

**Laparoscopic Antireflux Surgery vs  
Long-Term Esomeprazole Treatment for  
Chronic GERD. Final Results After 5  
Years of Follow up in the Lotus Study**

**Galmiche JP et al**

## Rationale

- PPI's are highly effective in the treatment of GERD
- Laparoscopic antireflux surgery (LARS) is widely used in the management of GERD
- Data comparing the long term efficacy of these two interventions re lacking

# LARS for GERD

- Reason for operation?
  - Heal esophagitis?, comparable to PPI (Lundell, BJS 2007)
  - Treat esophageal (HBT or regurgitation)?  
LRAS slightly superior in controlled data (Lundell BJS)
  - Treat extraesophageal symptoms (cough, asthma)? LARS superior by observational studies? (Sontag SJ, Am J Gastro 2003)

**Causality?**

# LARS for GERD

- Reason for operation?
  - Treat complications of GERD?
  - Treat pt's controlled on PPI's? (best candidates)
- Surgical experience? Referral centers vs community

# LARS for GERD: complications

- Mortality: 0.2%
- Life threatening complications: 1.5%
- Reoperations (Redo): 1.5 first 2 years
- Dysphagia (requiring dilatation): 3.5%

**Meta-analysis, specialized centers, Gastroenterology, 2008, 135:1392**



## Conclusions

- Interesting epidemiologic association
- Some biologic plausibility
- Weak magnitude of association
- Inconsistent findings
- Heterogeneous studies
- High potential for confounding



## Study Design/Methods

- 554 patients, mild, no more than grade B LA classification, responsive to PPI
- Primary end point: Treatment failure

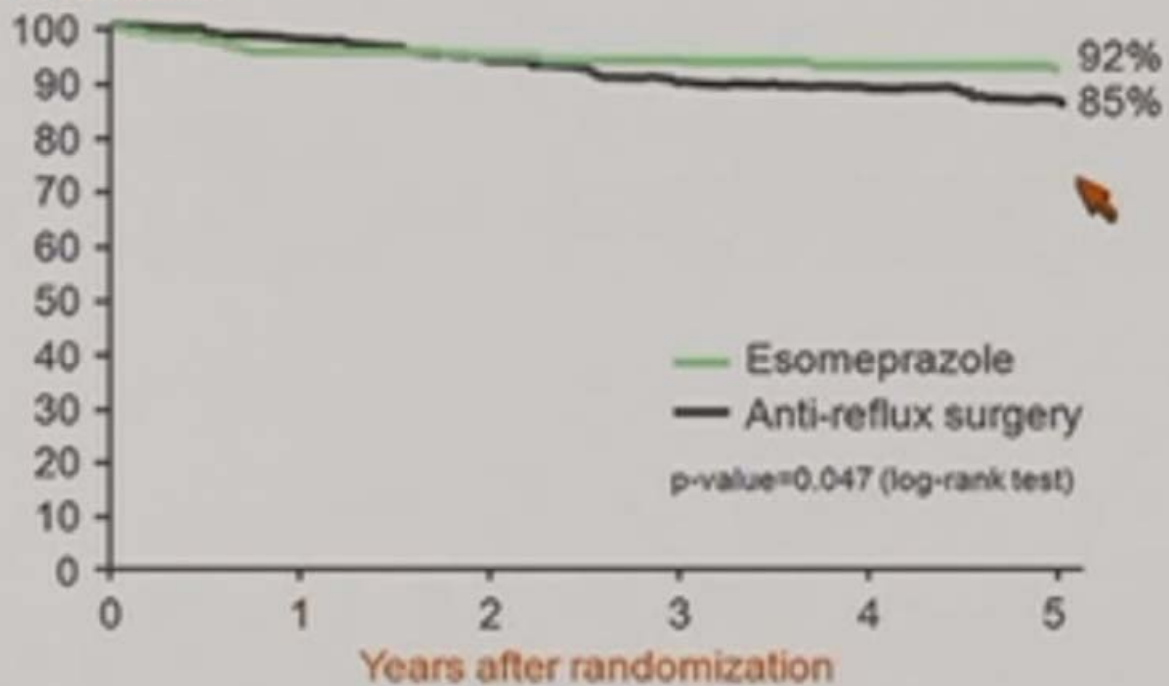
Medical: need to BID PPI's

Surgical: need for medical Rx, perioperative death, dysphagia ( <1 dilatation), reoperation for control of symptoms.

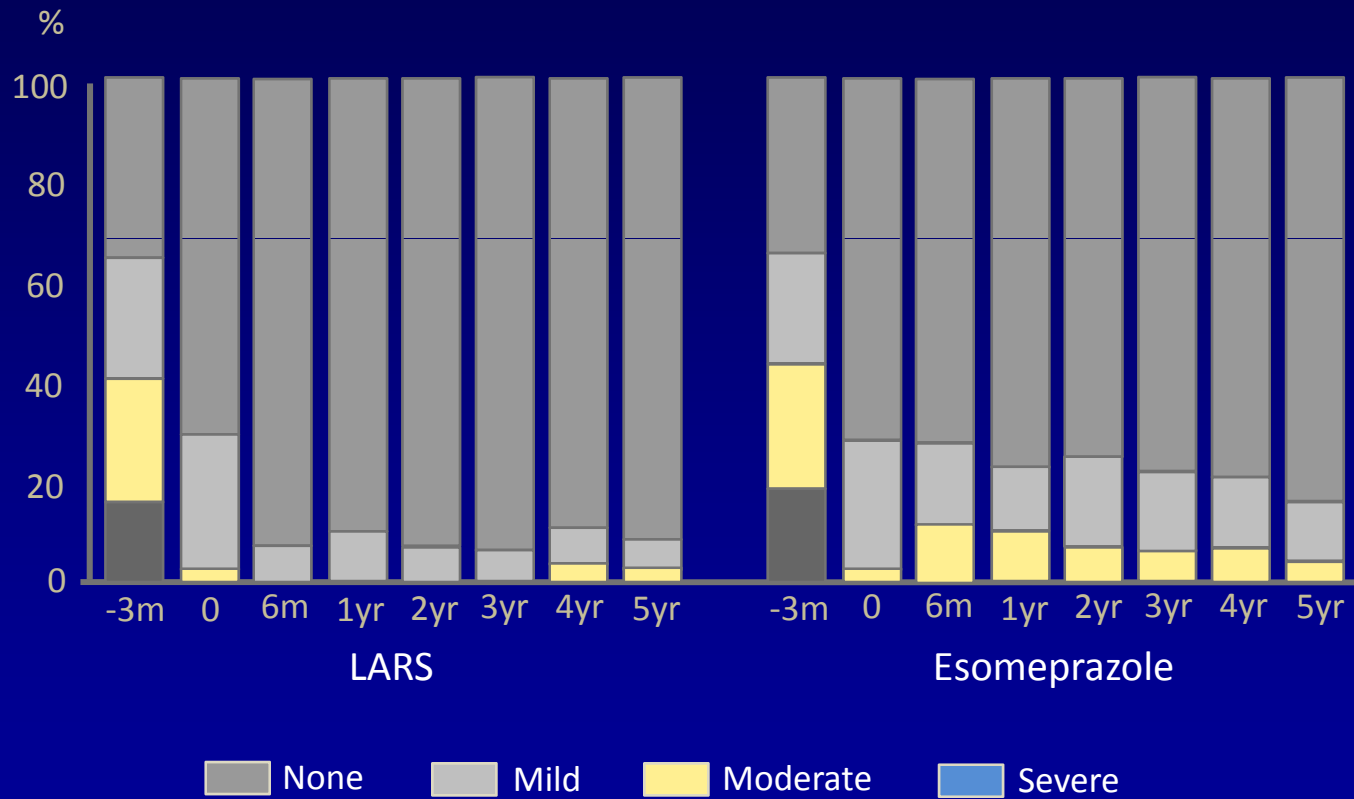
# Time to treatment failure-ITT Analysis

n=554

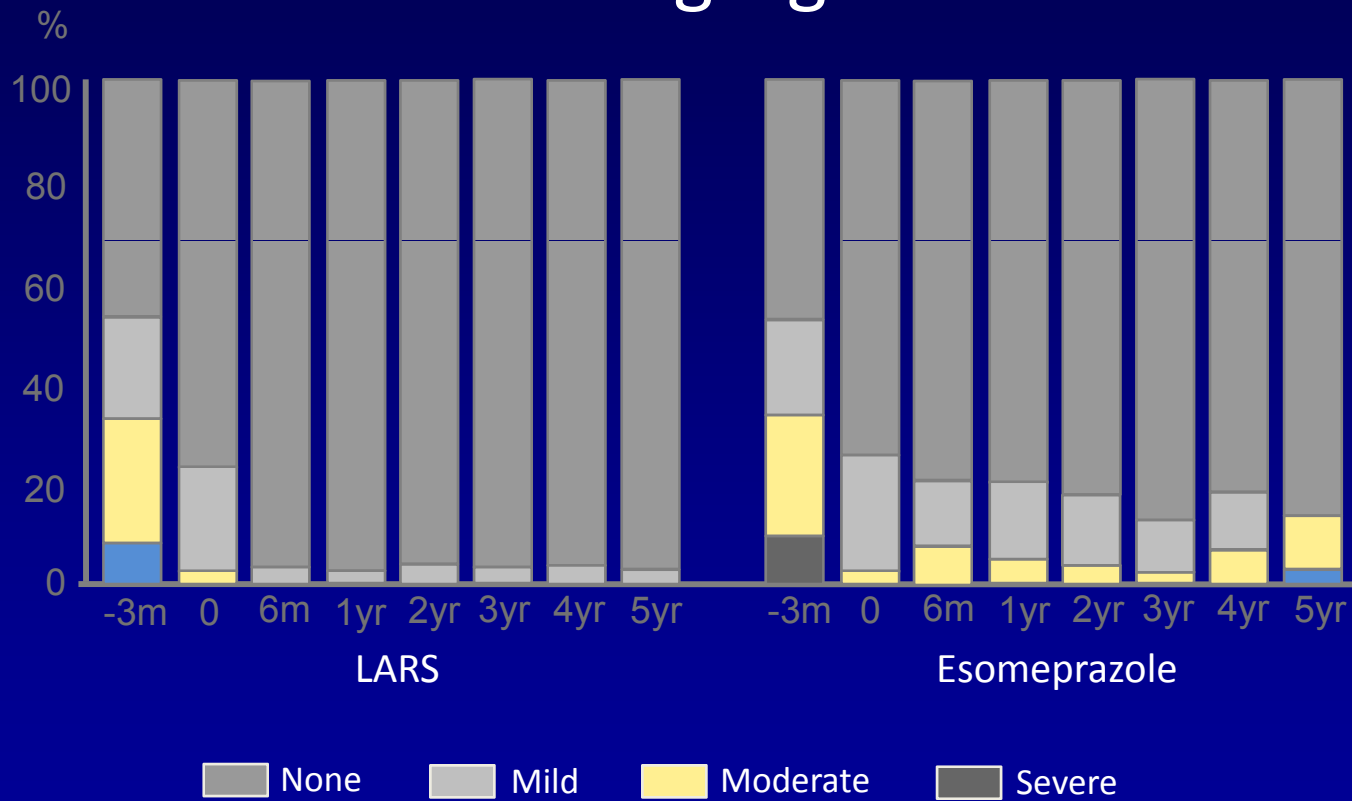
Estimated proportion  
in remission



# Proportion of Patients by Severity of Heartburn



# Proportion of Patients by Severity of Acid Regurgitation



# Safety

- No mortality
- Comparable serious adverse events in both groups

## Conclusions

- Long term control of chronic GERD can be very effectively achieved with either maintenance esomeprazole or LARS
- The real message:
  - patients who respond to PPI and wish to stop, can expect similar result form LARS
  - safety and efficacy of LARS in this group of patients,

**The European Achalasia Trial: A  
Randomized Multi-centre trial Comparing  
Endoscopic Pneumodilatation and  
Laparoscopic Myotomy as Primary  
Treatment of Idiopathic Achalasia**

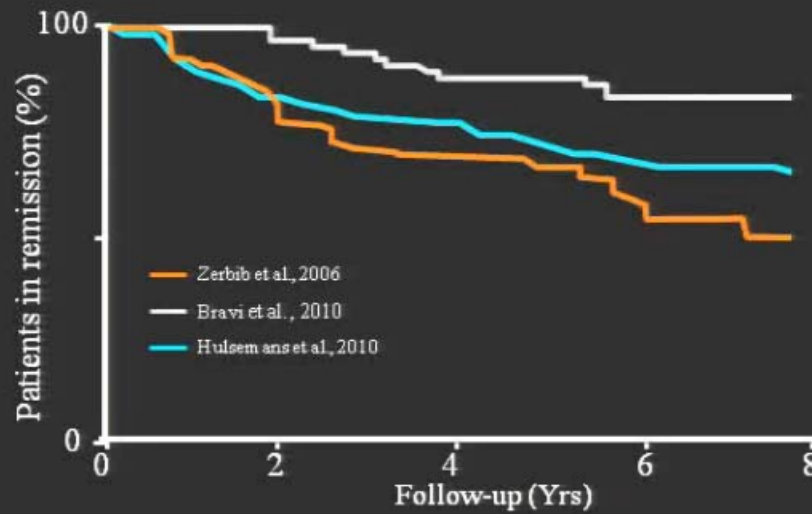
**Guy E Boeckstaens et al**

## Rationale: PD vs LHM

- Mostly retrospective studies
- Short follow up
- Different outcome measures
- Different protocols
- Single small study ( N=55) comparing both approaches (Kostic, World J Surg, 2007)

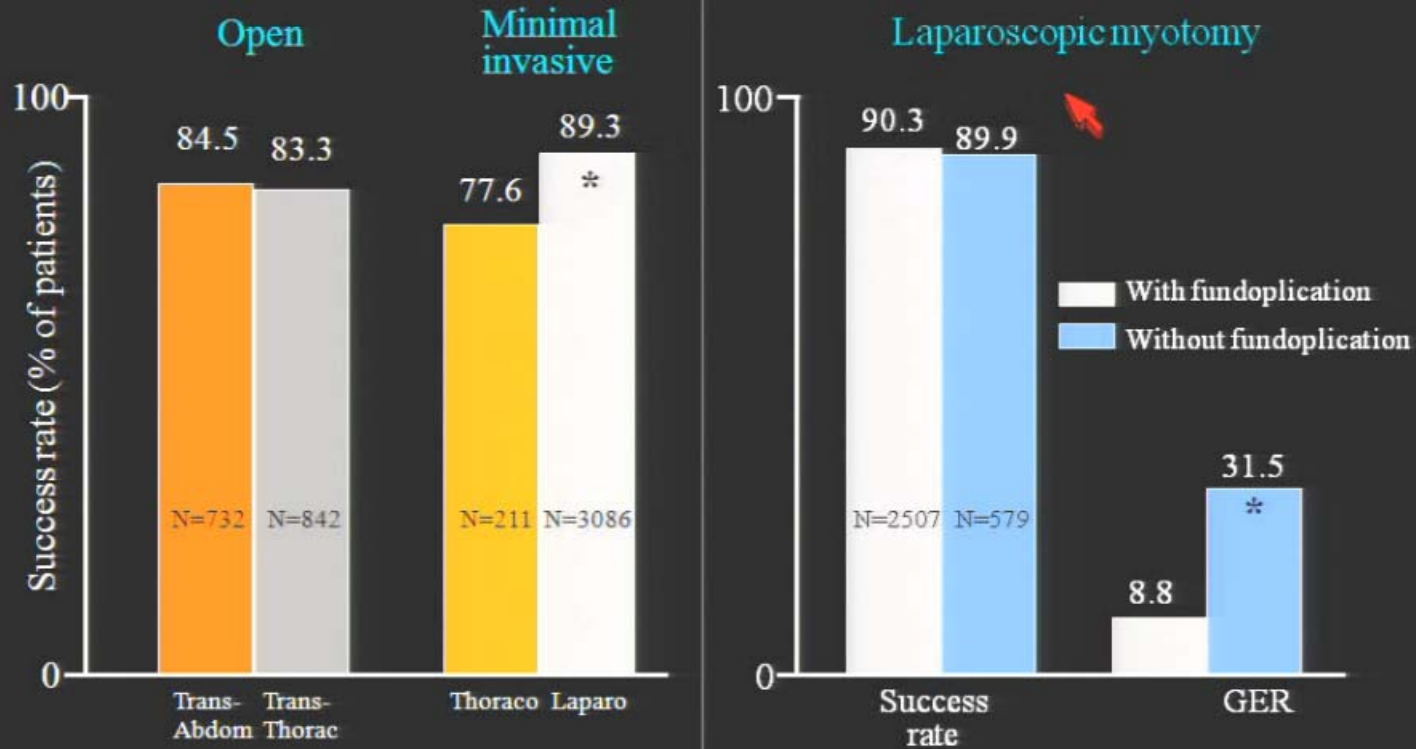
## Success rate of pneumatic dilation

- 7-11% do not respond to PD (referred for surgery)
- On average 1/3 of patients who do respond will have recurrent symptoms



Zarbib AM J Gastro 2006, Hulsemans CGH 2010, Bravi APT 2010

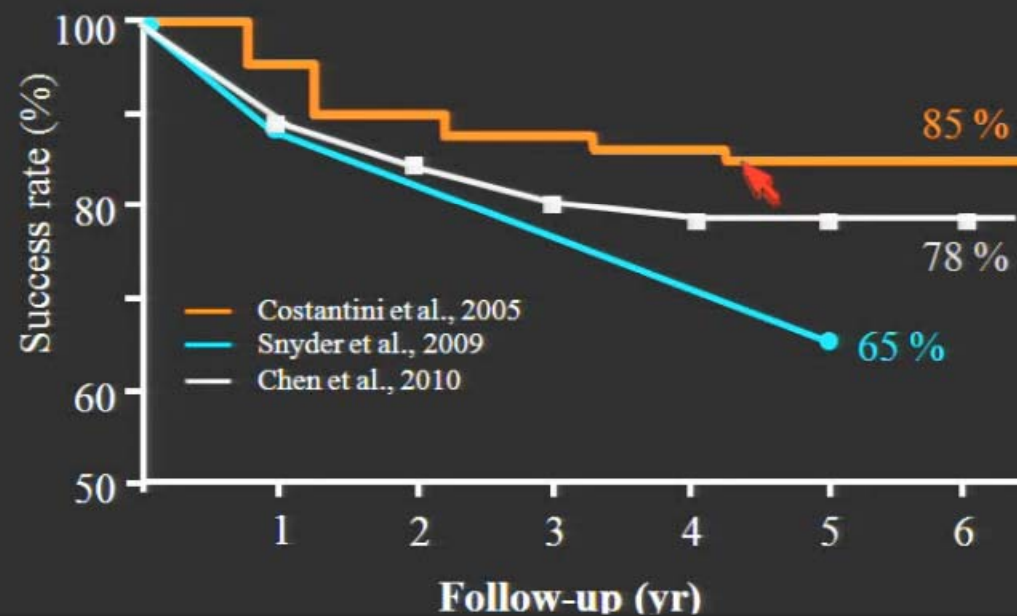
## Open vs minimal invasive, need for anti-reflux procedure?



Campos et al, Ann Surgery

## Success rate of Heller myotomy with fundoplication

- Early failure (<12 months): technical failure of myotomy (incomplete) or scarring at EGJ
- Late failure: peptic stricture, progression of disease



# complications

PD:

- perforation ~ 1-3%
- Reflux: 2% (Eckardt, GE, 1997)

LHM:

- mucosal perforation: 4-17%
- Conversion to open procedure:4-5%
- Mortality: 0.1 %
- Reflux: up to 10.6% (Frantzides , JACS, 2001)

# Treatment of Achalasia: Laparoscopic Myotomy vs Endoscopic Dilatation

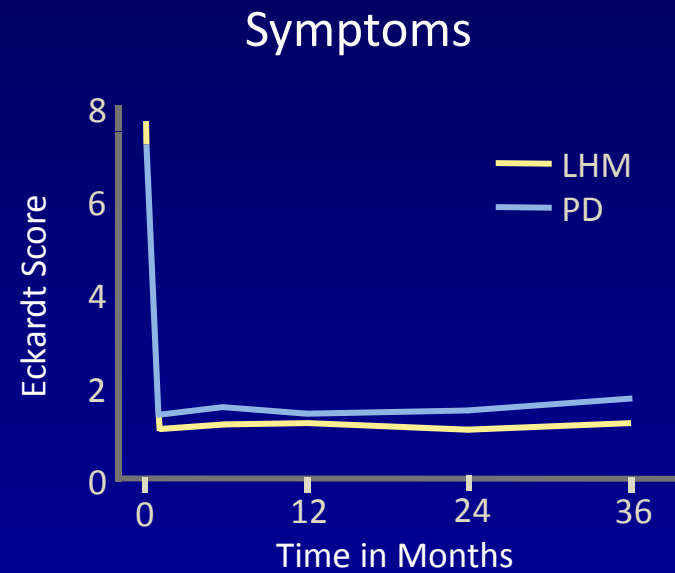
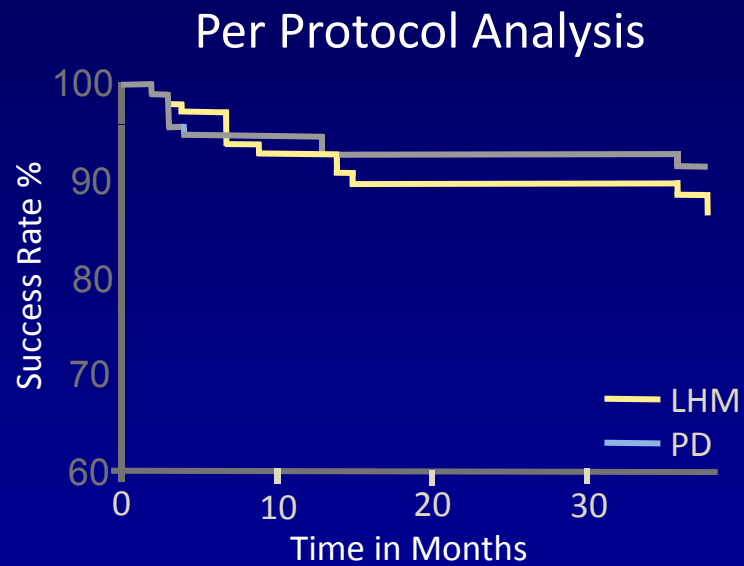
Large European multicenter, randomized prospective study:

- 200 patients with untreated achalasia, randomization between:
  - Laparoscopic Heller myotomy+Dor anti-reflux procedure
  - Pneumatic dilatation( Rigiflex dilator)
- Participating sites: referral centers with experience in both techniques

# Methods

- Comprehensive assessment of esophageal function
- Endpoints:
  - Primary: symptoms control ( combined score of regurgitation, dysphagia, weight loss, chest pain)
  - Secondary: QOL, complications, retreatment
- LHM: At least 6 cm above GEJ, 1:1/2 cm inferior over the stomach

# Primary Outcome Parameters

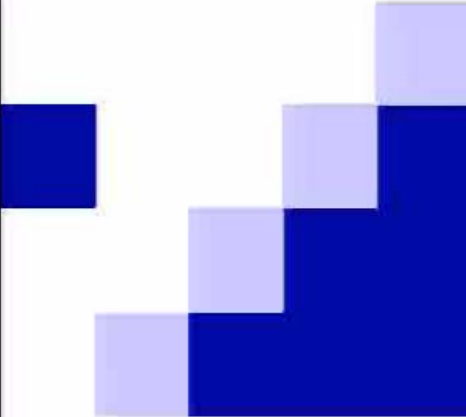


# Results

- Comparable results for:
  - endoscopic esophagitis
  - esophageal pH exposure
  - esophageal function (LESP, emptying)
  - QOL measures
- High reflux rate for both: 15/23%
- 25% required redilatation
- A/E: PD-4 perforations, LHM-11 mucosal perforations

## Conclusions

- PD LHM are comparable
- Young age, men, favor LHM
- Older age, women, favor PD
- Local expertise, a major determinant



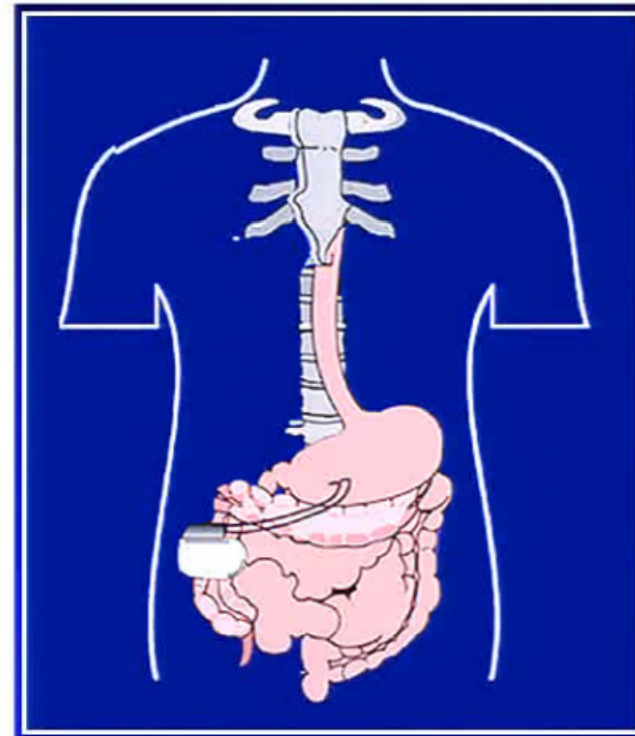
# Enterra® Gastric Electrical Stimulation for Idiopathic Gastroparesis: Results from a Multicenter Randomized Study

Richard W. McCallum<sup>1</sup>, William J. Snape<sup>2</sup>, John M. Wo<sup>3</sup>, Frederick J. Brody<sup>4</sup>, Henry P. Parkman<sup>5</sup>, Thomas V. Nowak<sup>6</sup>, Darin R. Lerew<sup>7</sup>, and Lisa A. Ruehlow<sup>7</sup>

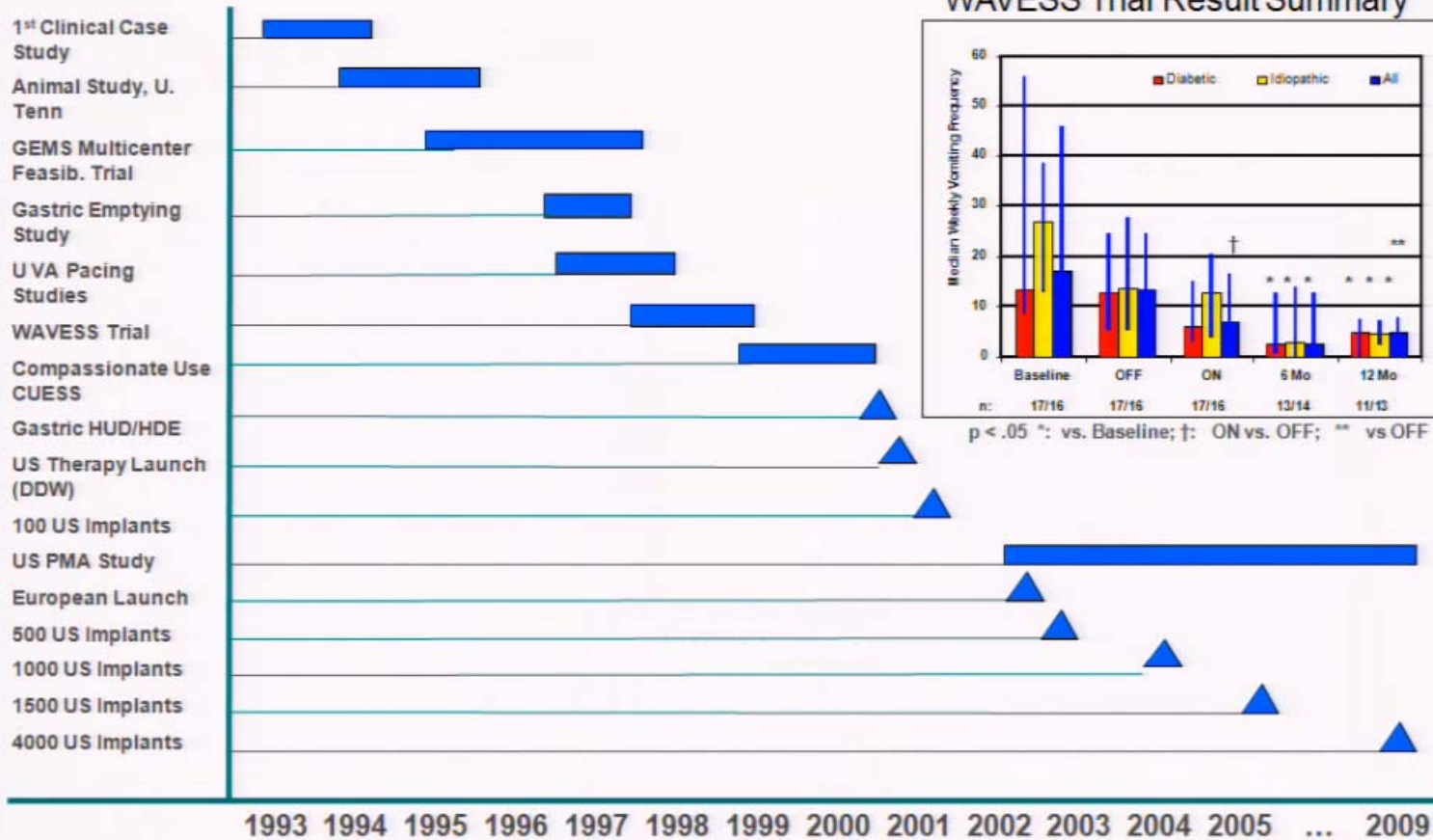
<sup>1</sup>University of Kansas Medical Center, <sup>2</sup>California Pacific Medical Center, <sup>3</sup>University of Louisville, <sup>4</sup>George Washington University, <sup>5</sup>Temple University Hospital, <sup>6</sup>Saint John's Research Institute, <sup>7</sup>Medtronic Inc.

# Gastric Electrical Stimulation Enterra® Therapy

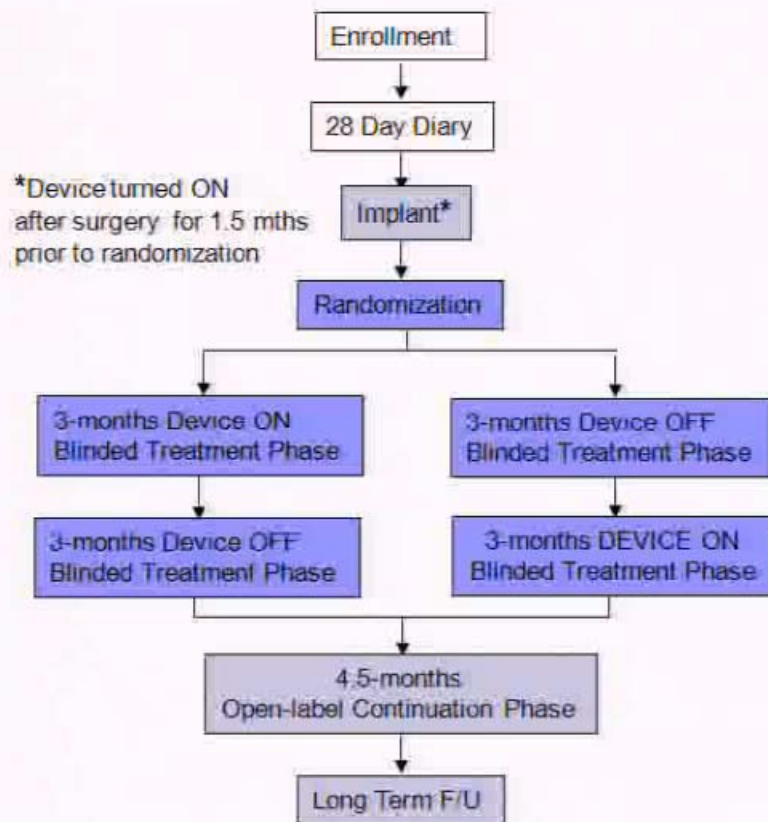
- Indicated for the treatment of chronic, intractable nausea and vomiting secondary to diabetic or idiopathic gastroparesis under a Humanitarian Device Exemption (HDE).
- System includes:
  - Implantable neurostimulator: Medtronic Model 7425G or 3116
  - Neuromuscular leads (2): Medtronic Model 4351
- Stimulation Parameters
  - Amplitude: 5 milliamps
  - Pulse Width: 330  $\mu$ sec
  - Rate: 14 Hz
  - Cycle On Time: 0.1 sec
  - Cycle Off Time: 5.0 sec



# Gastric Stimulation Program History



# Enterra<sup>®</sup> Therapy Clinical Study Design



**Purpose:** Prospective, multi-center, double blinded, randomized, controlled, two-period crossover study designed to evaluate the safety and efficacy of Enterra Therapy in the treatment of chronic intractable (drug-refractory) nausea and vomiting secondary to gastroparesis of idiopathic etiology

**Primary Endpoint:** To demonstrate a reduction in weekly vomiting frequency when the device is turned ON, relative to when the device is turned OFF

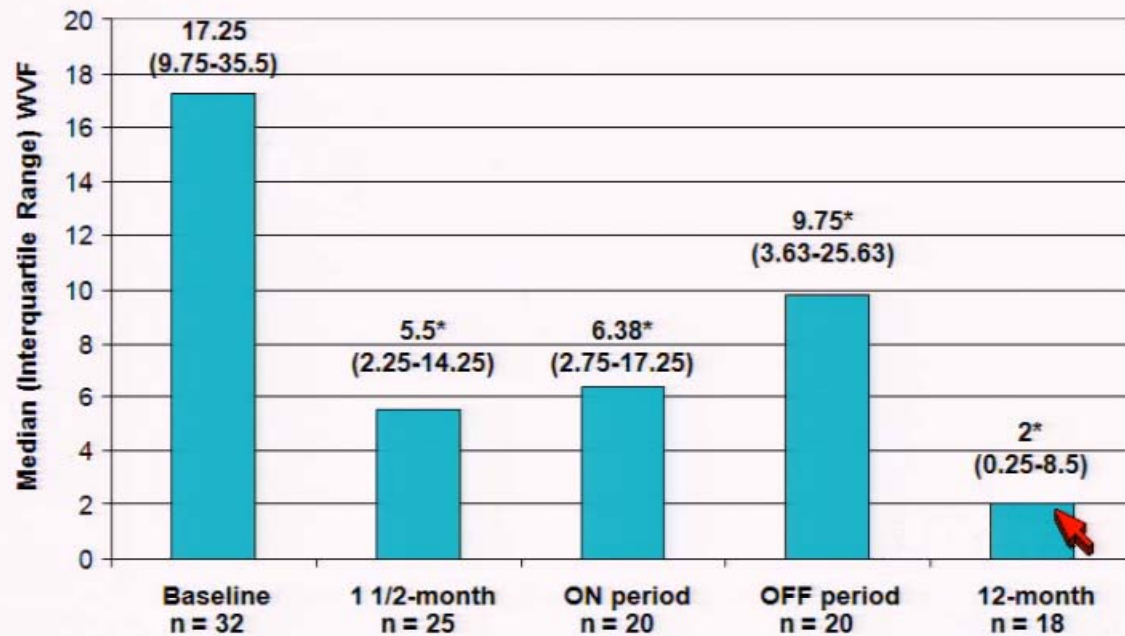
**Secondary Objectives:** To demonstrate a reduction in symptom score when the device is turned ON, relative to when the device is turned OFF. To demonstrate a reduction in weekly vomiting frequency at 12 months, relative to baseline.

**Additional Goals:** 1) To demonstrate change in symptom score, quality of life, number of days in hospital, and gastric emptying at 12 months, relative to baseline. 2) To assess safety by characterizing adverse events.

# Demographic Data

- N= 32 patients
- Female: 26 (81%)
- Age: Average 39.4 years (range: 22-64)
- Years of Gastroparesis symptoms before enrollment
  - Average 7.7 years (range 1.5-28 years)
- Supplemental nutritional support
  - Oral: 4 (12.5%), J-tube: 5 (15.6%), Parenteral: 1 (3.1%)
- BMI: Average 25.1 kg/m<sup>2</sup> (range 13.6-39.4 kg/m<sup>2</sup>)

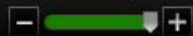
# Weekly Vomiting Frequency (WVF)



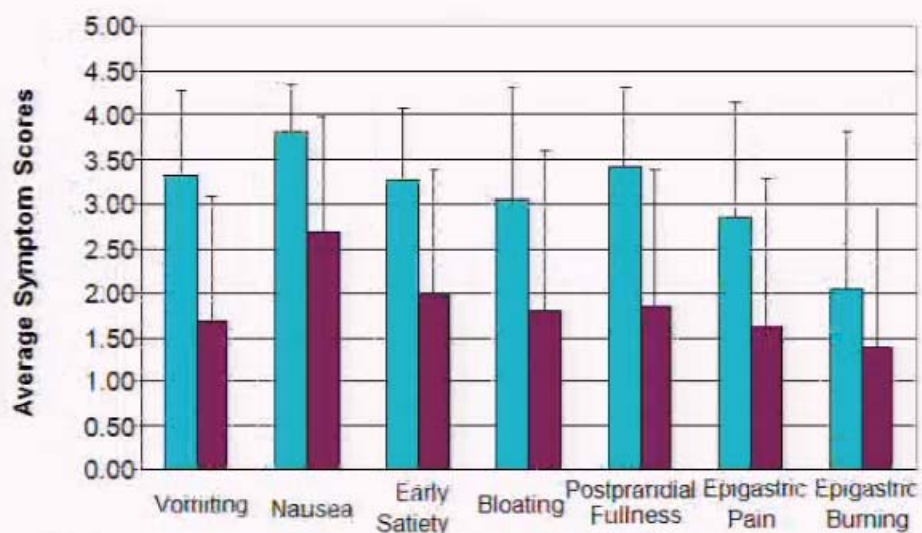
\*p < 0.05 versus baseline

There was no significant difference ON vs OFF (primary endpoint)

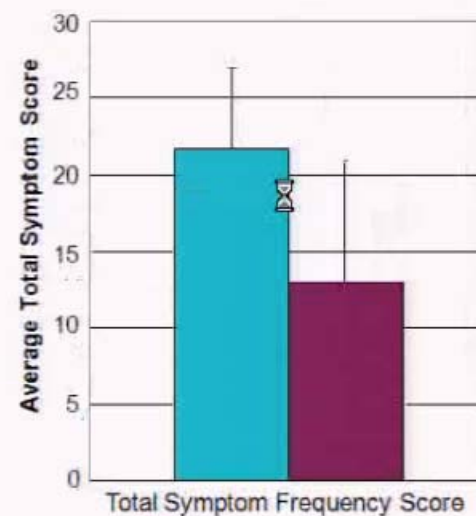
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## Additional Measure: 12-month Change in Symptom Frequency Scores



■ Baseline	3.32	3.79	3.26	3.05	3.42	2.84	2.05
■ 12 month	1.68	2.68	2.00	1.79	1.84	1.63	1.37
	P=0.001	P=0.005	P=0.001	P=0.005	P<0.001	P=0.002	P=NS



■ Baseline	21.74
■ 12-month	13.00
	P<0.001

## Results

- Improvement in HRQL at 12 months compared to baseline
- Reduced number of in hospital days

# Conclusions

- Enterra Rx results in rapid and sustained improvement of symptoms of gastroparesis
- However, no difference between ON and OFF periods
- **Small number. Carry over effect?**