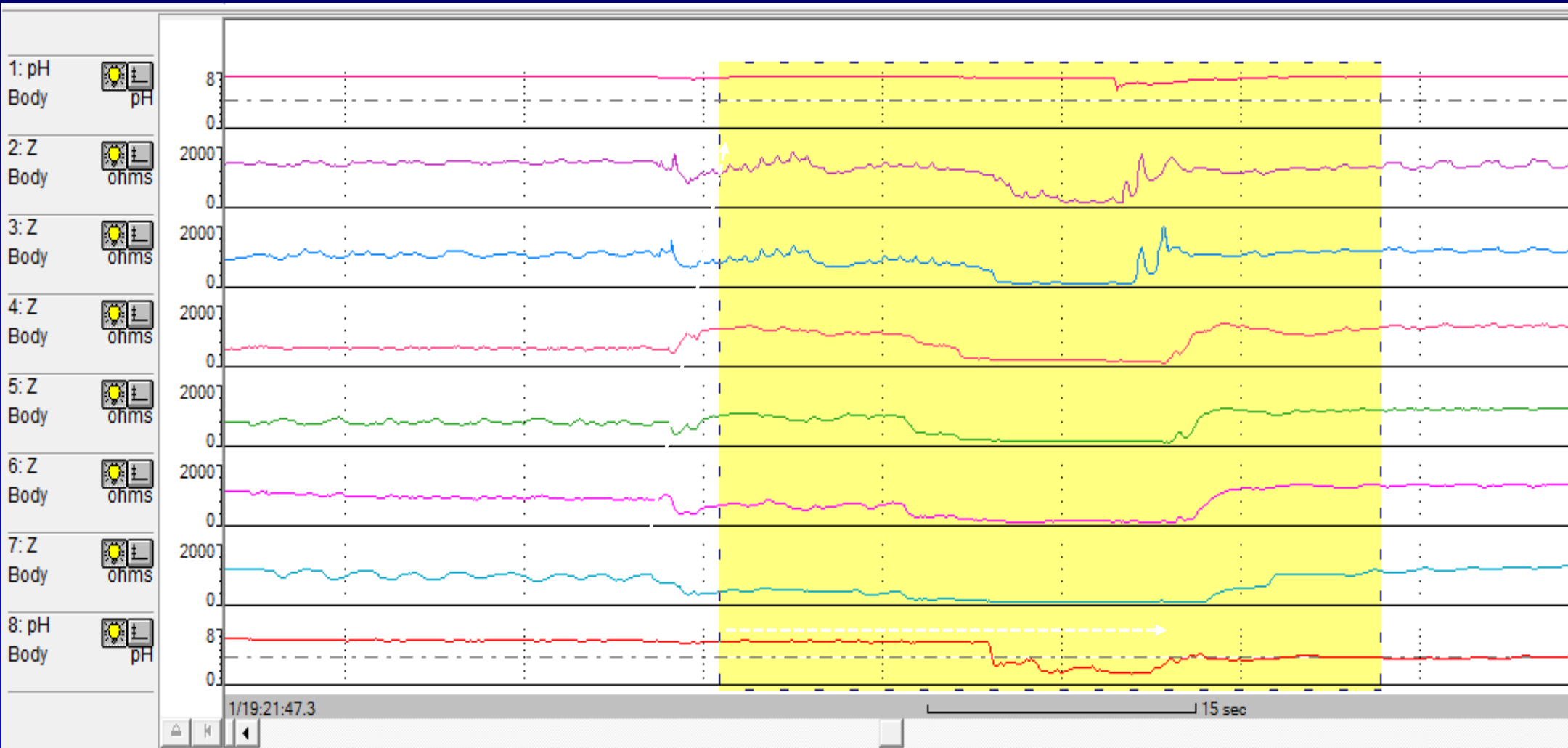
Single-Probe, Triple-sensor pH Monitoring for LPR



Ambulatory pH-Impedance Monitoring



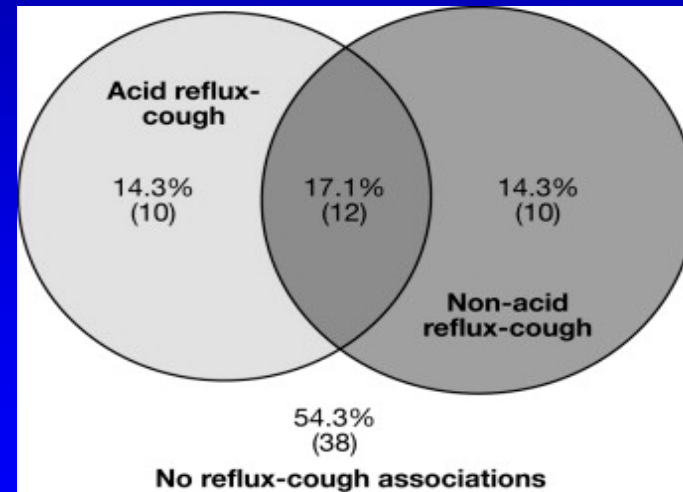
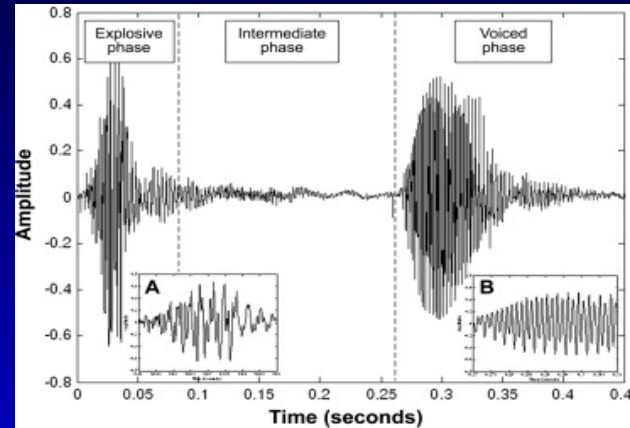
Ambulatory pH-Impedance Testing: Acid (pH<4), Weakly Acid (pH 4-7), Non-Acid reflux (pH>7)



How to order Ambulatory pH-Impedance Monitoring?

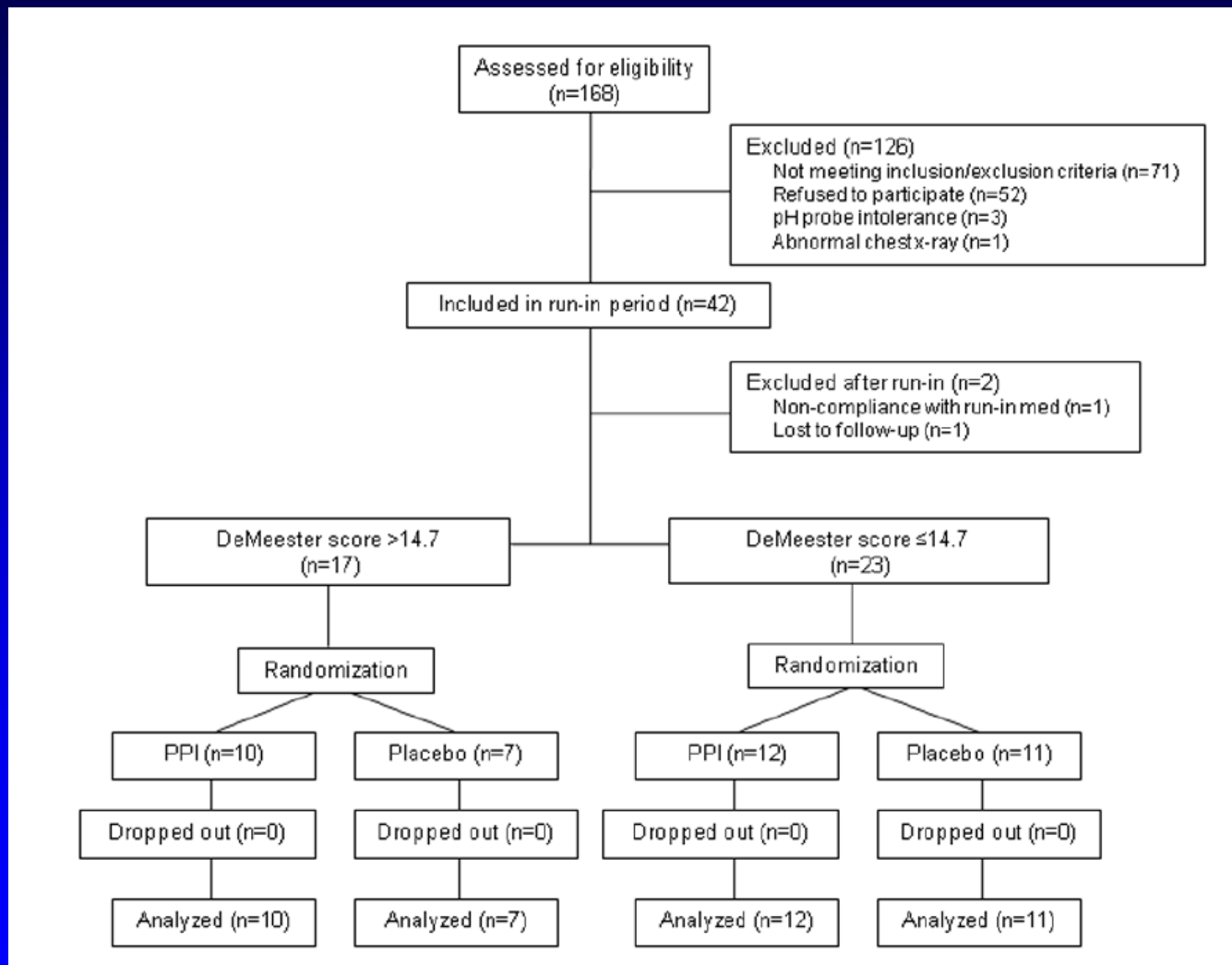
- Testing OFF PPI
 - Exclude GERD
- Testing ON PPI
 - Differentiate “adequate” vs. “inadequate” reflux suppression
 - Need a trial of sufficient therapy before test
 - 3 months of double-dose PPI
 - But still need correlation between symptoms & reflux

Reflux and Acoustic Monitoring for Chronic Cough:

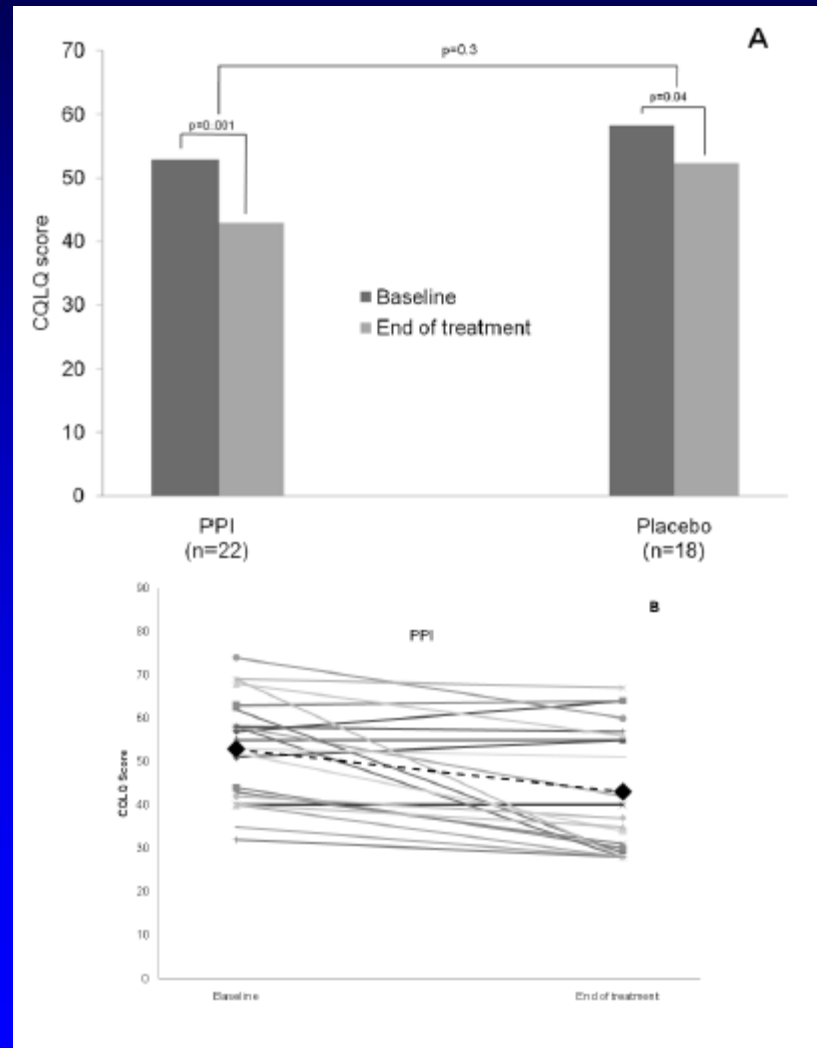


Treatment

RCT of PPI for Chronic Cough



RCT of PPI for Chronic Cough

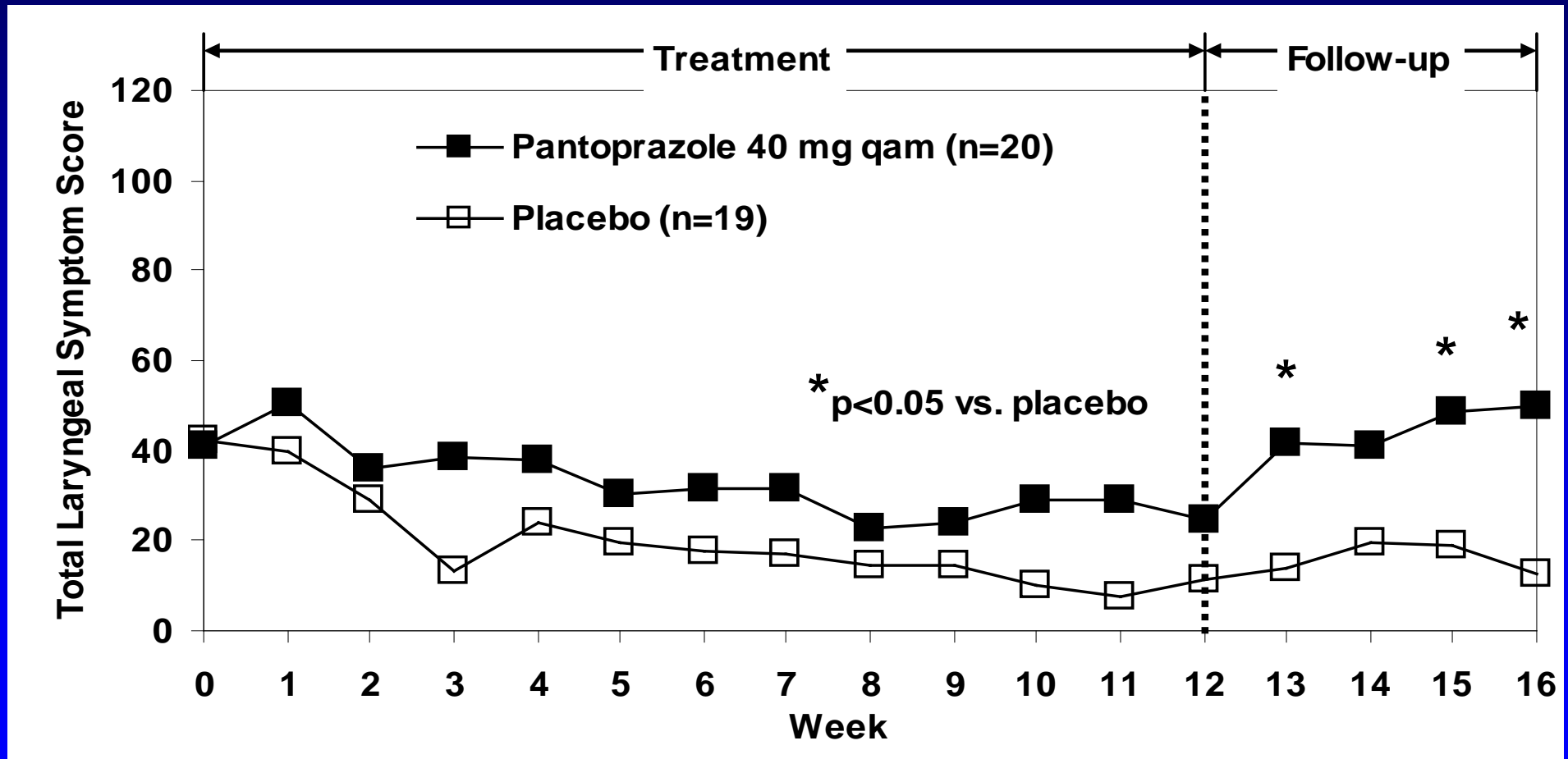


Antireflux Therapy for GERD-Related Chronic Cough

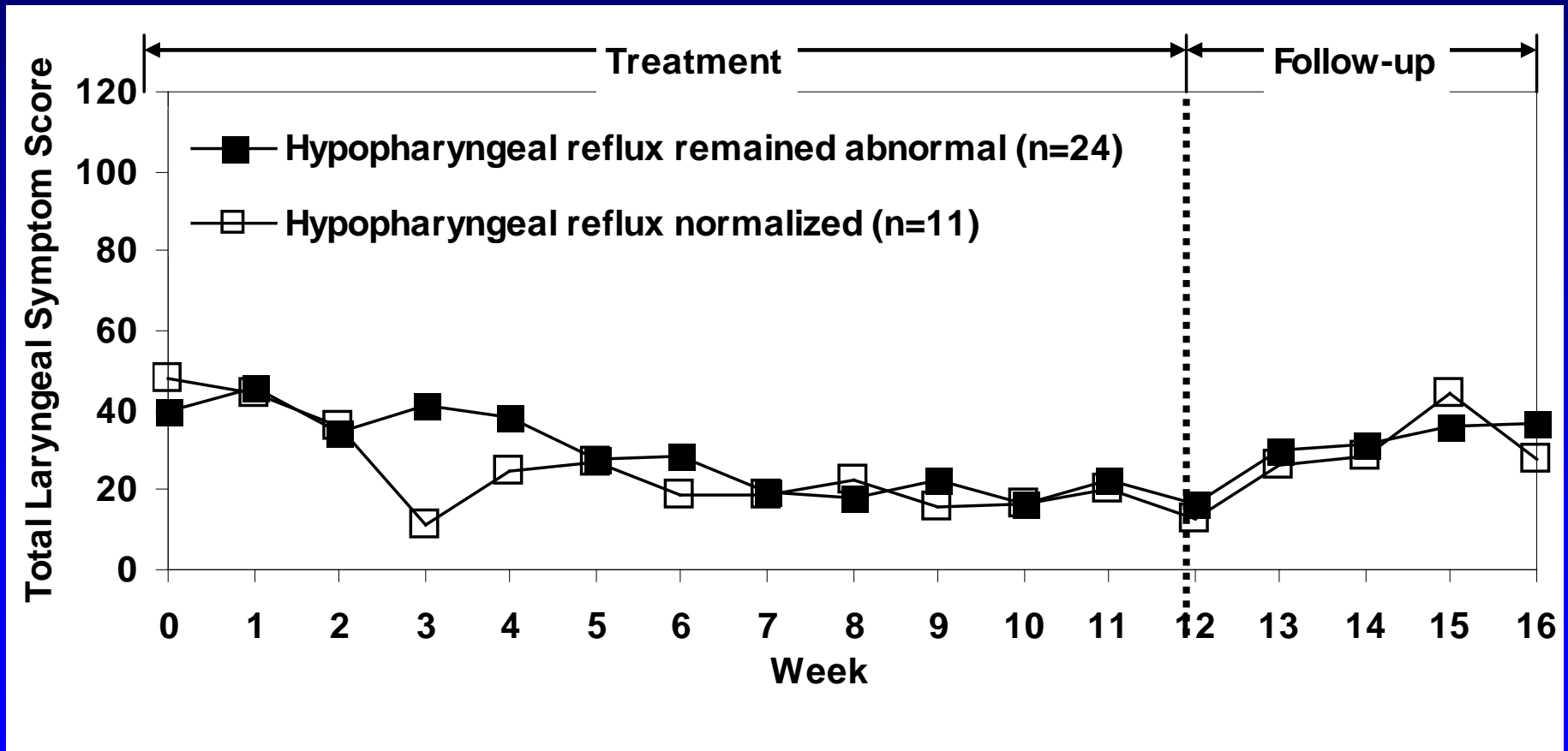
- Randomized controlled trials (RCTs) are limited; small numbers of patients
- Meta-analysis of RCTs in adults with GERD-related chronic cough gave inconclusive results¹

¹Chang et al. Cochrane Database Syst Rev 2005;CD004823.

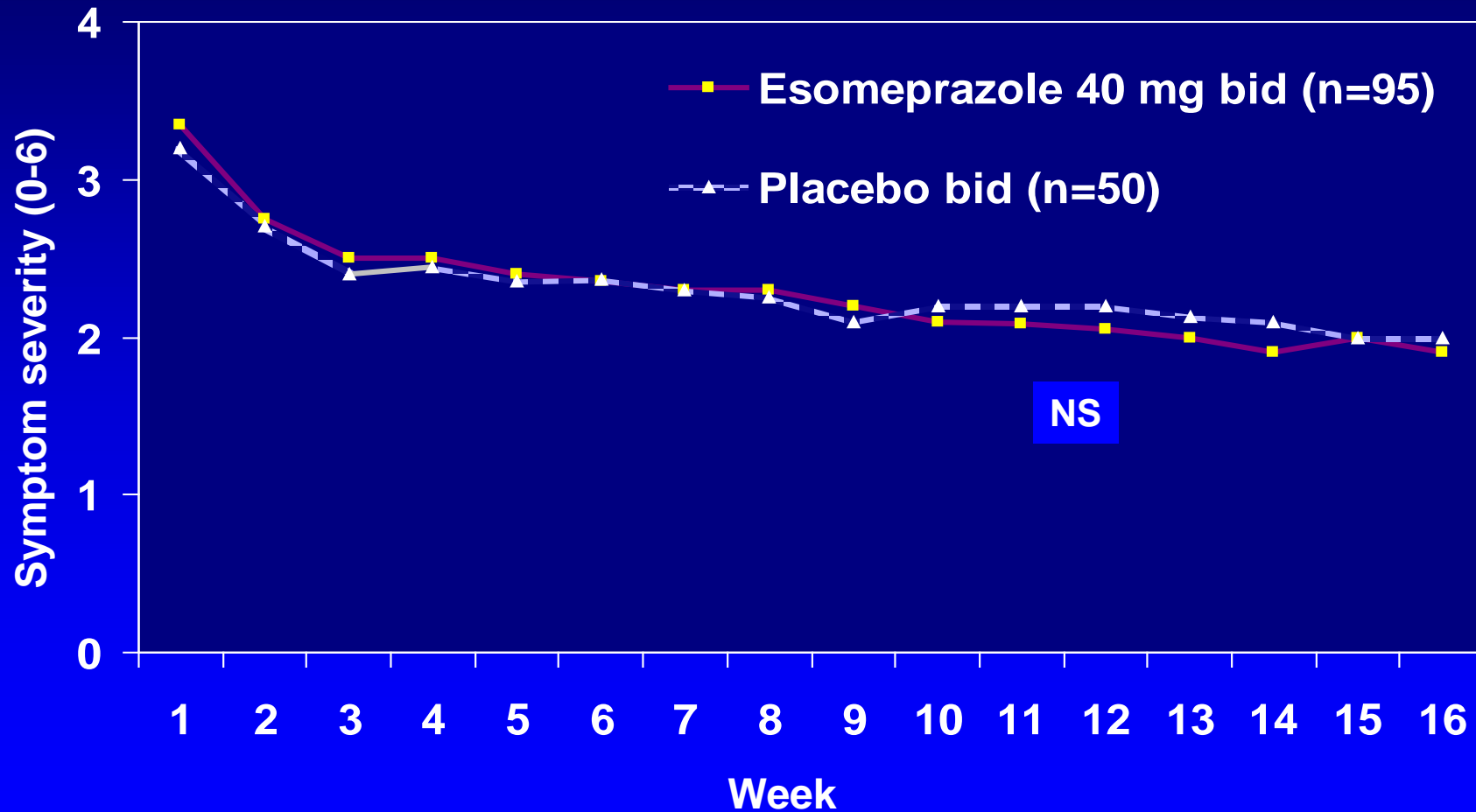
Randomized, Placebo-Controlled Trial in Patients with LPR with +pH Test



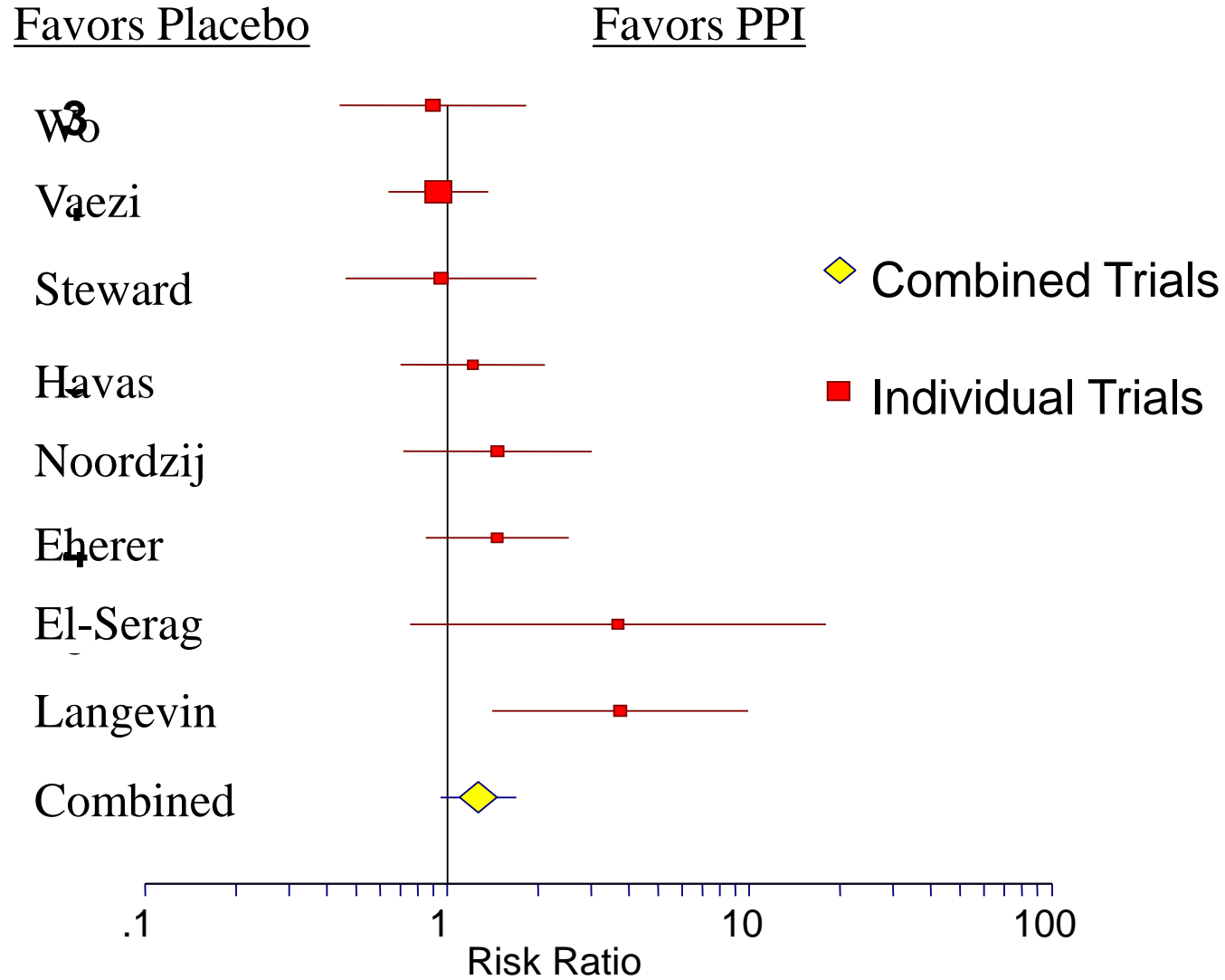
Treatment Response Do Not Correlate with Acid Suppression



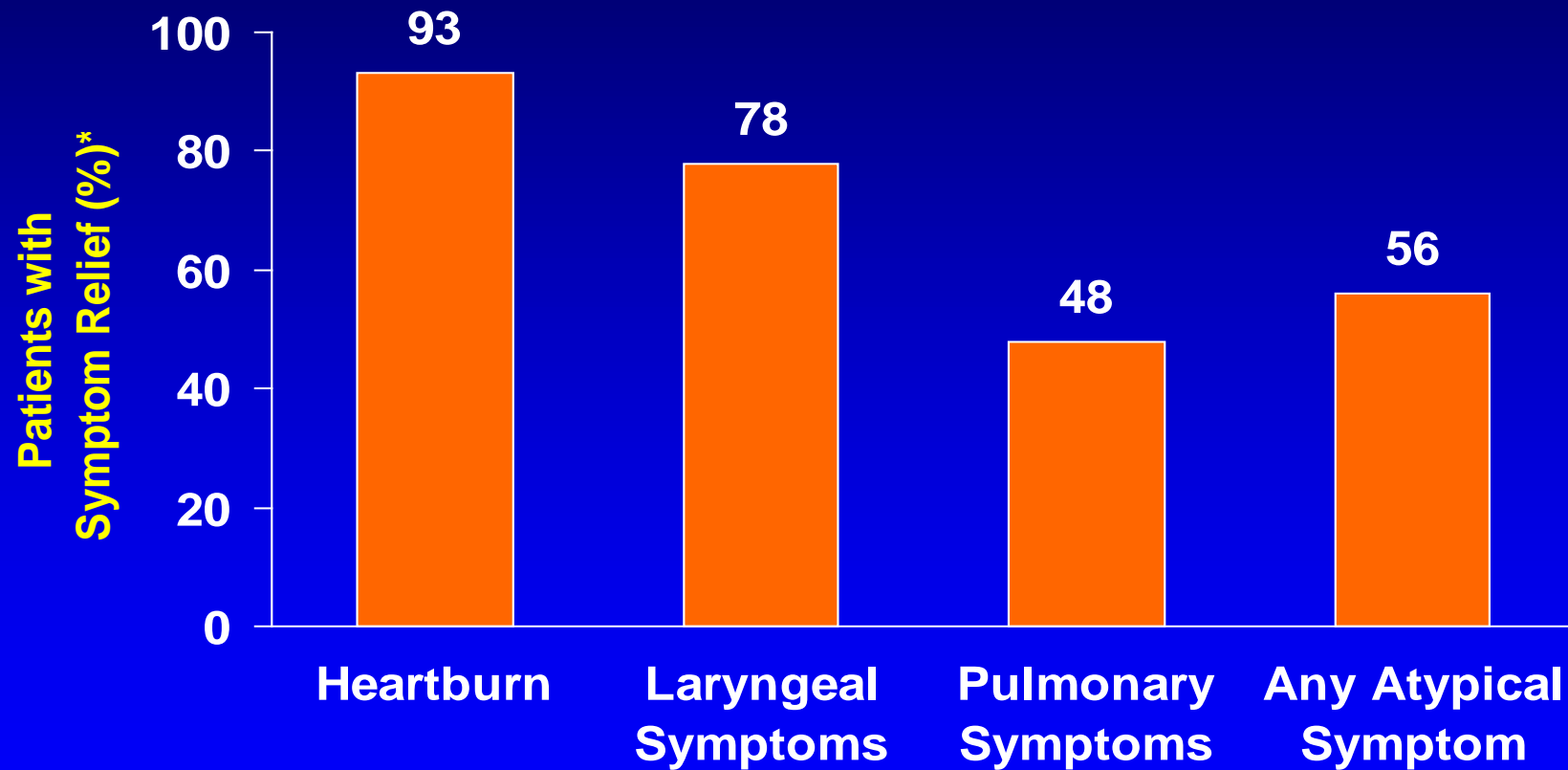
Randomized, Placebo-Controlled Trial in Patients with Suspected LPR



Meta-Analysis of RCT for LPR



Fundoplication: Efficacy in Relief of Atypical GERD Symptoms




N = 150 (35 with atypical symptoms).

So et al. *Surgery*. 1998;124:28-32.

Antireflux Surgery for GERD-Related Cough and LPR

- Limited experience
- Long term efficacy unknown
- Complete response uncommon
- Fundoplication for selected patients only
 - Large hiatal hernia
 - Presence of heartburn
 - Aspiration
 - No contraindications



Summary: Chronic Cough and Laryngopharyngeal Reflux

- Typical heartburn is often absent
- Causes are multifactorial
 - GERD & non-GERD factors
- Empiric PPI for 2-3 months is recommended, but efficacy is weak based on RCT's
- Ambulatory pH-impedance monitoring should be reserved for PPI non-responders