

GERD Pathophysiology: Motility Conference

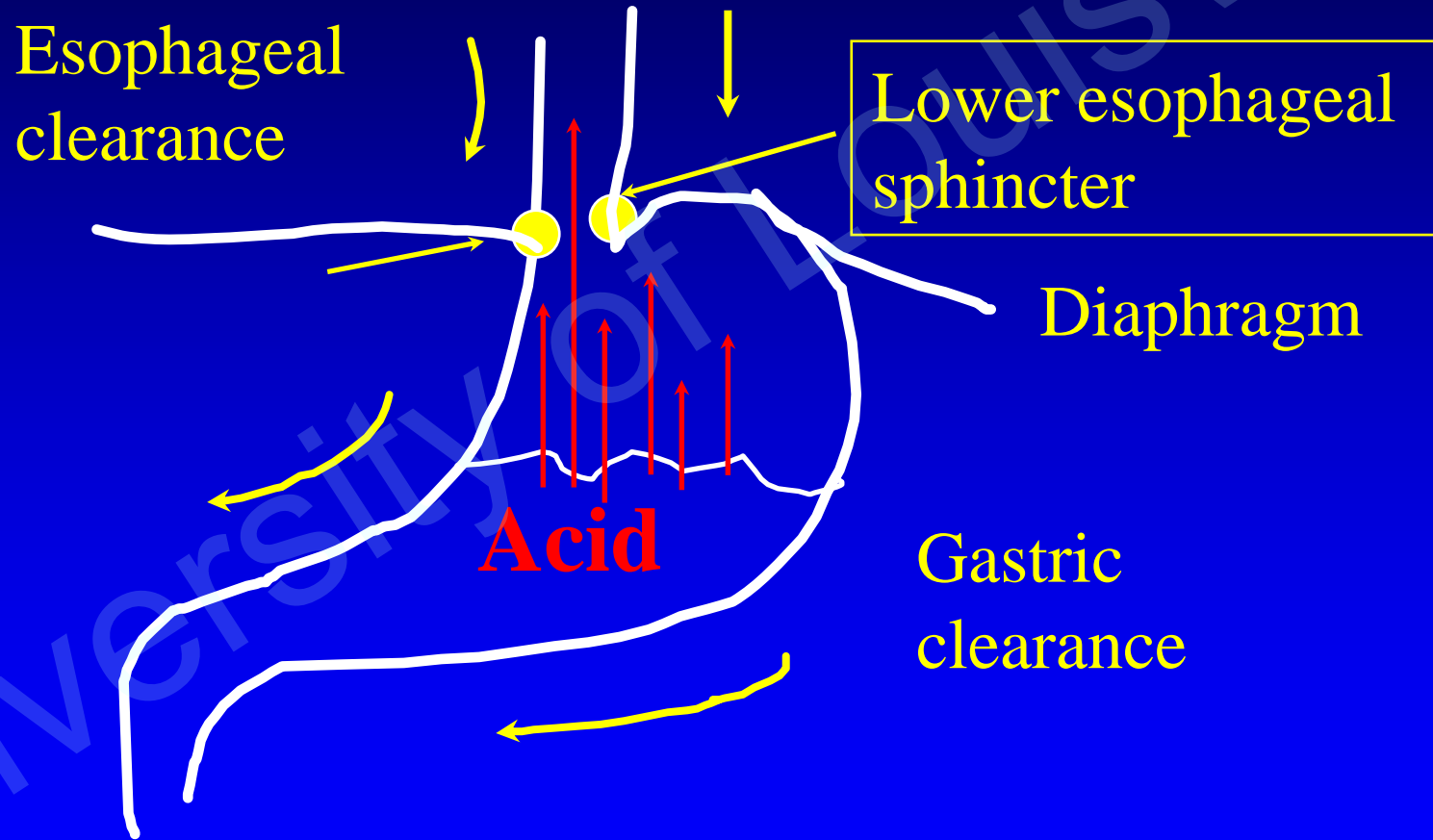
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Division of Gastroenterology/Hepatology

April 15, 2008



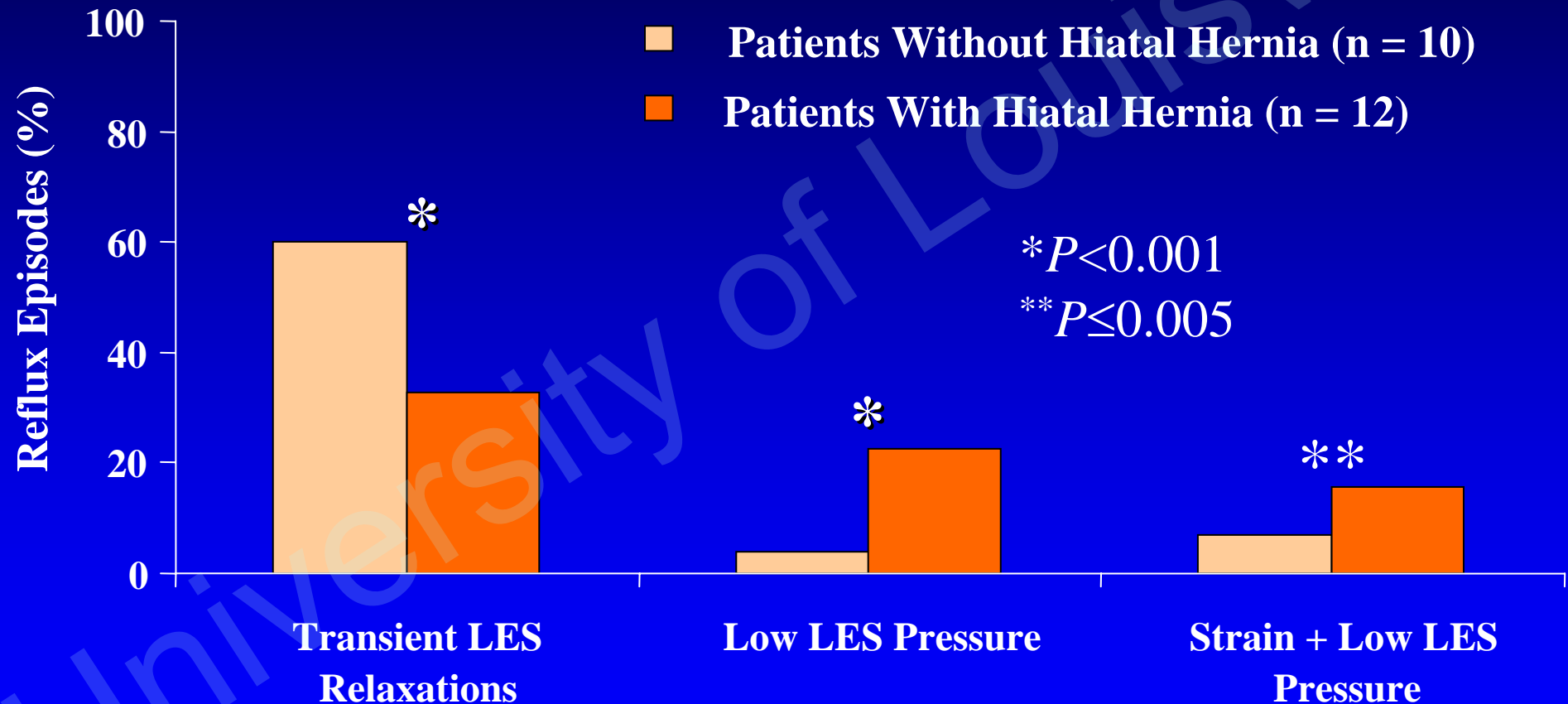
Protection from Acid Reflux



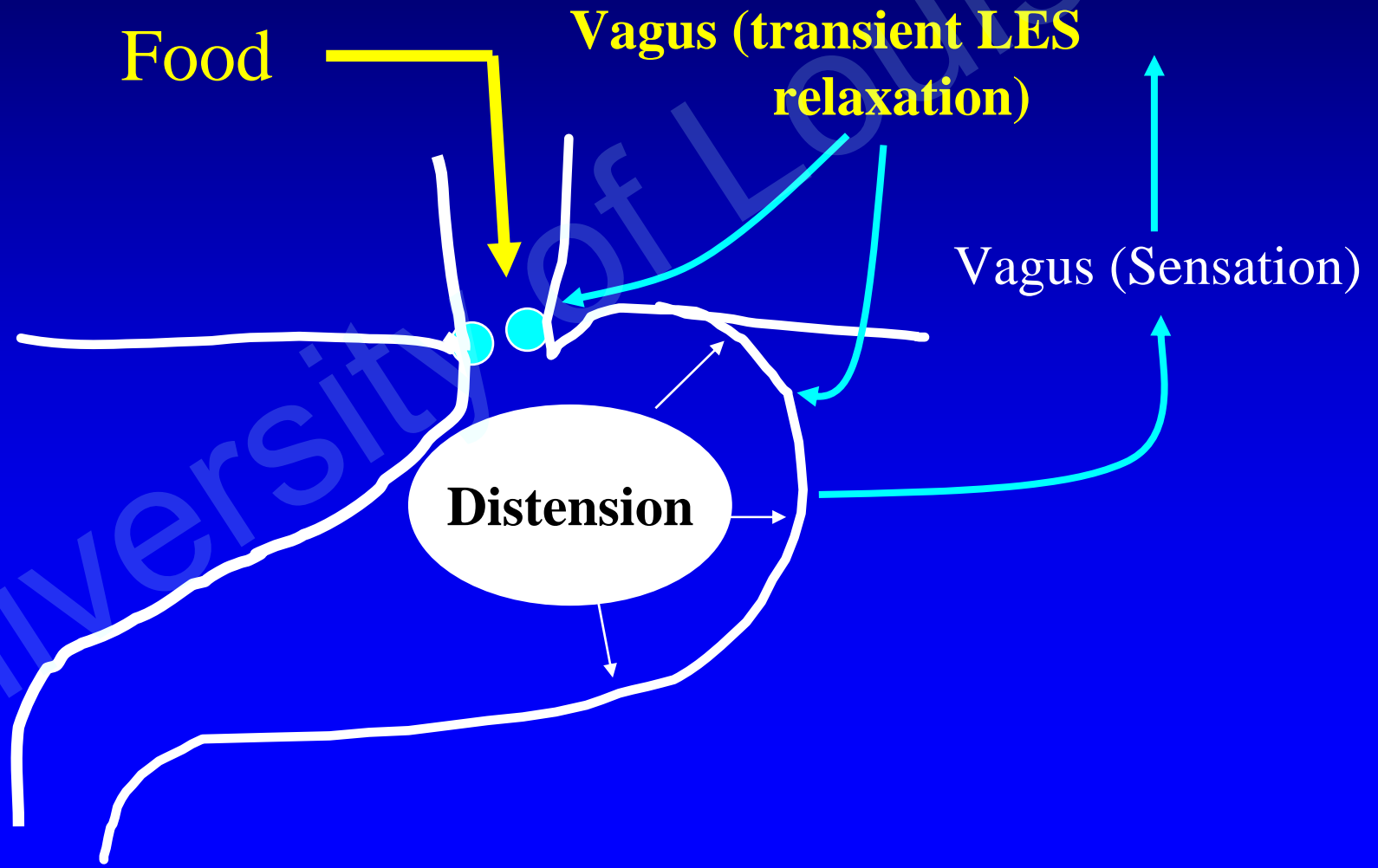
Significance of Intragastric pH >4 in GERD

- Pepsin is inactive at pH >4
- Most bile acids and pancreatic enzymes inactive at pH >4
- Esophageal mucosa injury is rare at pH >4

Three Mechanisms Causing Pathologic Acid Reflux

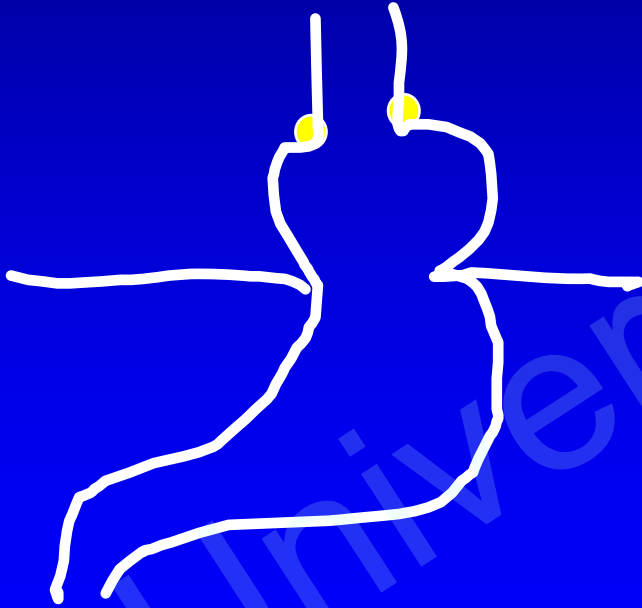


Transient LES Relaxation

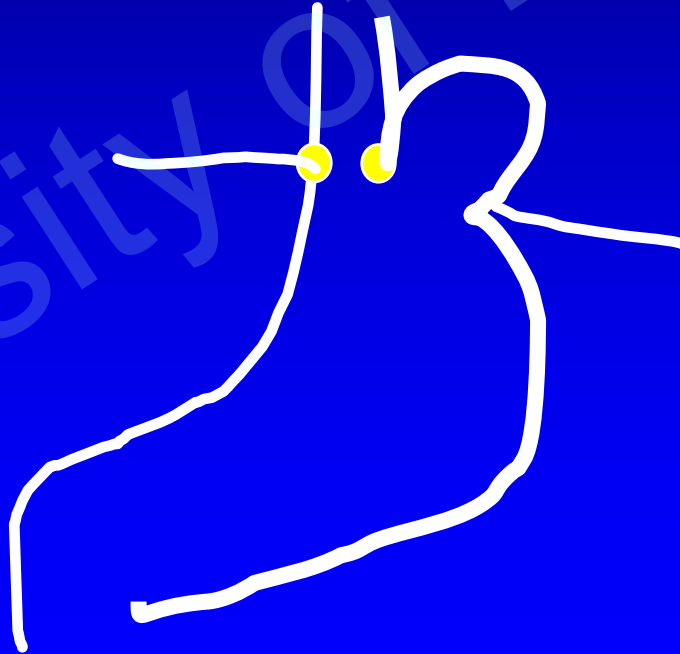


Hiatal Hernia

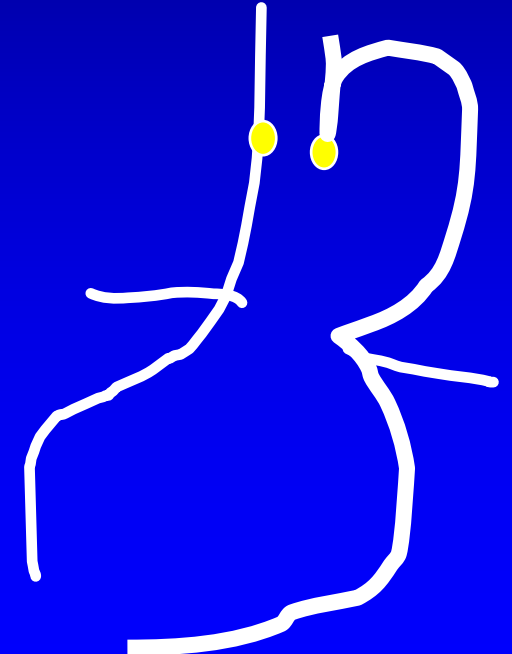
Type 1
Sliding hernia



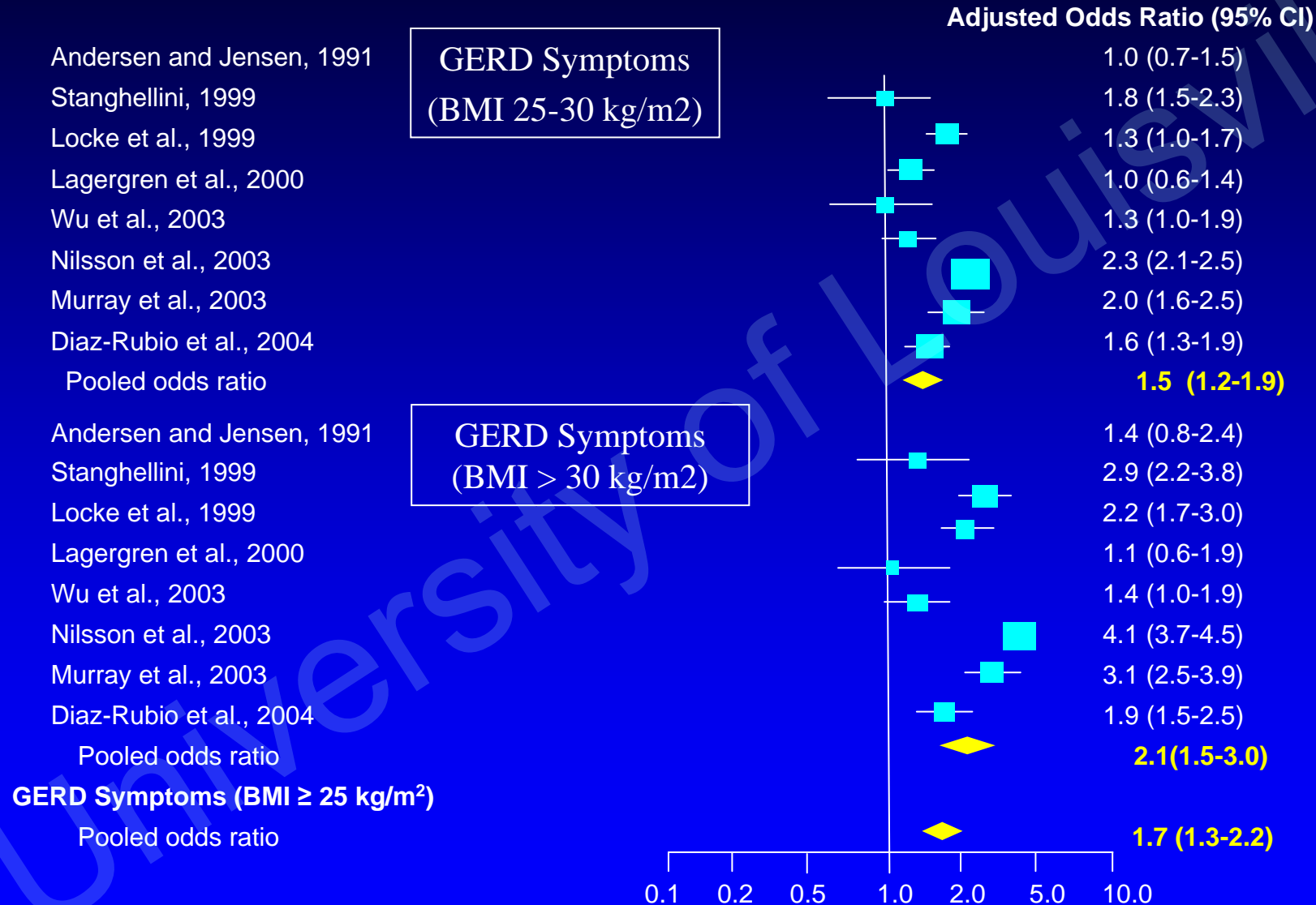
Type 2
True
paraesophageal
hernia



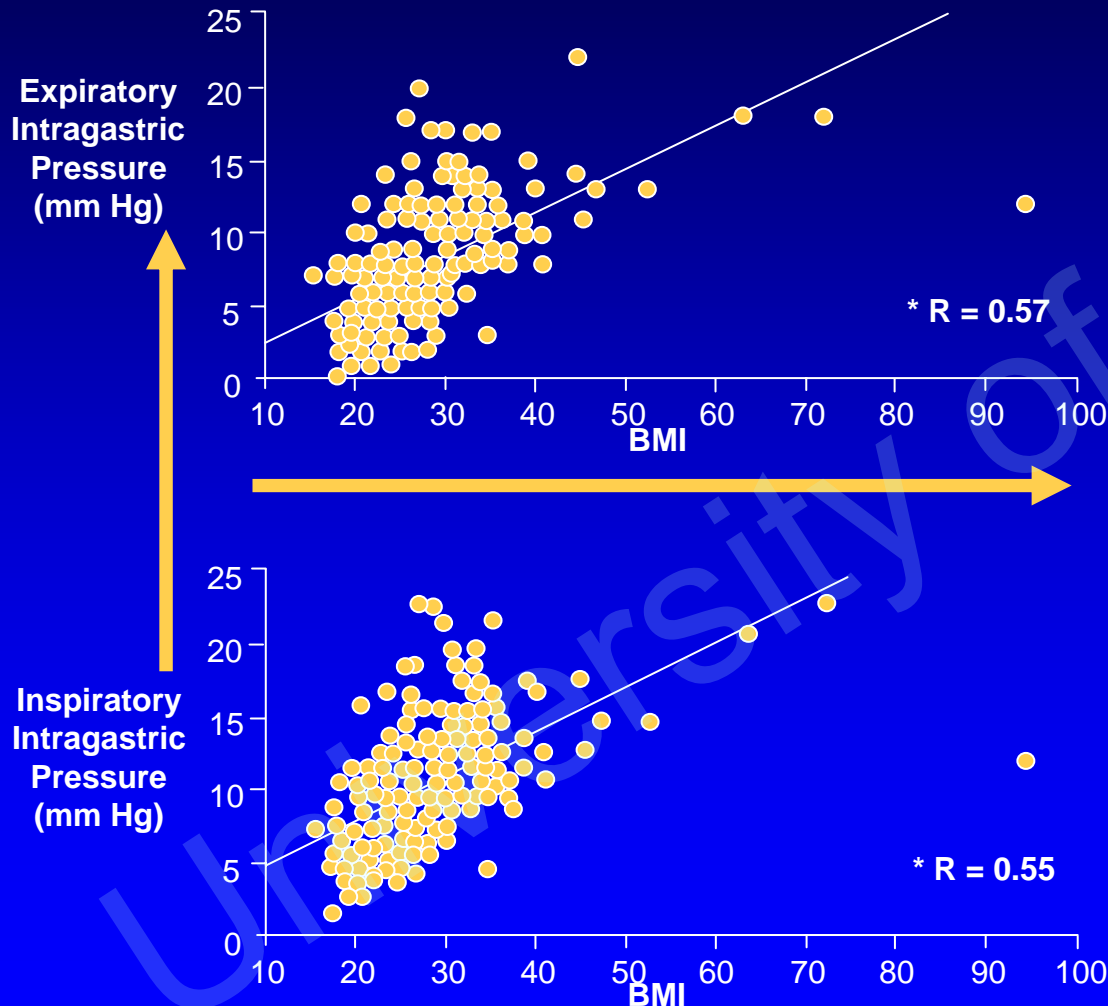
Type 3
Mixed
paraesophageal
hernia



GERD Symptoms are Associated with Obesity in Meta-Analysis Study

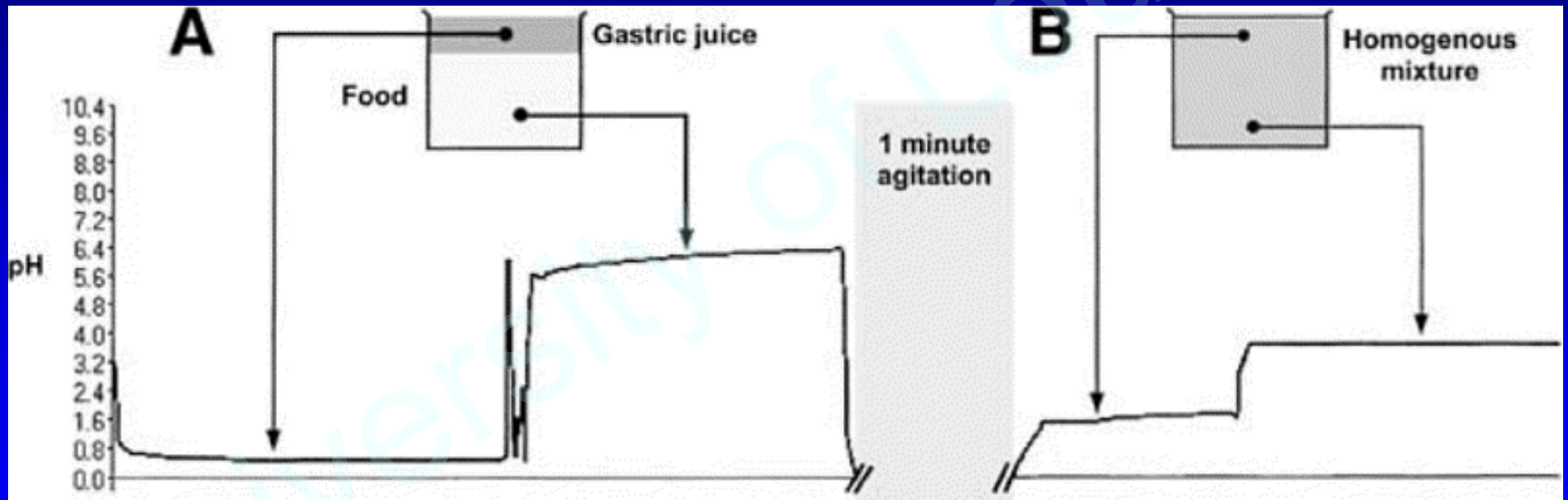


Increased Intra gastric Pressure and BMI

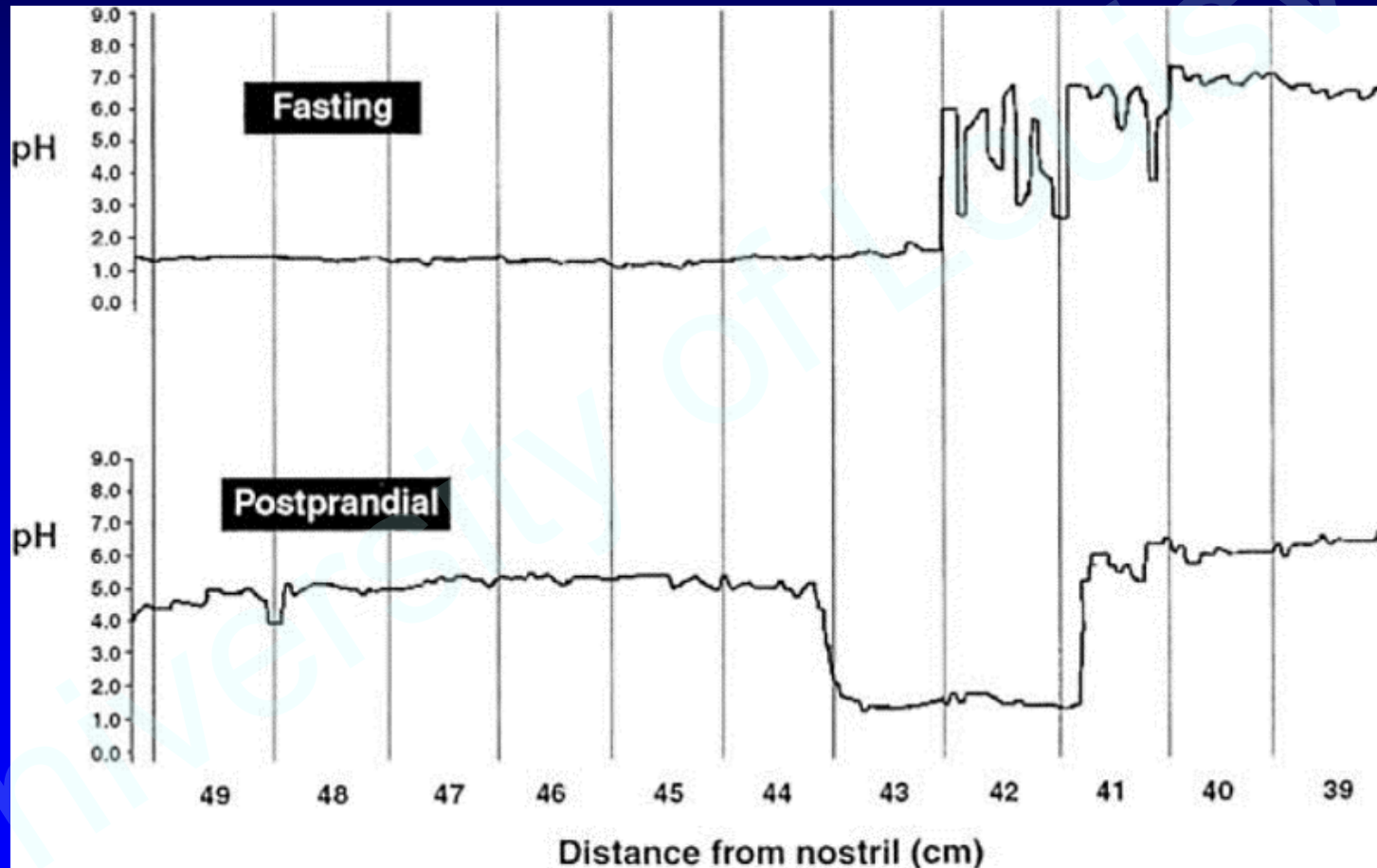


- Higher intra-gastric pressure may increase the chance that gastric contents will ascend into the esophagus

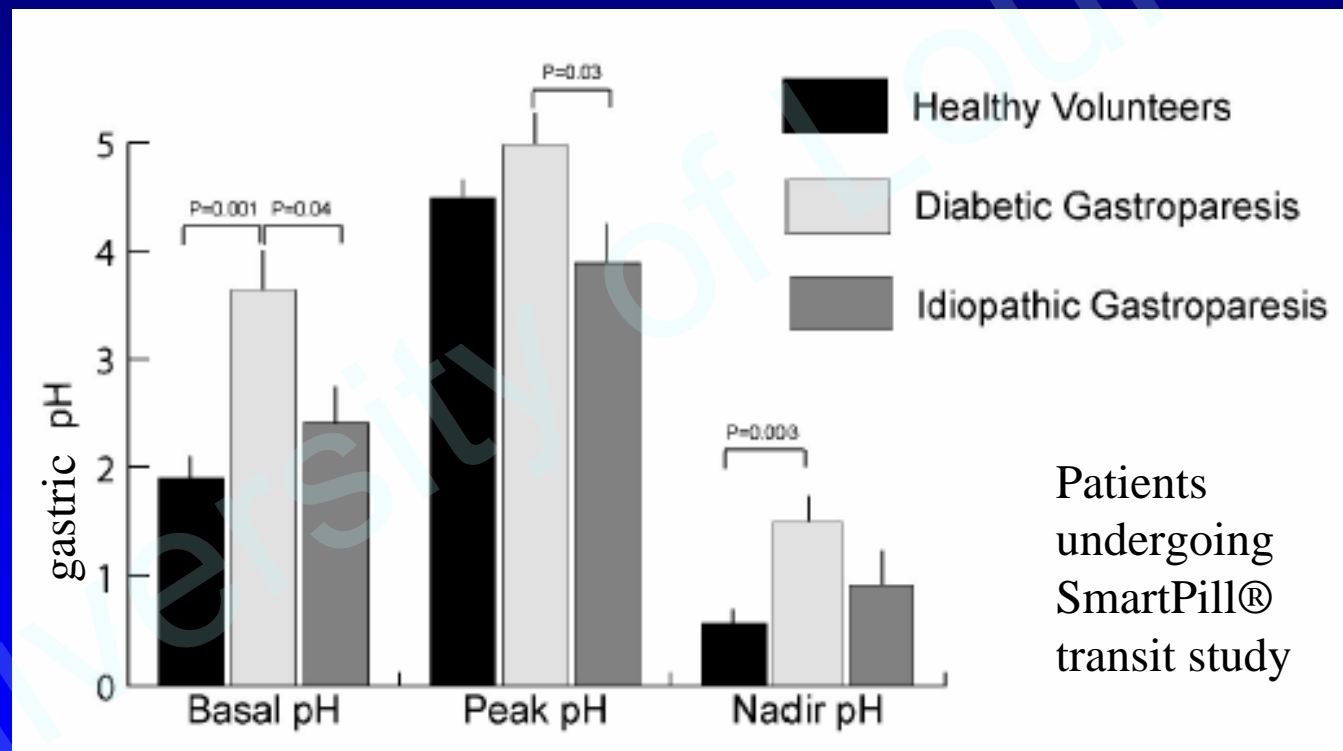
Gastric Acid Buffering by Food



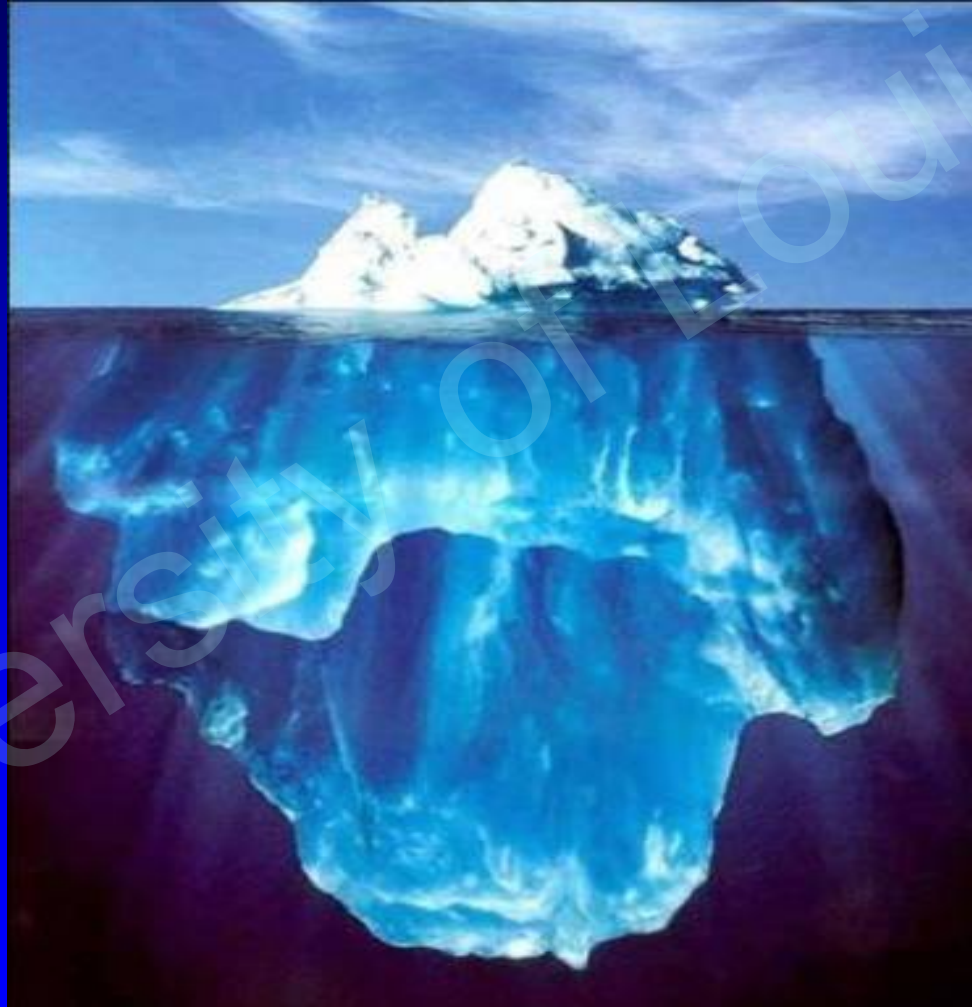
Acid Pocket After Meals Below the GEJ



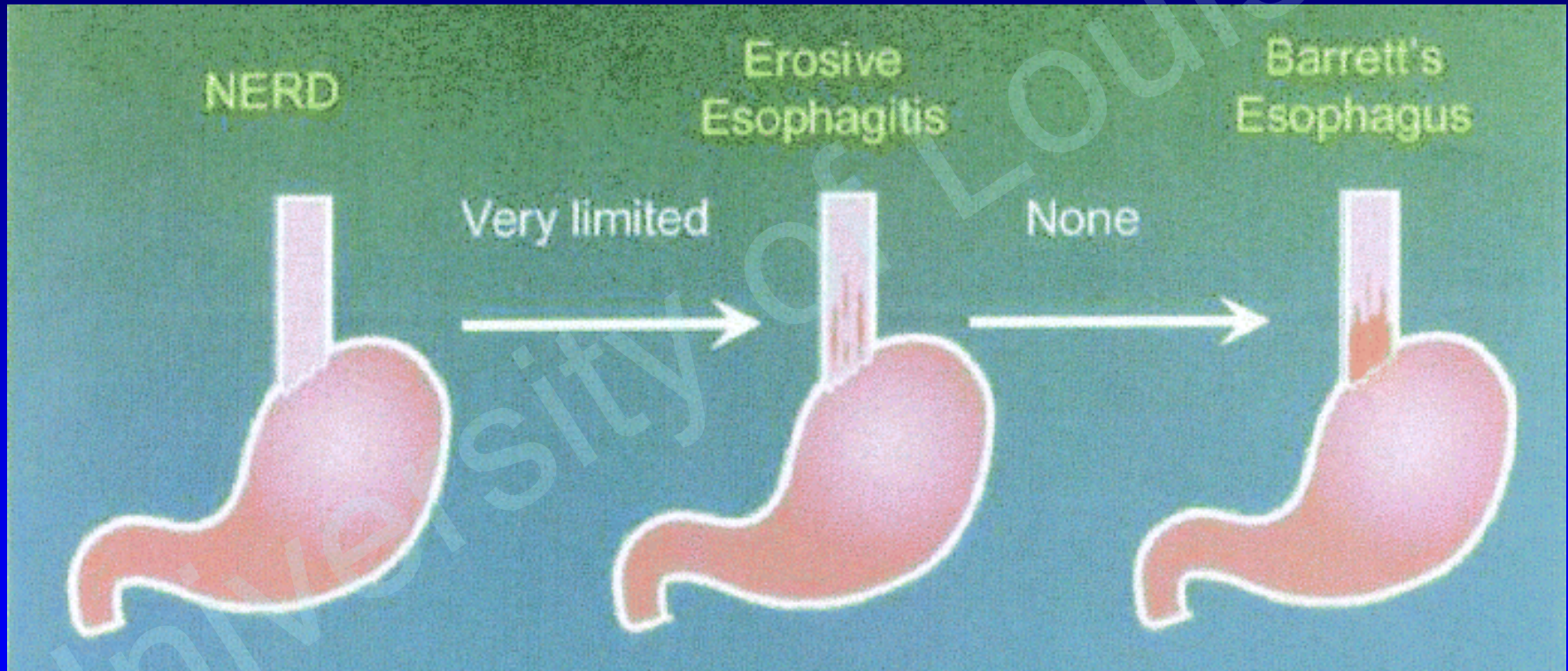
Gastric Acid Buffering is Amplified by Gastroparesis



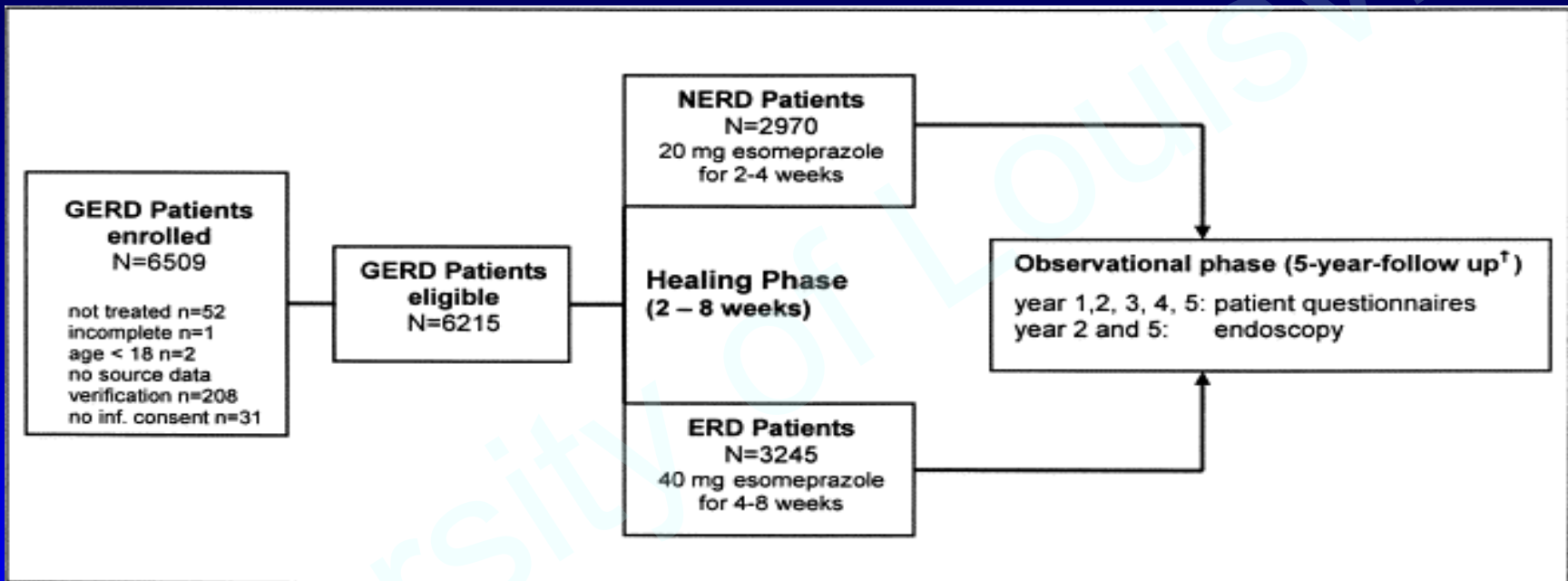
Traditional GERD Iceberg



GERD—A Spectrum of Disease?



Pro-GERD Epidemiological Study from Germany, Austria, and Switzerland



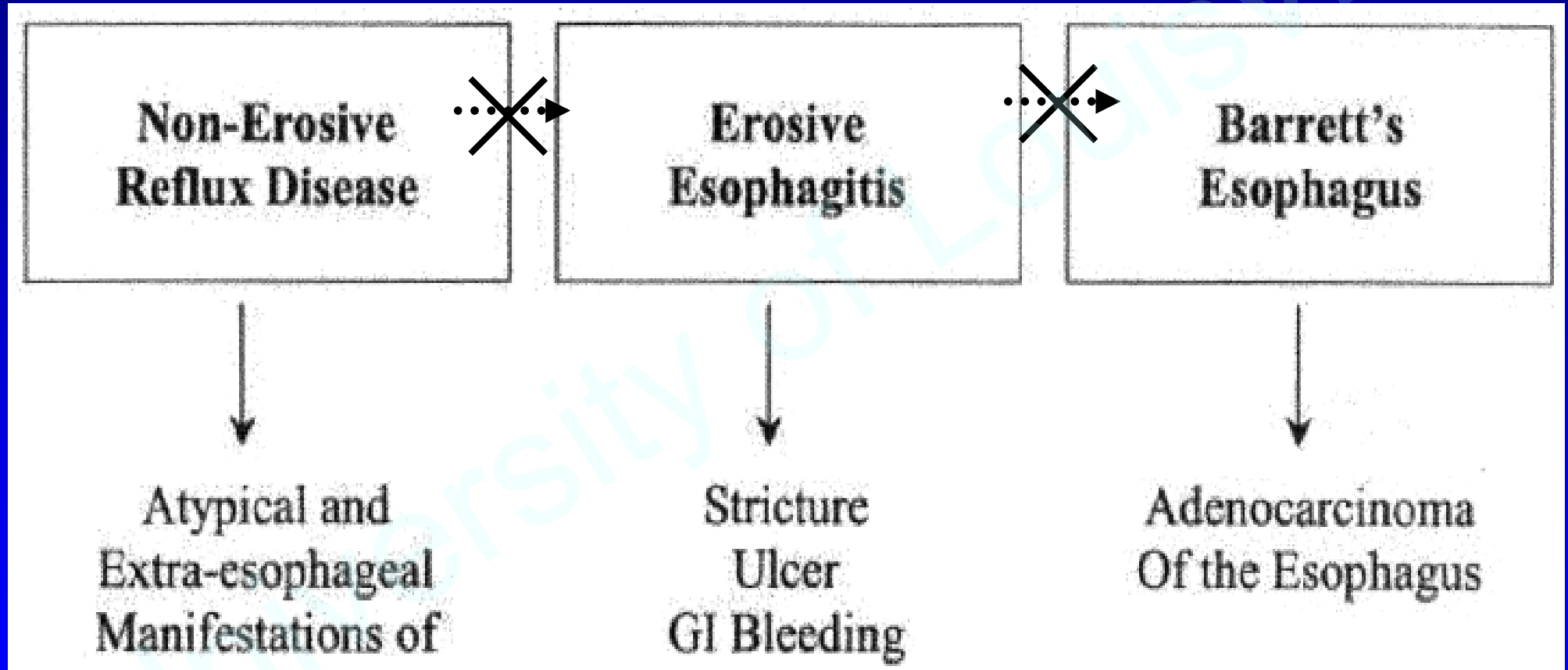
† Treatment is given at discretion of the doctor.

	week				year					
	0	2	4	8						
Patient Evaluation	x	x	x [†]	(x)	x	x	x	x	x	x
Physician Contact	x	x	x [†]	(x)		x				x

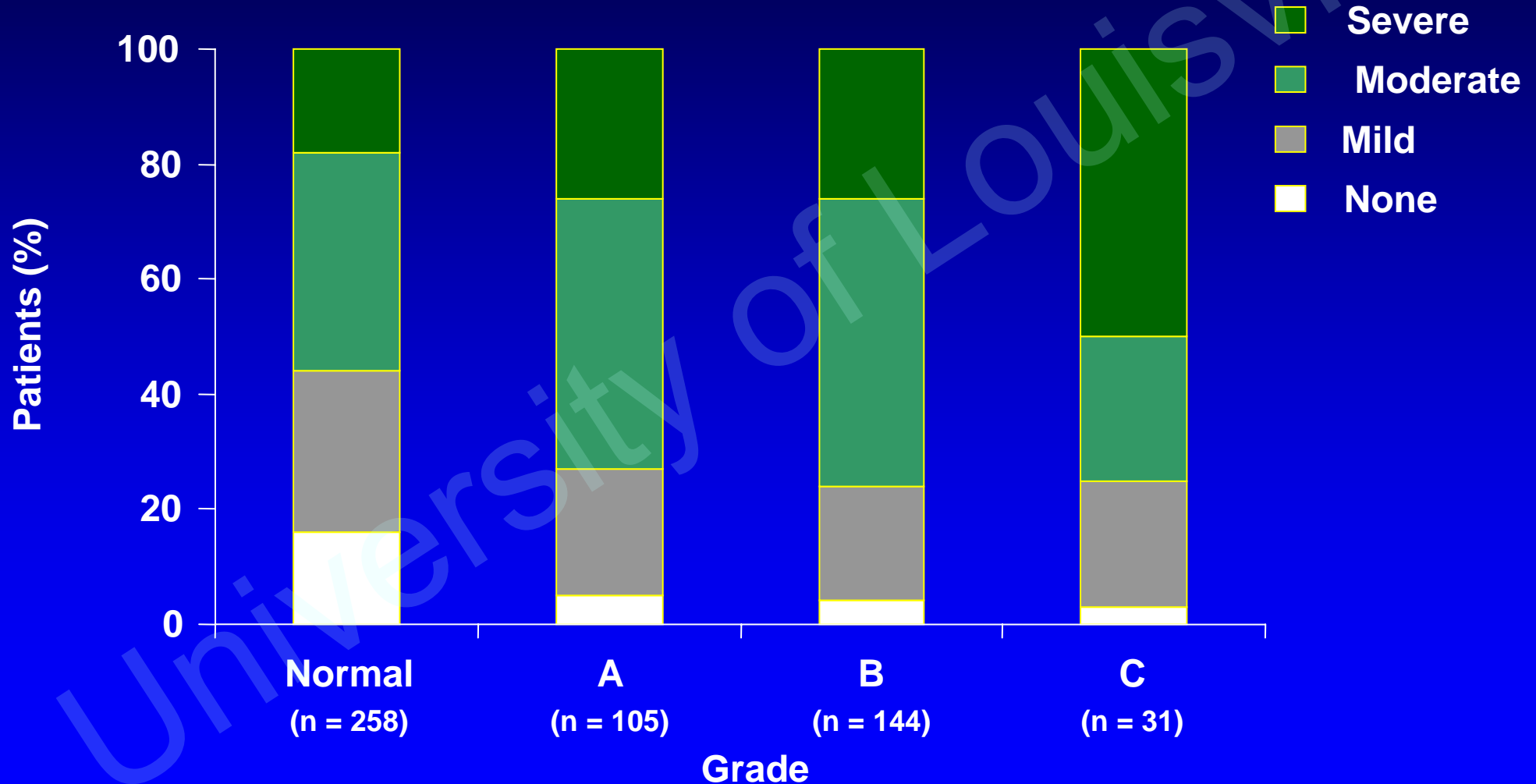
† for NERD patients only if not yet healed

(x) for ERD patients only if not yet healed

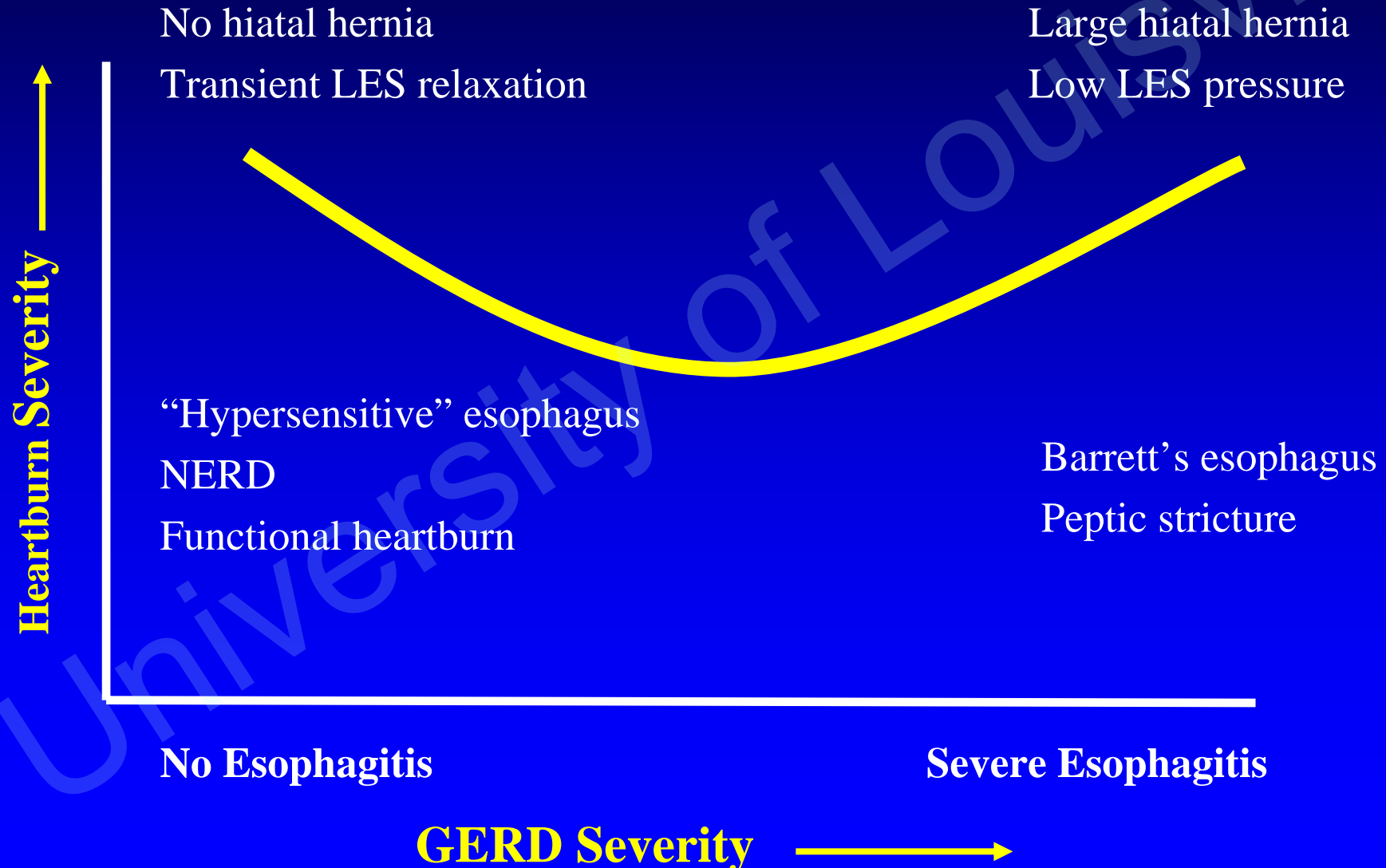
New Conceptual Model for GERD



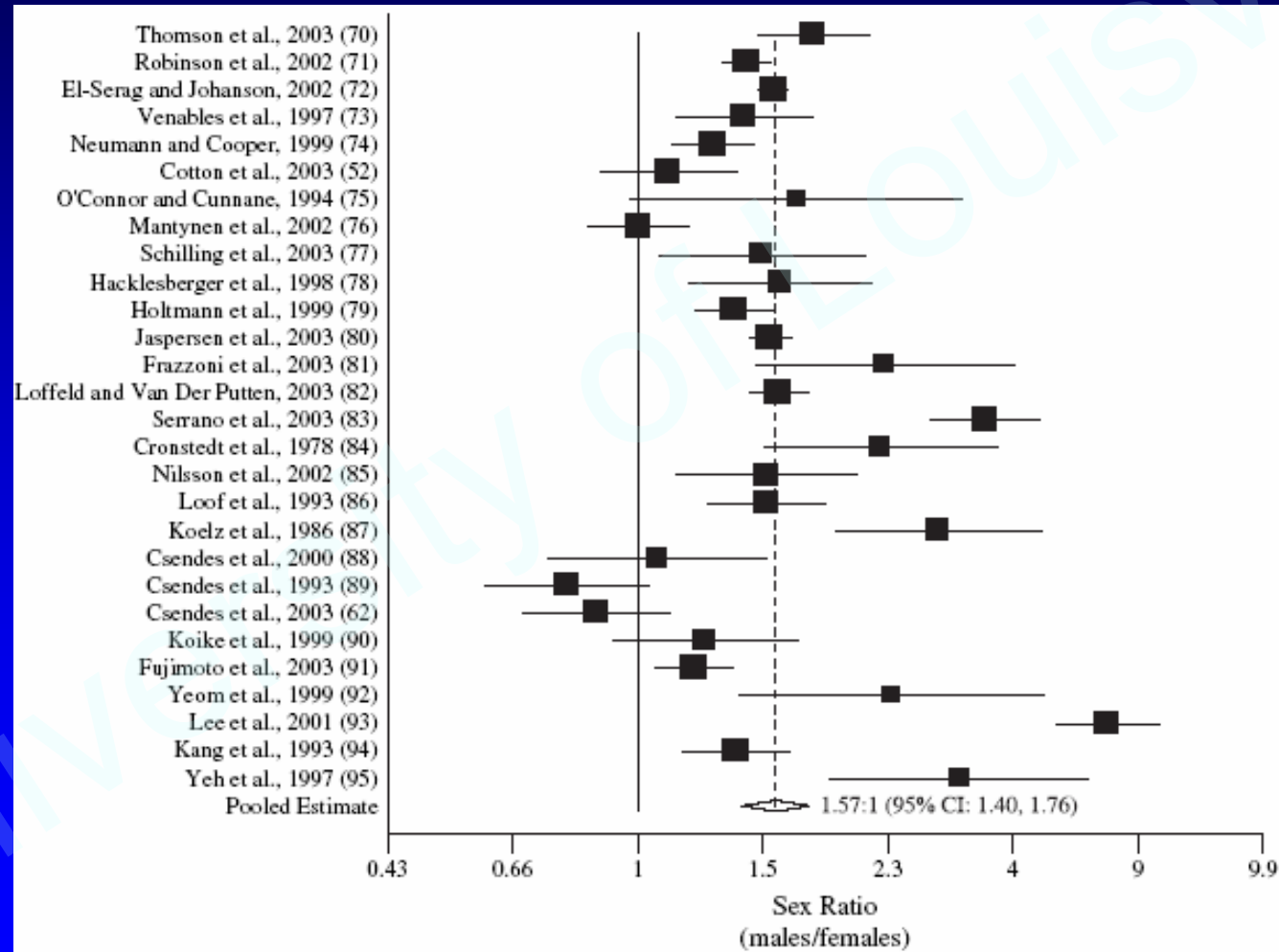
Heartburn Severity Does Not Correlate with Erosive Esophagitis



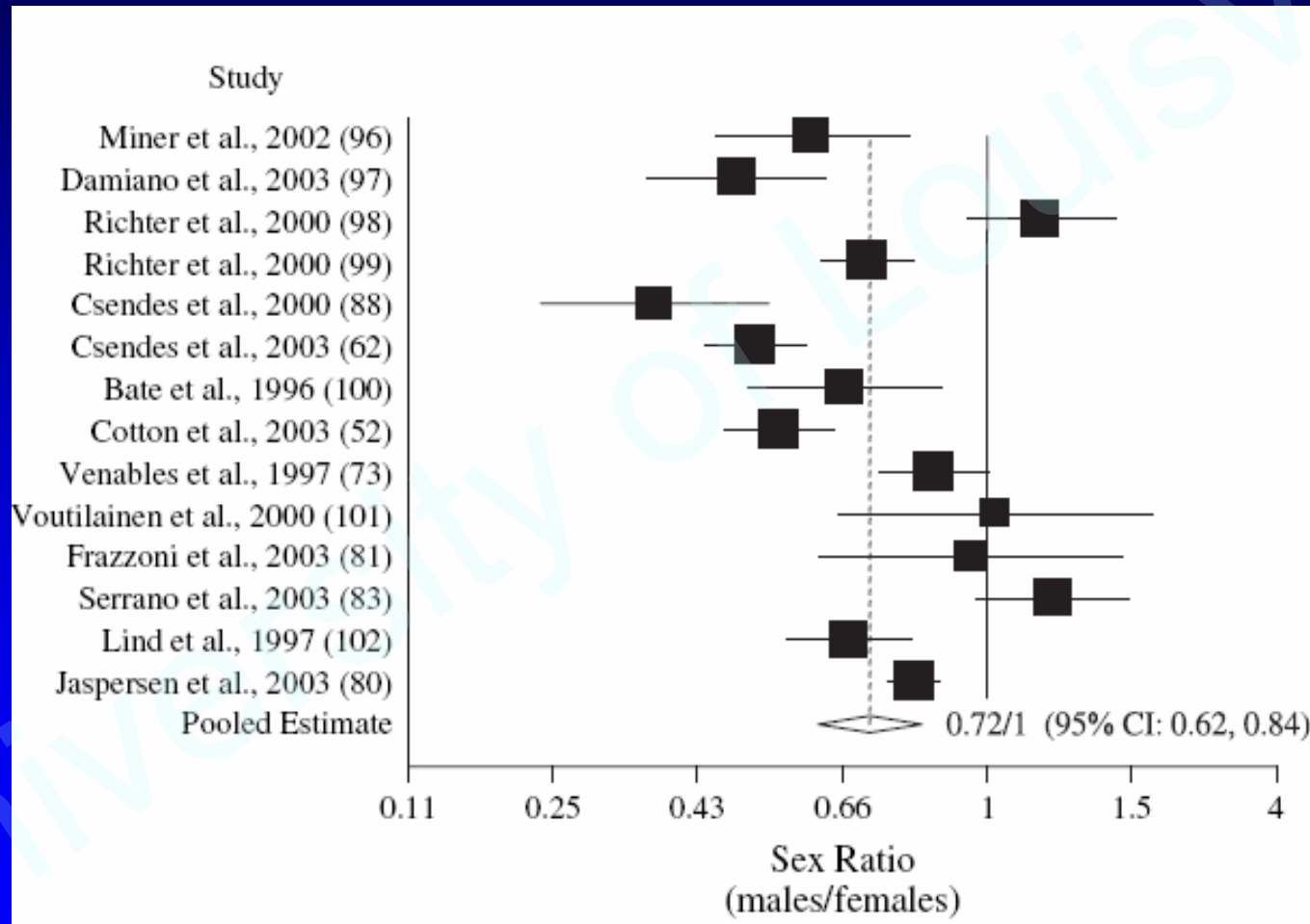
Heartburn Severity May Not Correlate with Disease Severity in GERD



GERD is More Common in Males

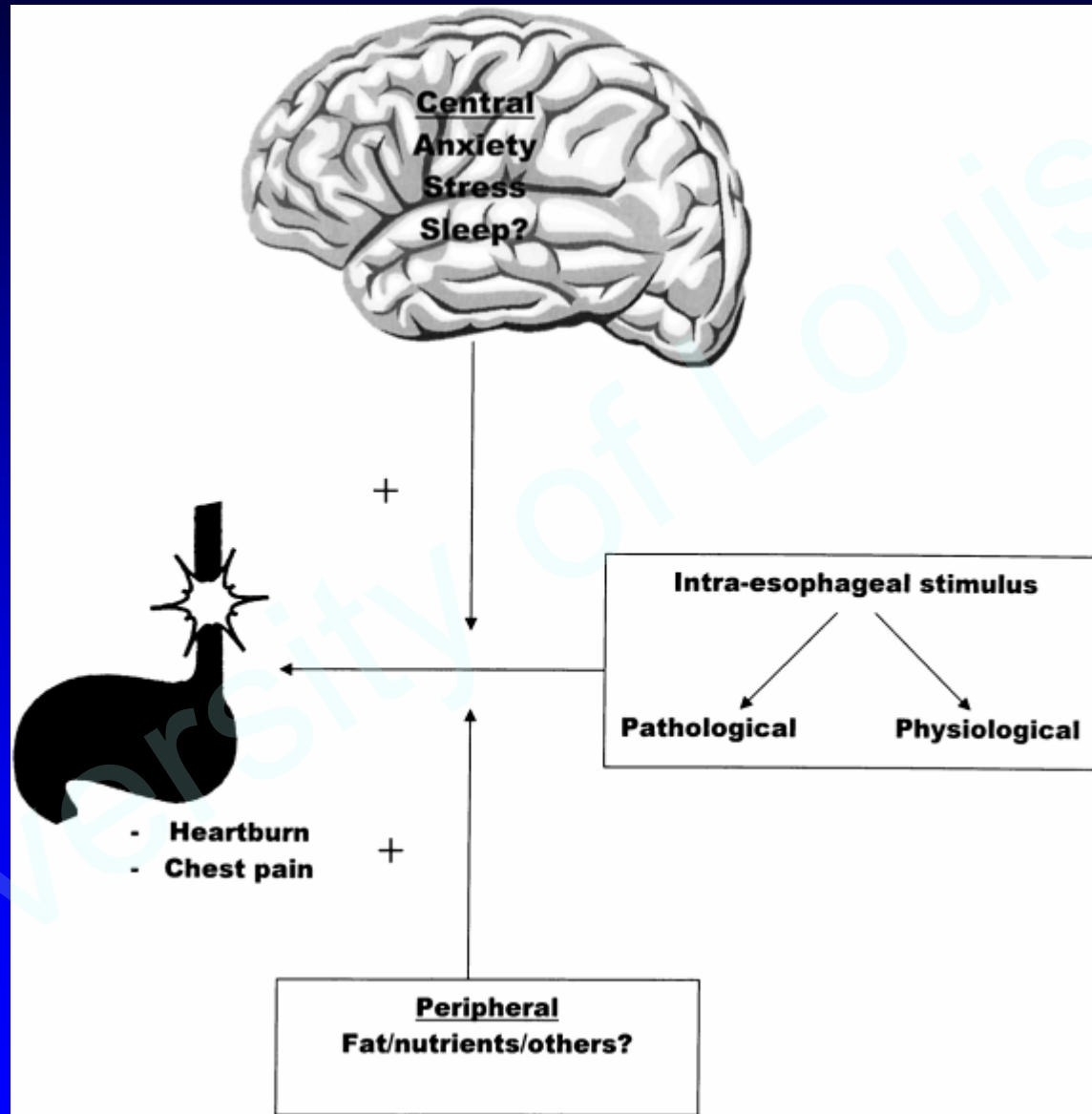


NERD is More Common in Females

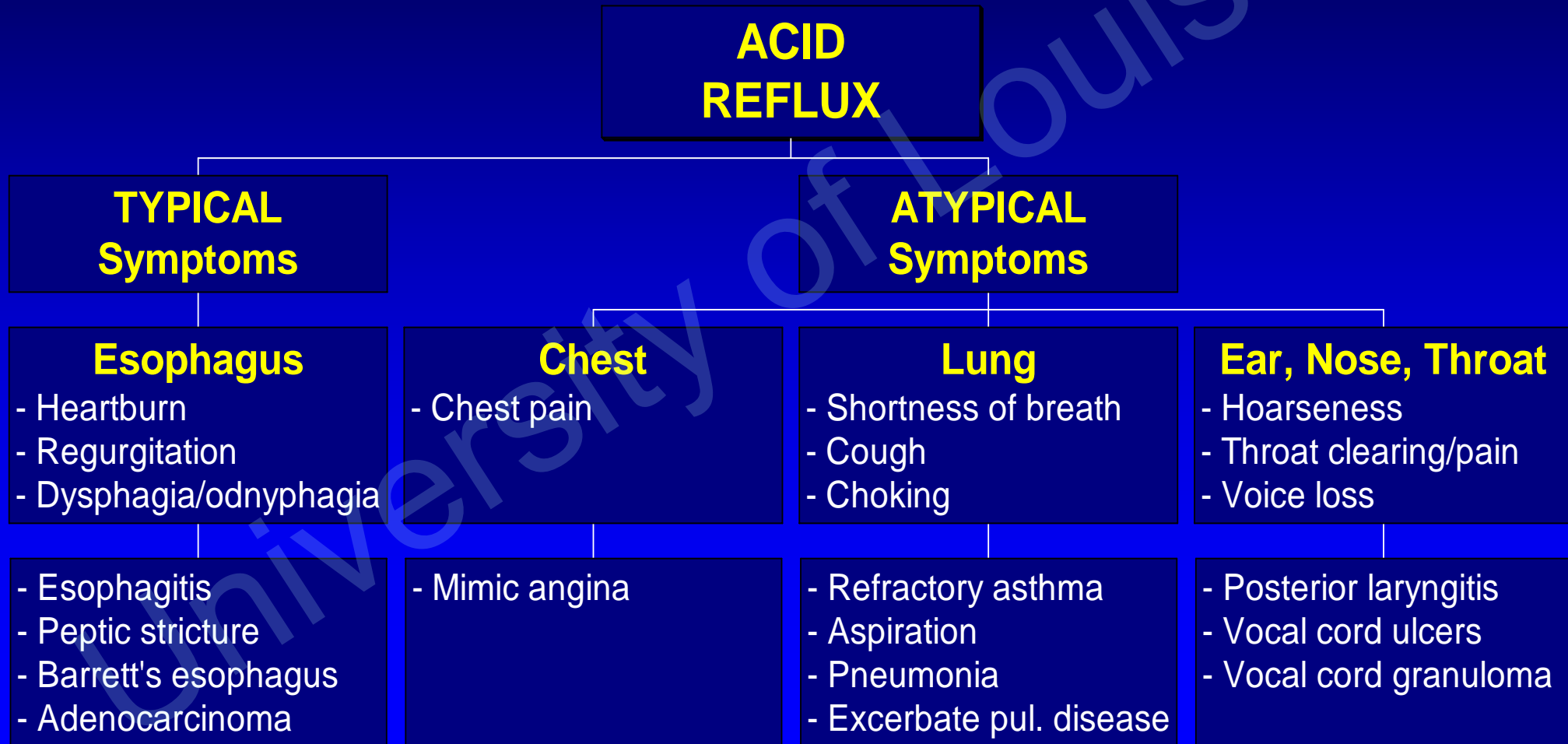


Brain-Gut Axis for Non-Erosive Reflux Disease

Acid
Hypersensitivity



Acid Reflux is More Than Just Heartburn



Typical vs. Atypical GERD

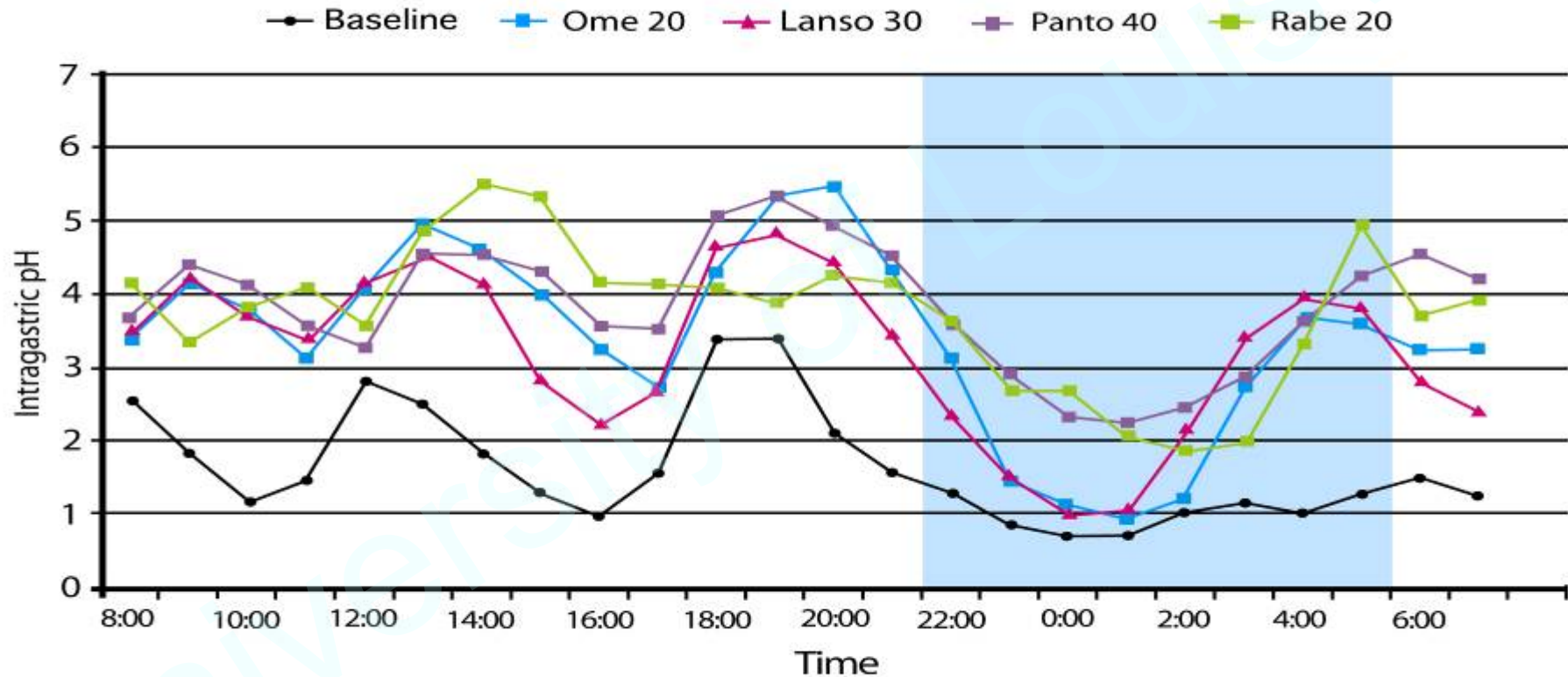
	<u>Typical</u>	<u>Atypical</u>
Symptoms	consistent	variable
Esophagitis/Barrett's	common	uncommon
Causes	reflux	<u>Multifactorial</u>
Treatment response	rapid	variable
Therapy	step-therapy	more aggressive + longer duration

Why PPI is not Working?

Six Most Common Reasons for Why PPI Is Not Working

1. Inadequate acid suppression – pH test on meds
2. Not taking medication correctly - history
3. Large hiatal hernia - EGD
4. Impaired esophageal motility - manometry
5. Gastroparesis – 4-hr GET
6. Wrong diagnosis – pH test off meds & further w/u

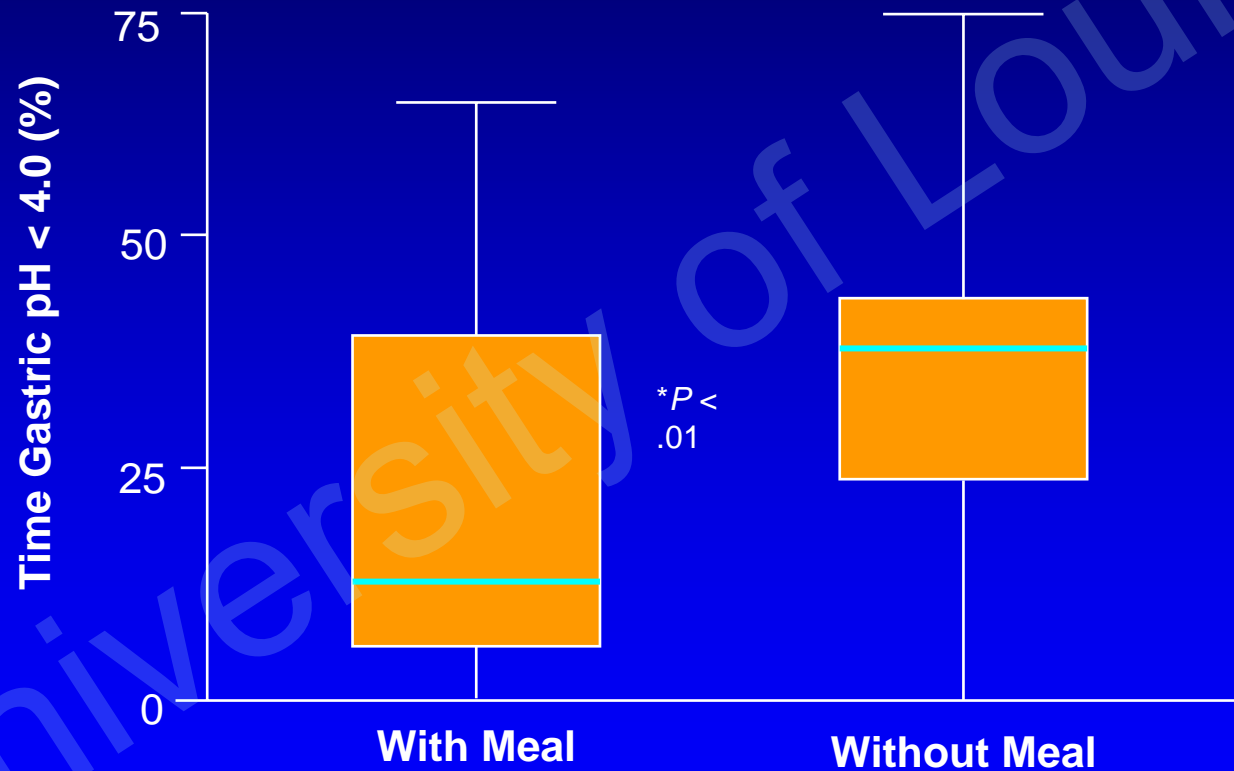
Inadequate Acid Suppression by PPI



Adapted from Tutuian et al. Med Gen Med 6(4), 2004.

¹ Hammer et al. Aliment Pharmacol Ther. 2004 15;

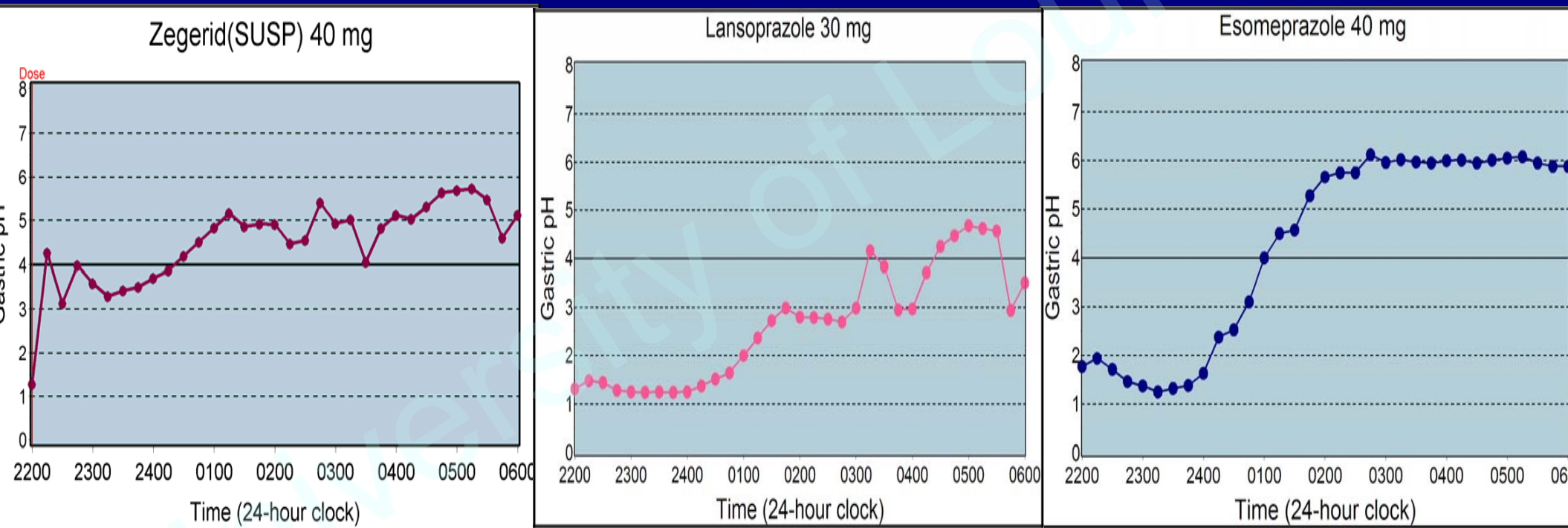
Not Taking the PPT before Meals



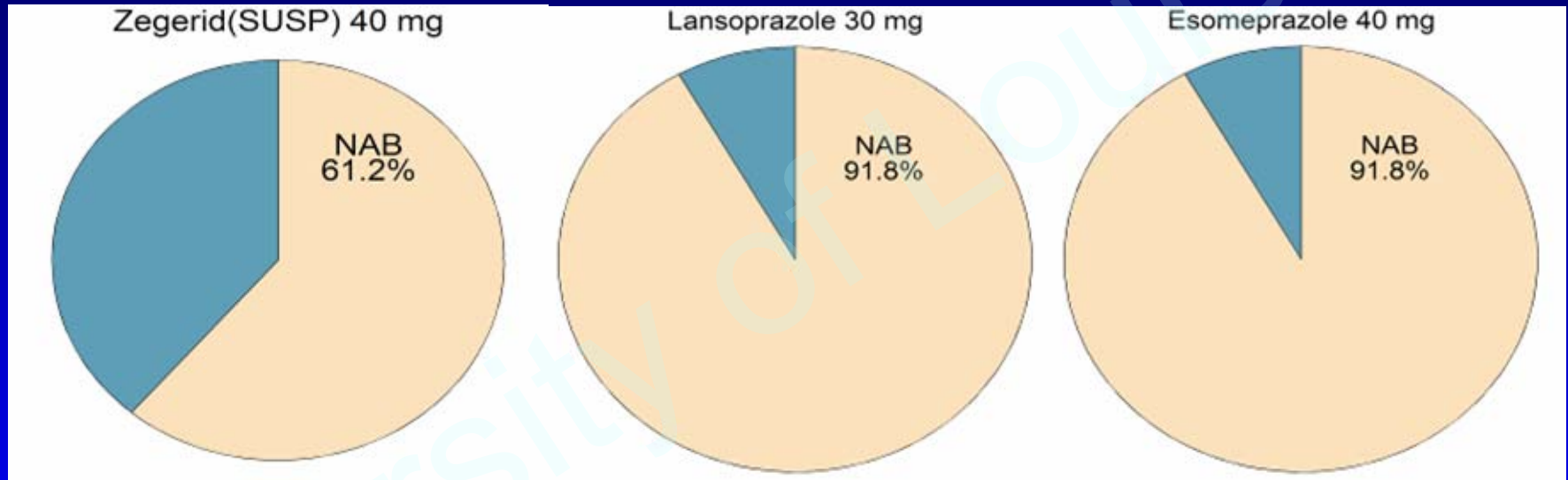
PPI Oral Formulation

- Delayed-release PPI
 - Tablet
 - Capsule
 - Powder
 - Dissolvable
- Immediate-release PPI
 - Tablet
 - Powder

Median Gastric pH During Night PPI Dosing q.h.s. (Day 7)



Qhs “Before Bed” Dosing is Not Appropriate with Delayed-Release PPI*



(n=49)

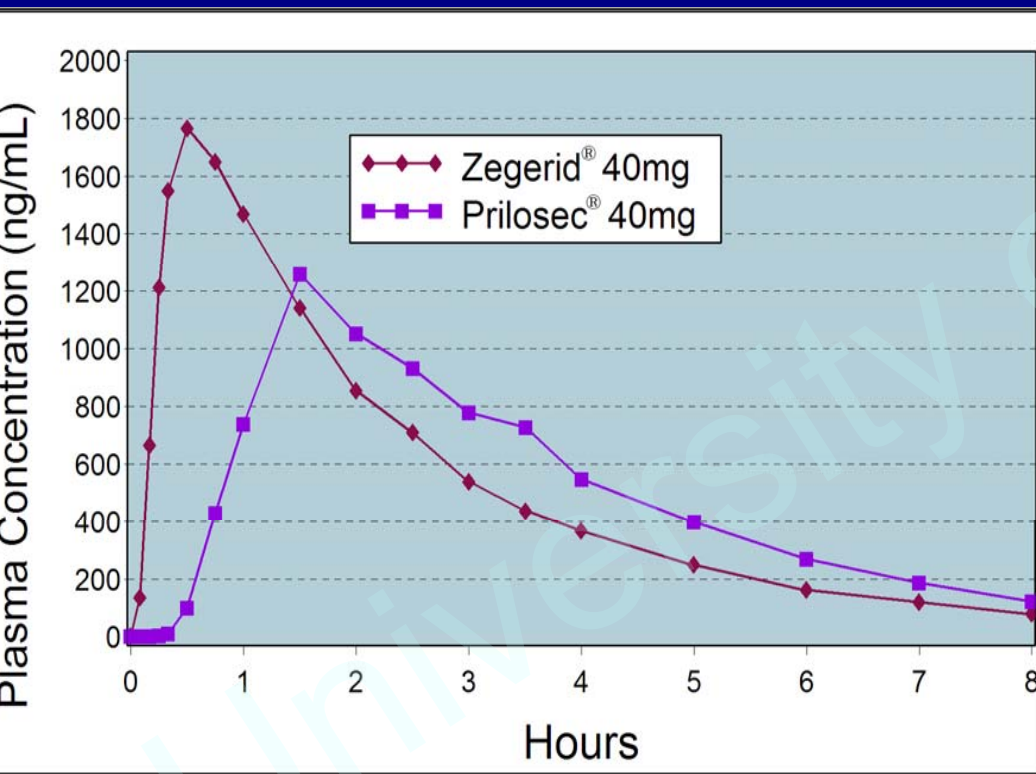
Zegerid vs. lansoprazole p-value <0.001

Zegerid vs. esomeprazole p-value <0.001

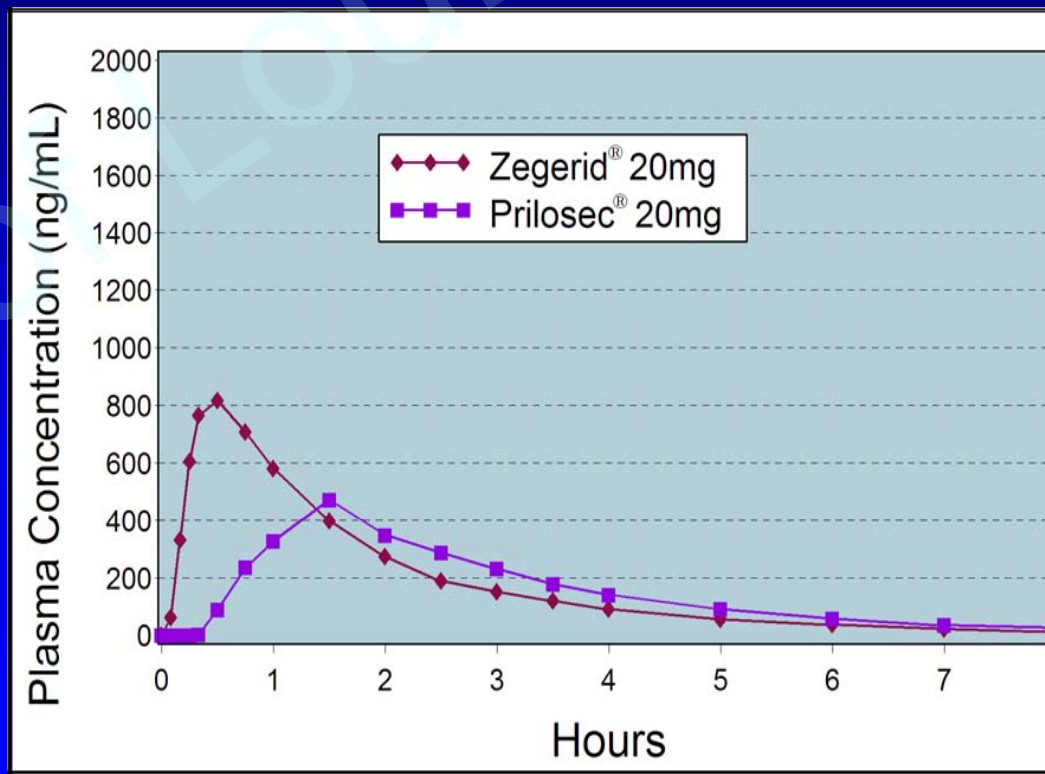
*Nighttime Interval (2200-0600) on day 7

Pharmacokinetics of Immediate-release and Delayed-release Omeprazole

40mg



20mg



N=31, open label cross-over, after 7 days of study drug

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

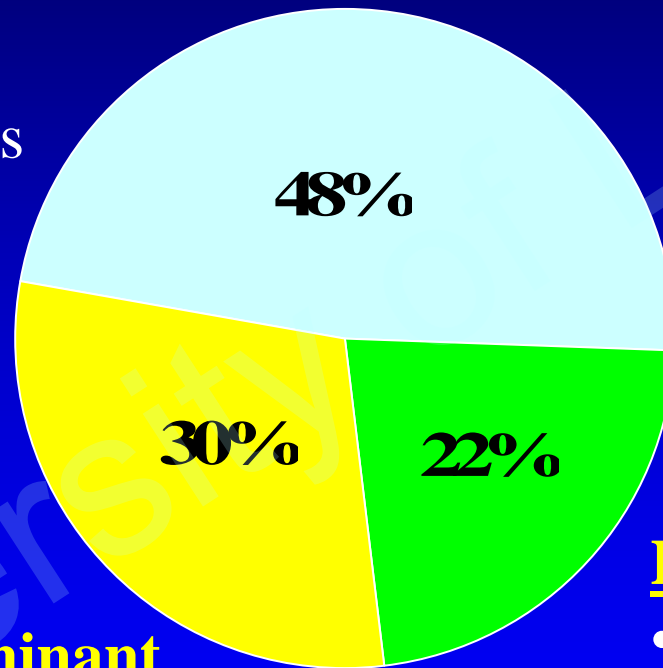
*Depends on clinical suspicion

Presentation of Gastroparesis

Vomiting-Predominant

- Vomiting
- Dehydration
- Hospitalizations
- Weight loss

N=338 patients
presenting to University
of Louisville



Dyspepsia-Predominant

- Epigastric pain
- Bloating
- Abdominal distension

Regurgitation-Predominant

- Heartburn
- Effortless regurgitation

Bravo Wireless pH Telemetry



- **Strength**
 - Patient friendly
 - 48-hr test
- **Weakness**
 - Single sensor



Transnasal pH monitoring



- **Strength**
 - Most sensitive and specific test for GERD
 - Useful for atypical GERD
- **Weakness**
 - Patient discomfort
 - Costly

Conclusion

- All GERD patients are not the same
 - NERD vs. EE vs. BE
- Causes of GERD are multifactorial
- Six most common reason for refractory typical or atypical GERD are