

Epidemiology of GERD

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Professor of Medicine

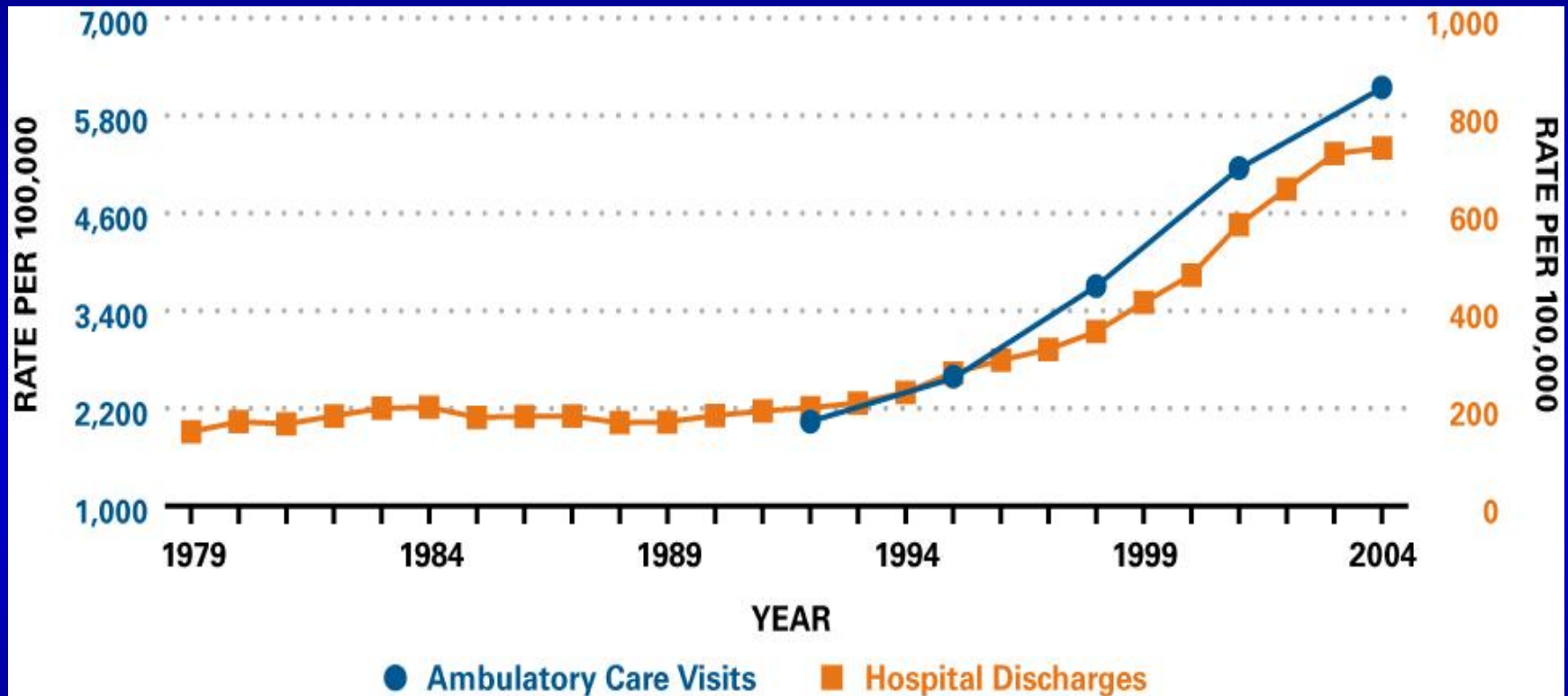
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The Trends

Gastroesophageal Reflux Disease: Age-Adjusted Rates of Ambulatory Care Visits and Hospital Discharges With All-Listed Diagnoses in the United States, 1979–2004



SOURCE: National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS) (averages 1992-1993, 1994-1996, 1997-1999, 2000-2002, 2003-2005), and National Hospital Discharge Survey (NHDS)

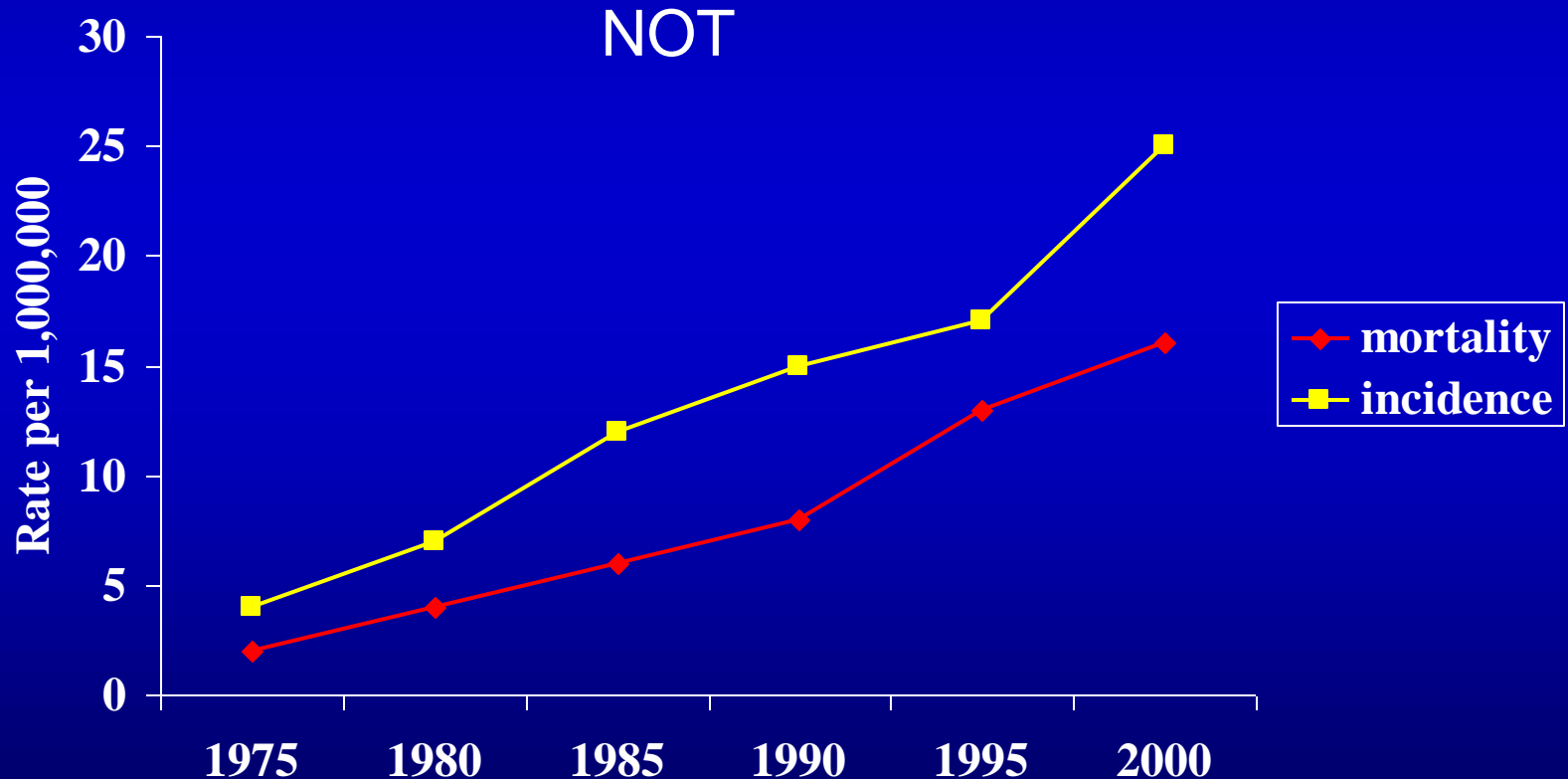
Esophageal Adenocarcinoma



Over-diagnosis?

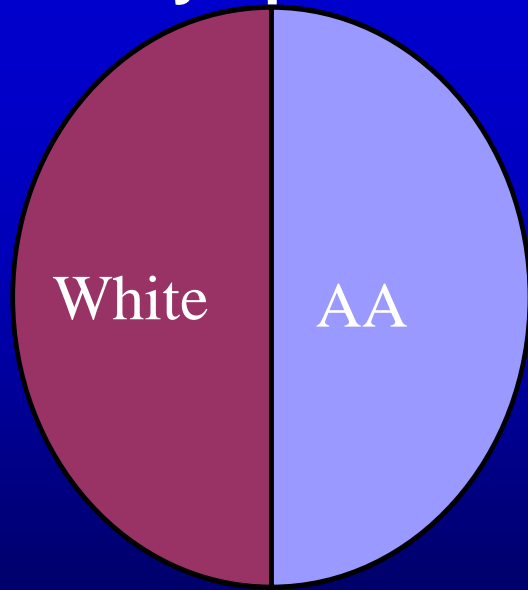
Mortality to Incidence Ratio

If over diagnosis is responsible for increased incidence, disease specific mortality would not increase

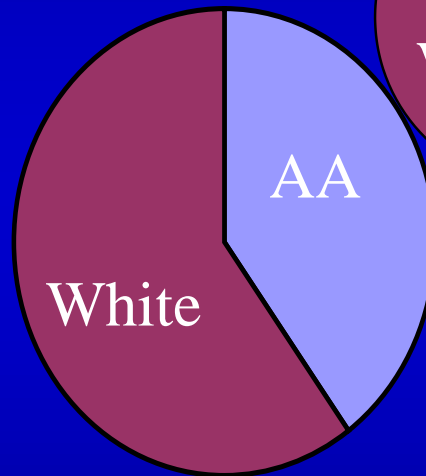


Racial Variations along the Spectrum of GERD

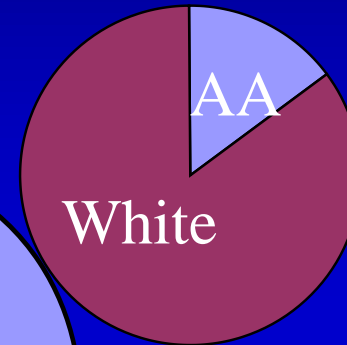
GERD Symptoms



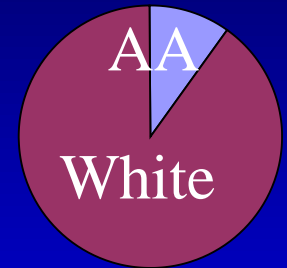
Erosive Esophagitis



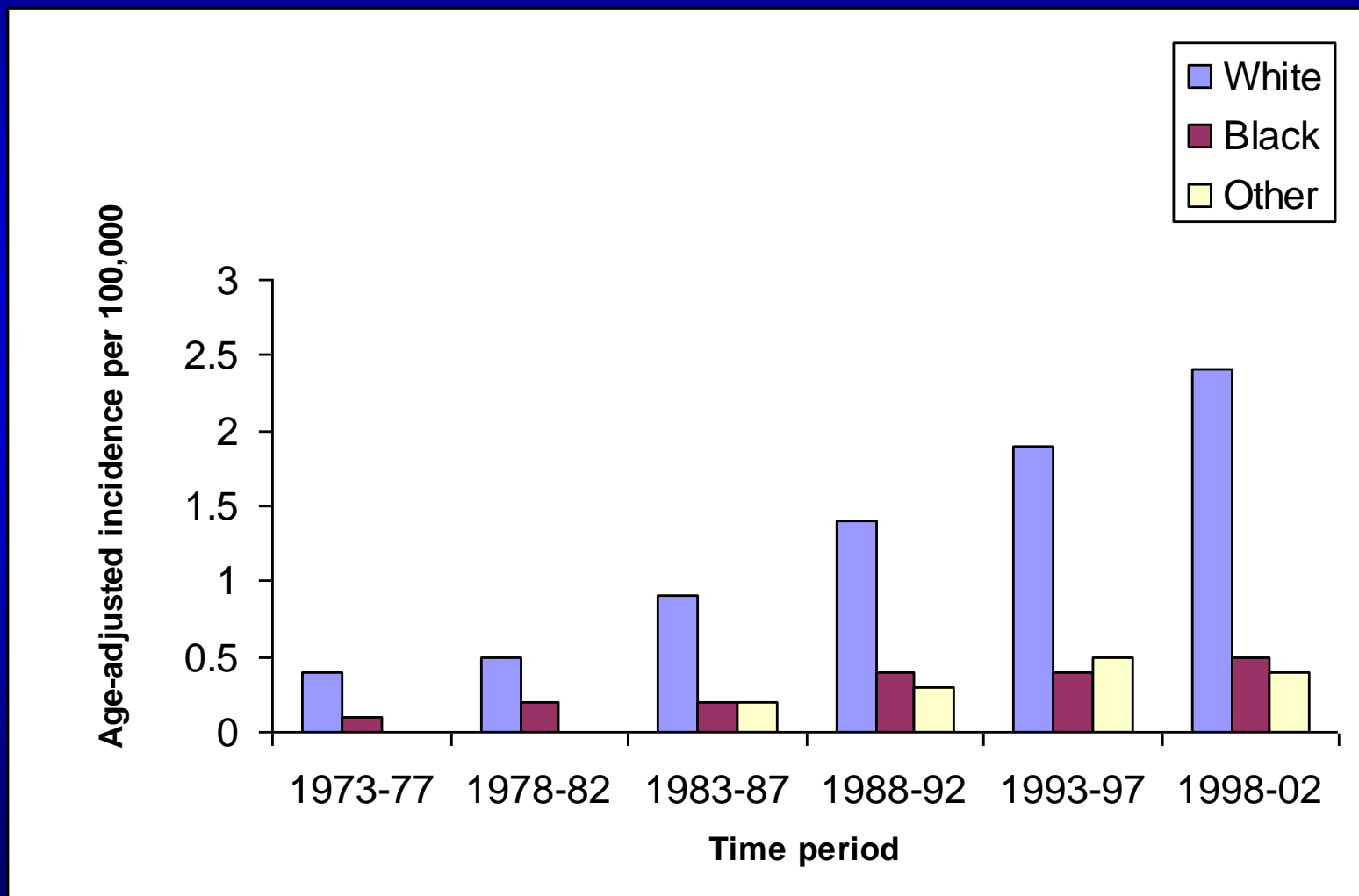
Barrett's



Esophageal adenocarcinoma

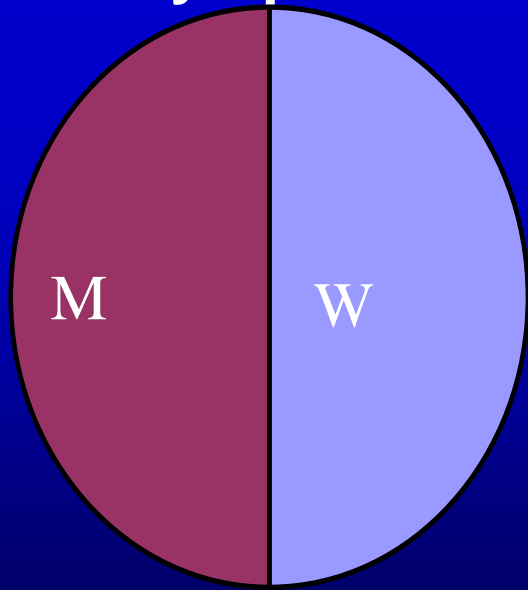


Esophageal Adenocarcinoma in the United States (SEER Data)

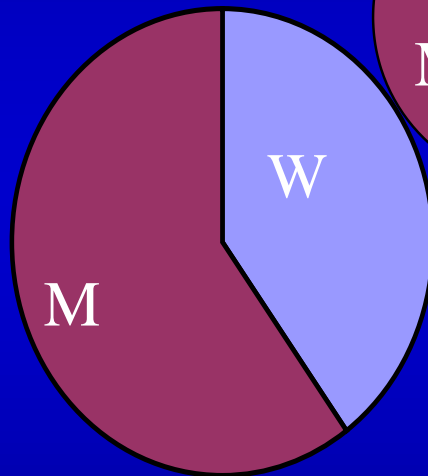


Sex Variations along the Spectrum of GERD

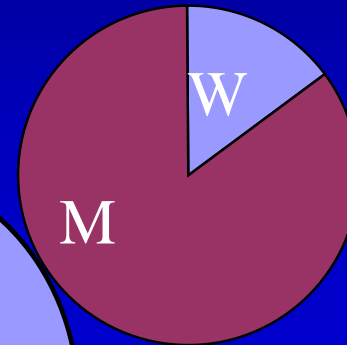
GERD Symptoms



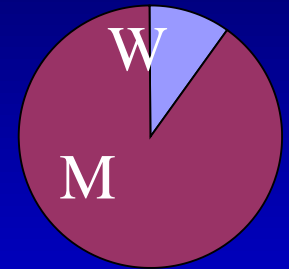
Erosive Esophagitis



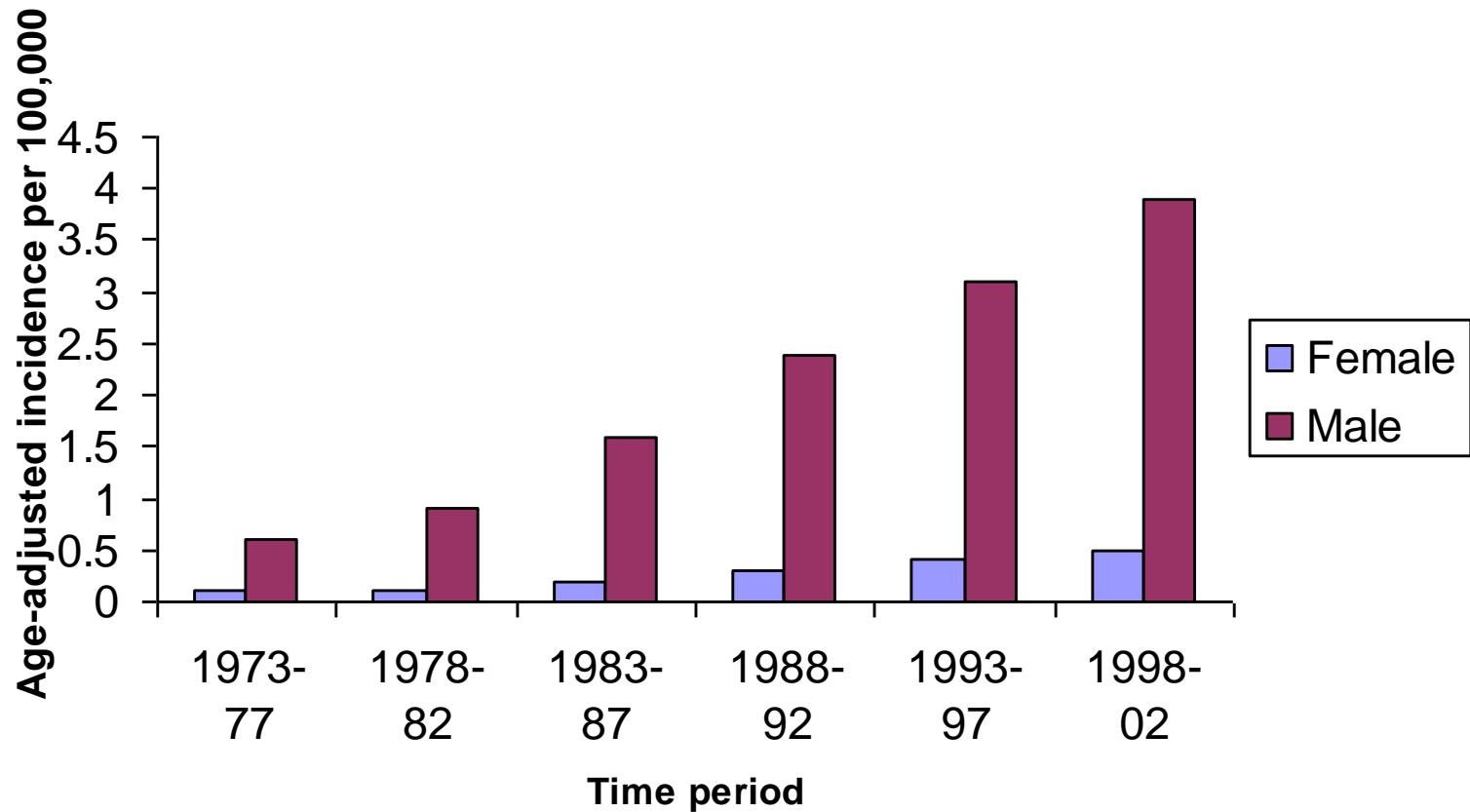
Barrett's



Esophageal adenocarcinoma

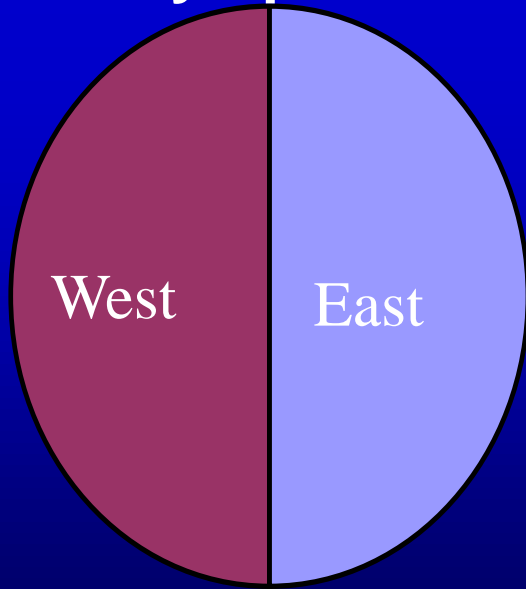


Esophageal Adenocarcinoma in the United States (SEER Data)

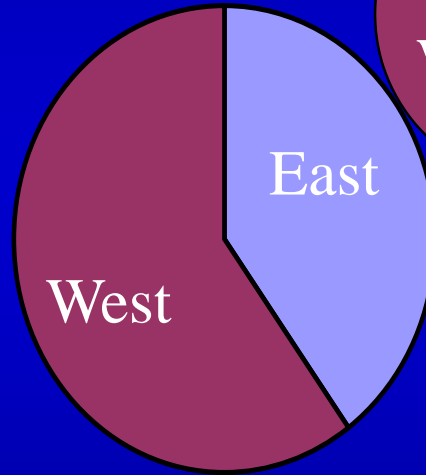


Geographic Variations along the Spectrum of GERD

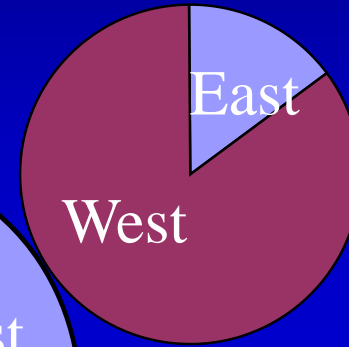
GERD Symptoms



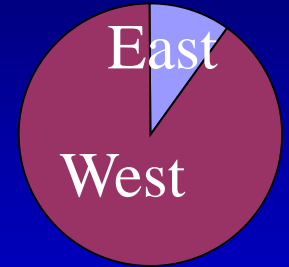
Erosive Esophagitis



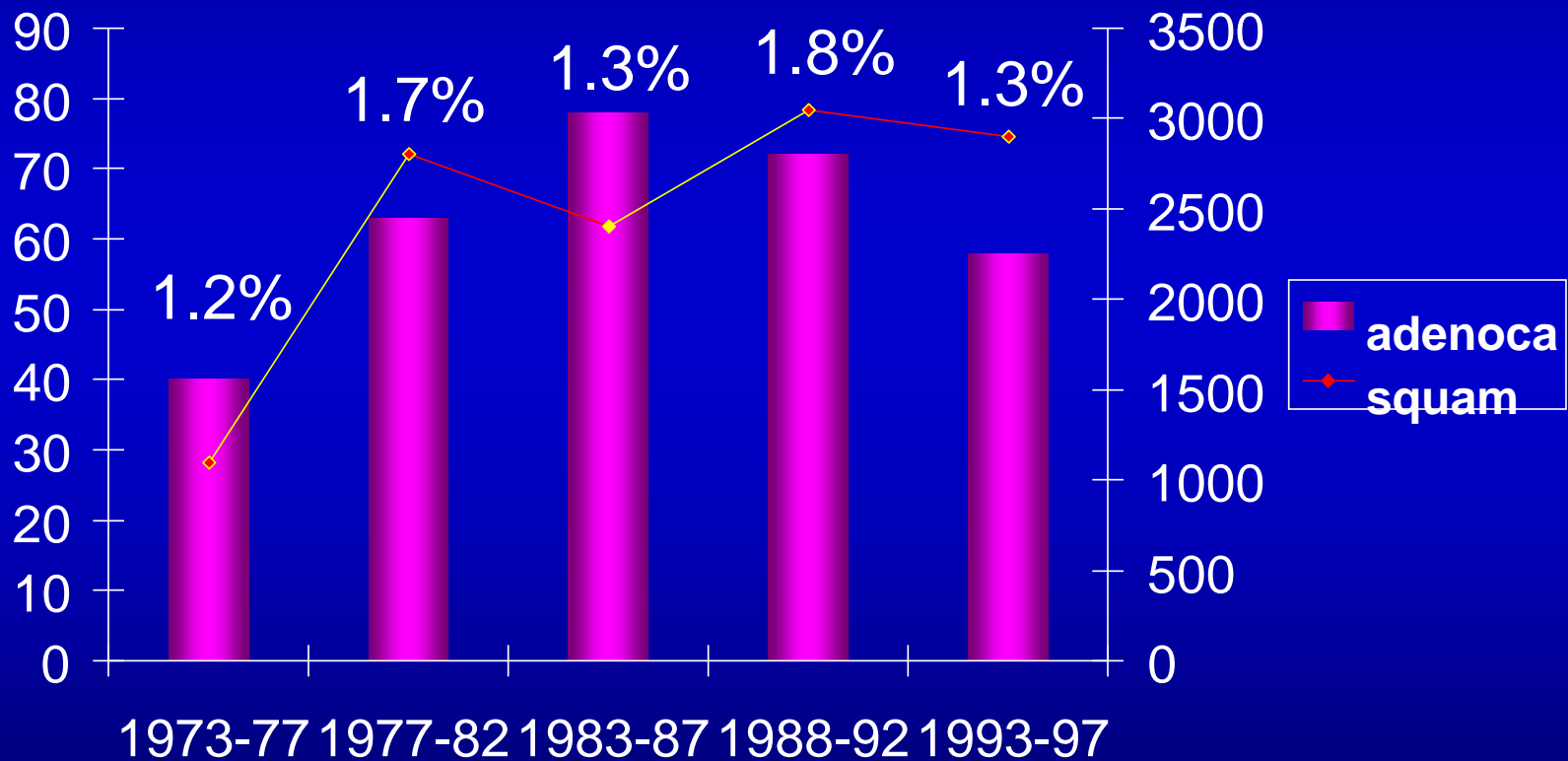
Barrett's



Esophageal adenocarcinoma



Esophageal Cancer in Japan



Hongo et al, J Gastroenterol 2003

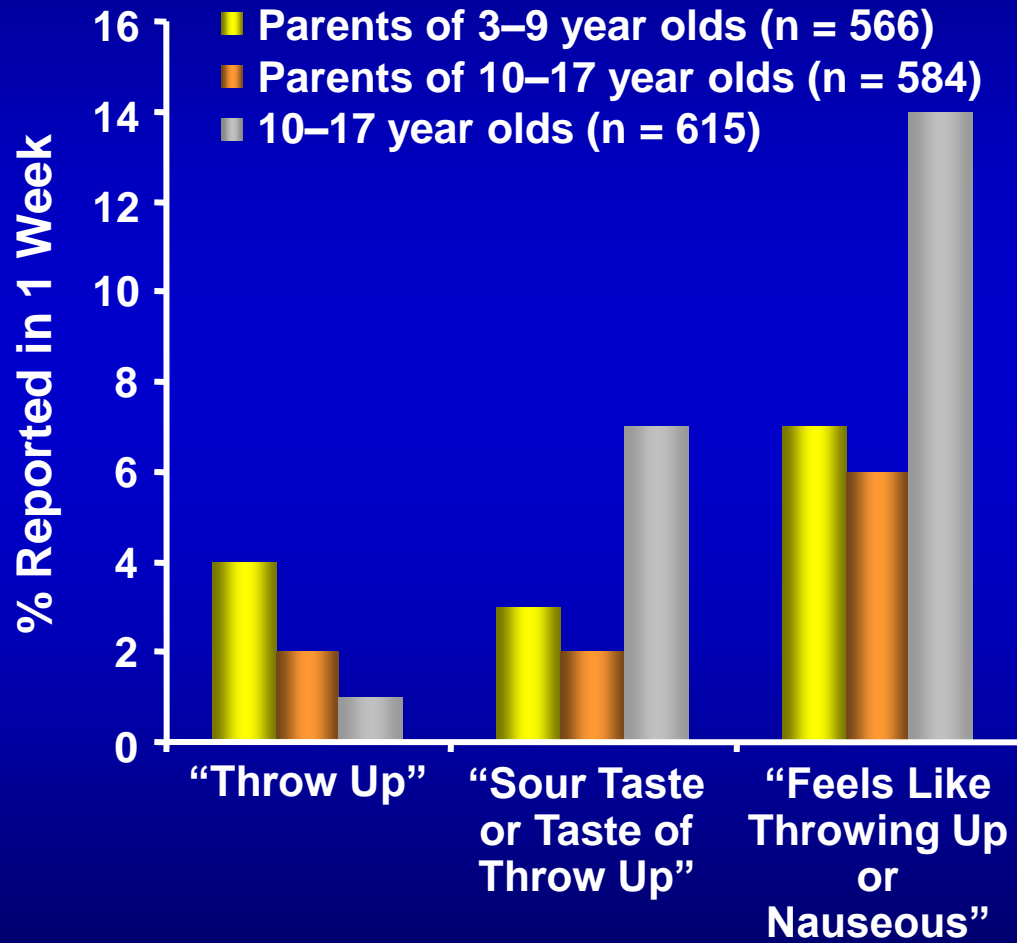
Stories Behind the Trend

Story I

GERD Symptom Duration and Risk of Esophageal Adenocarcinoma

Symptom <i>Duration</i> (Years)	Esophageal Adenocarcinoma Odds Ratio
No symptoms	1.0
<12	7.5
12-20	5.2
>20	16.4

Prevalence of Reflux Symptoms in Infants and Children: GER or GERD

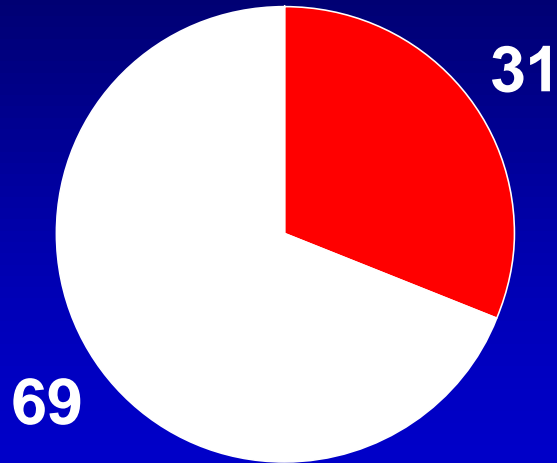


Clinical Course of Childhood GERD

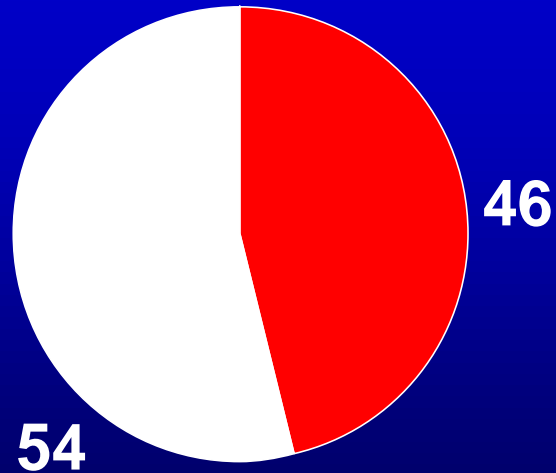
- **Study 1** *El-Serag HB, et al. Am J Gastroenterol 2004*
 - 207 patients contacted
 - 80 patients enrolled (39%)
 - GERD reported at a mean age of 5 years
 - Follow up at mean age of 20 years
- **Study 2** *El-Serag HB, et al. Clin Gastro Hepatol 2007*
 - 160 patients contacted
 - 113 enrolled (71%)
 - GERD reported at a mean age of 7
 - Follow up at mean age of 17 years

Weekly Heartburn and/or Regurgitation

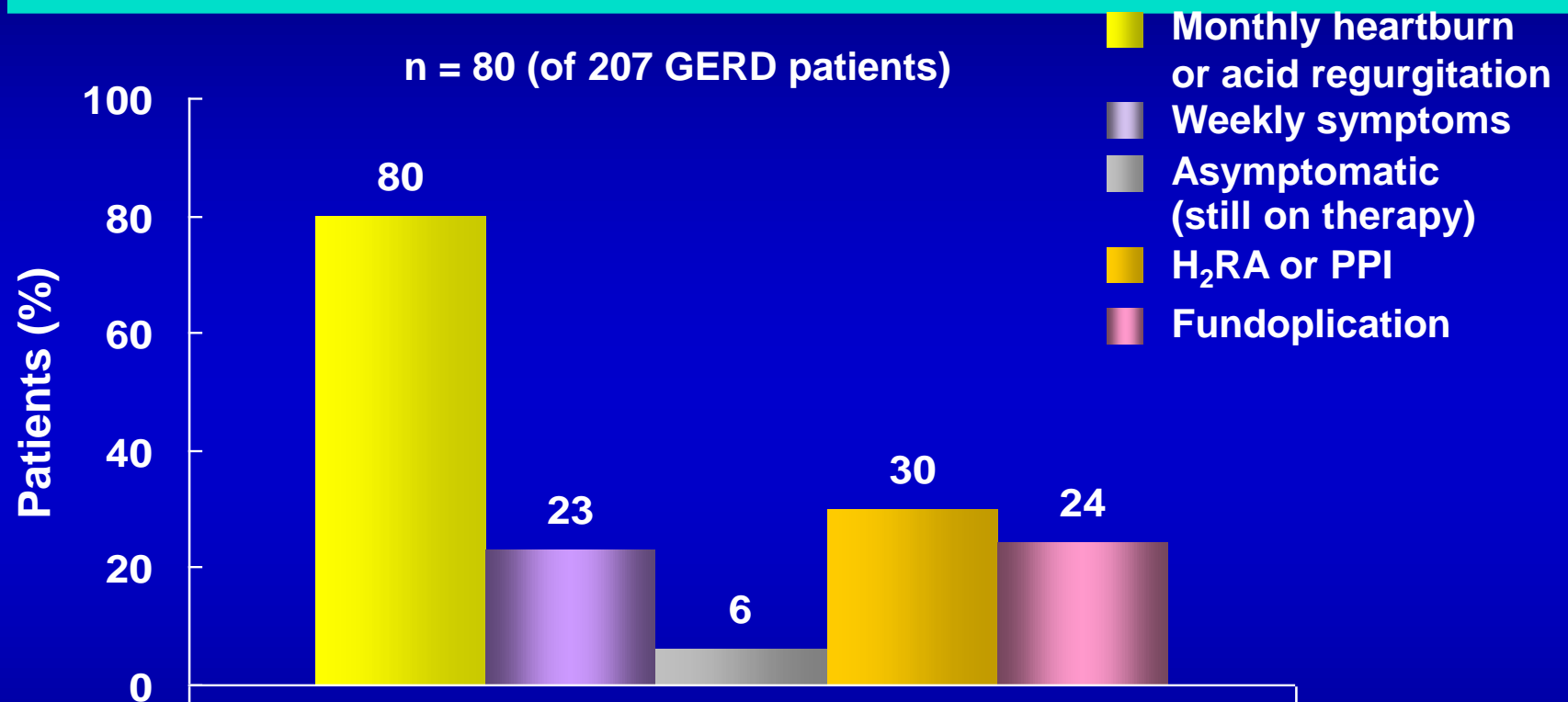
**Study 1
(n=80)**



**Study 2
(N=113)**



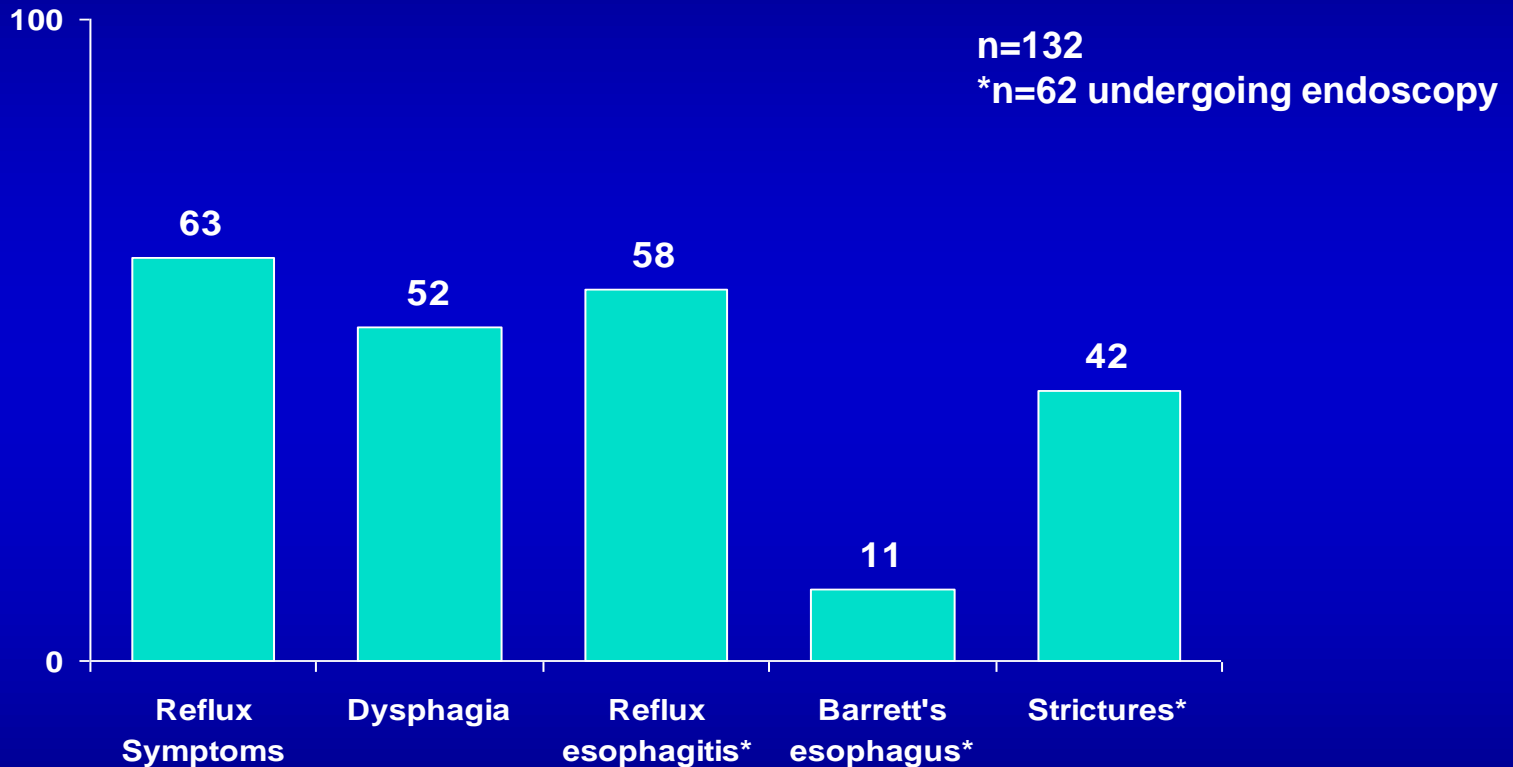
Childhood GERD Follow-up: Long-term



No differences among those with monthly, weekly, or no GERD symptoms in demographic features, age of GERD onset, receipt of fundoplication, or current GERD treatment

Long-term follow-up of adults born with esophageal atresia

Patients (%)



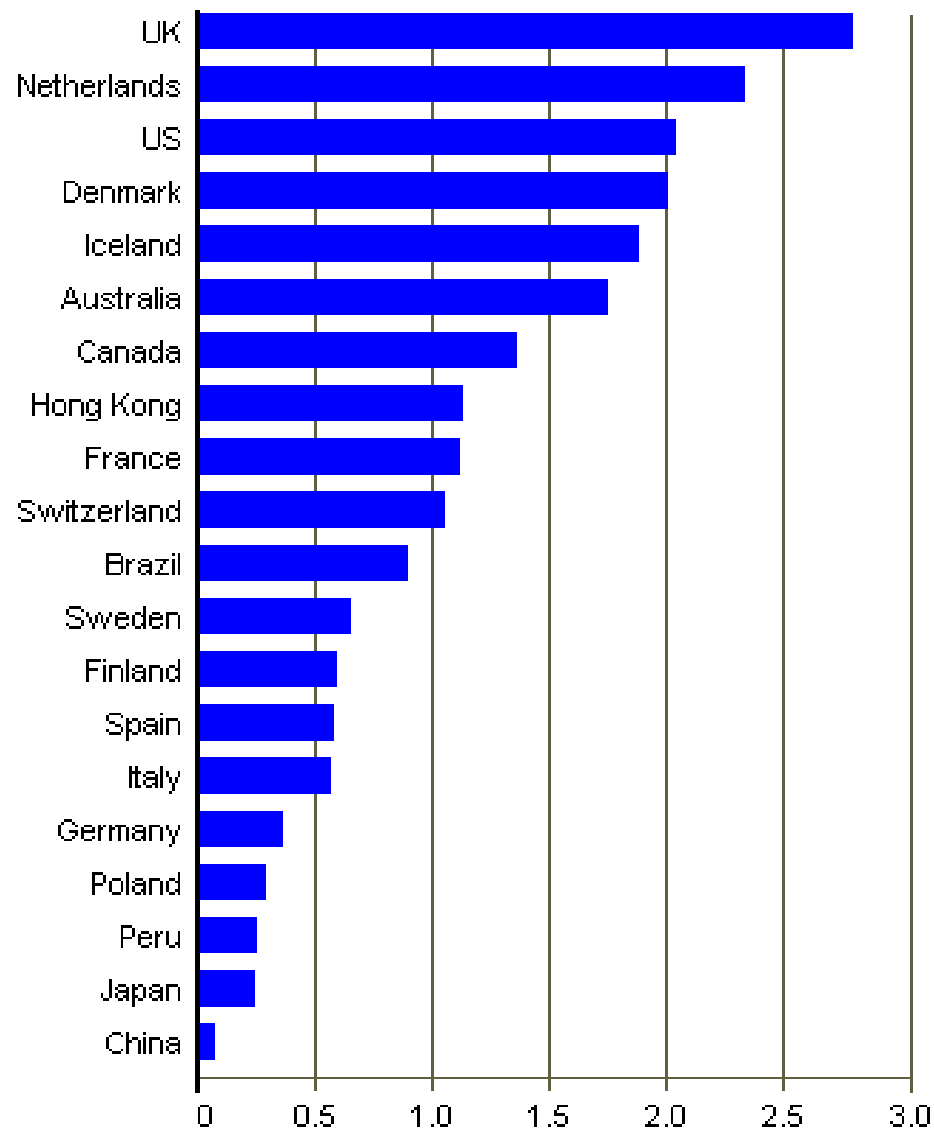
- Reflux symptoms, esophagitis and Barrett's esophagus are common in adults born with esophageal atresia



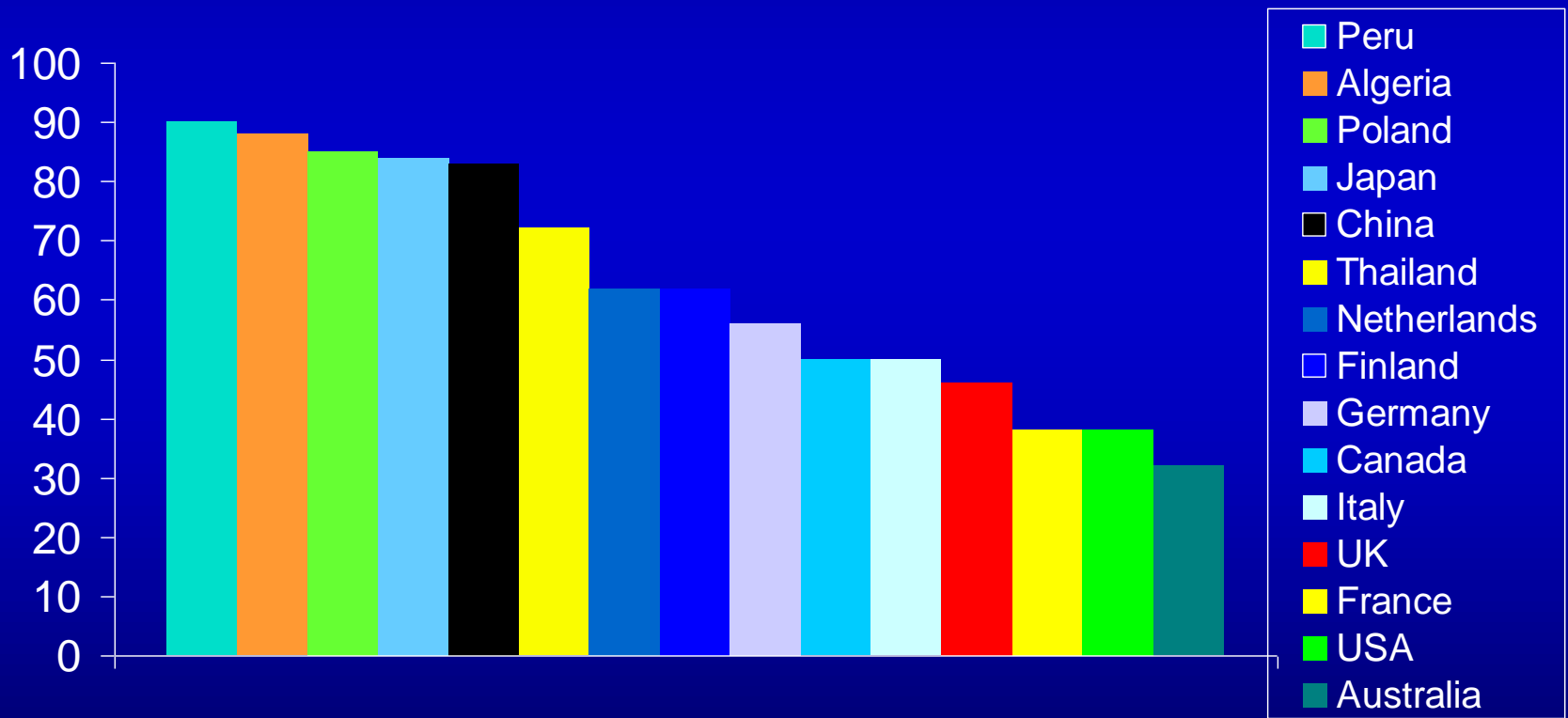
Stories Behind the Trend

Story II

Incidence of Esophageal Adenocarcinoma



Geographical Differences in the Prevalence of *H. pylori* (age > 20)



Ecological Fallacy ?

- Both trends (\downarrow H_p & \uparrow GERD) are true on a *population* level, but are they related to each other on the *individuals* level?

GERD and *Helicobacter pylori* (Hp)

- GERD symptoms: no consistent association with Hp
 - Cross-sectional studies
 - Longitudinal post Hp treatment
- Esophageal erosions
 - Weak inverse association with Hp
- BE and esophageal adenocarcinoma
 - More consistent inverse association

H. pylori and Esophageal Adenocarcinoma: Beyond Ecological Association

- Five studies
 - No significant association
 - One case-control study ¹
 - Significant “protective” association
 - One case-control study (only *Cag A* positive strains) ²
 - One case-control study (OR: 0.3, 95% CI: 0.2-0.6) ³
 - Nested case-control study (both types of esophageal cancer) ⁴
 - Nested case-control study (OR: 0.37, 95% CI: 0.16-0.88) ⁵

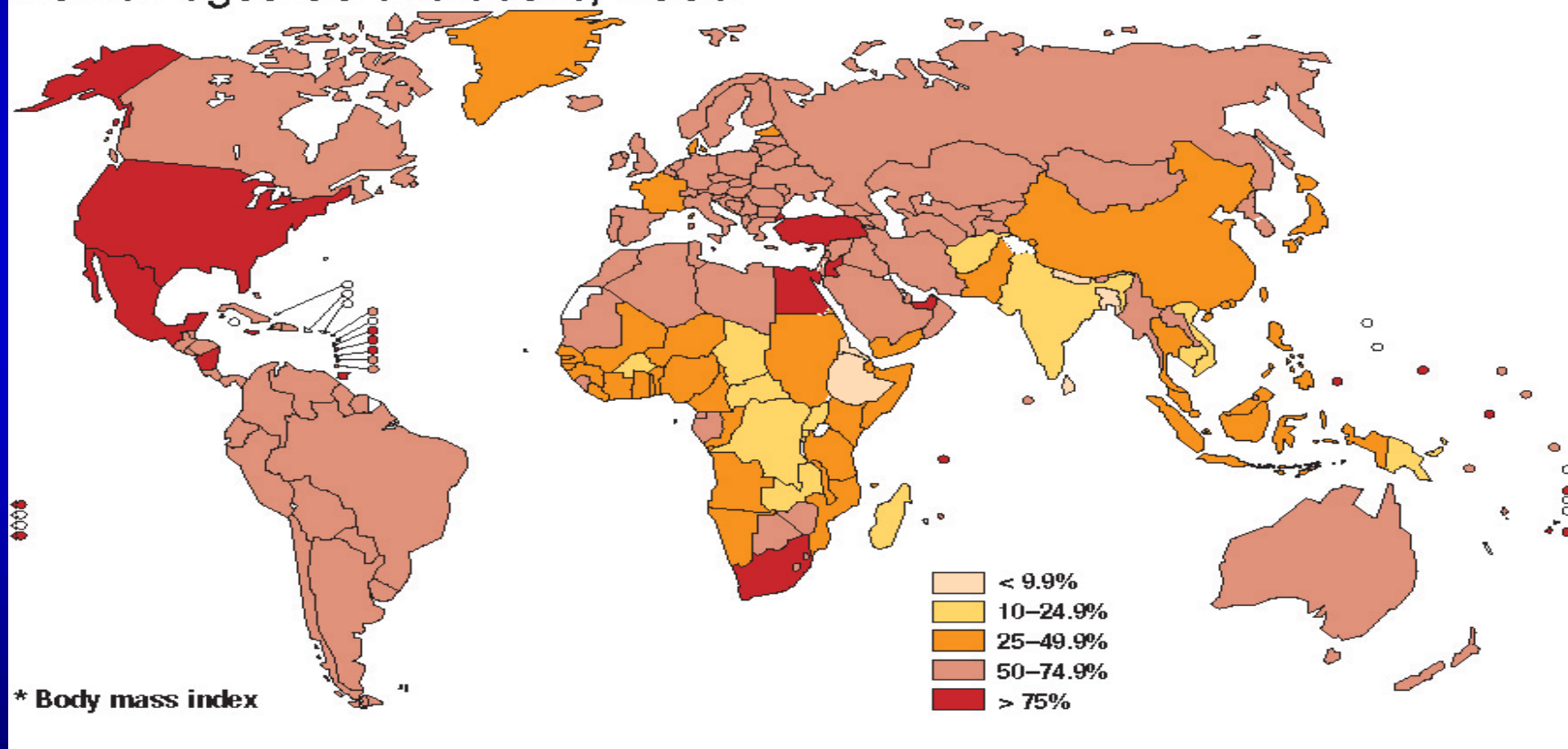
1. Chow et al (USA), 1998
2. Wu et al (USA), 2003
3. Ye et al (Sweden), 2004
4. Henrik Siman et al (Sweden), 2001
5. De Martel (USA), 2005

Stories Behind the Trend

Story III

Obesity Is a Global Problem

Projected prevalence of overweight (BMI* ≥ 25 kg/m²), women aged 30 and above, 2005



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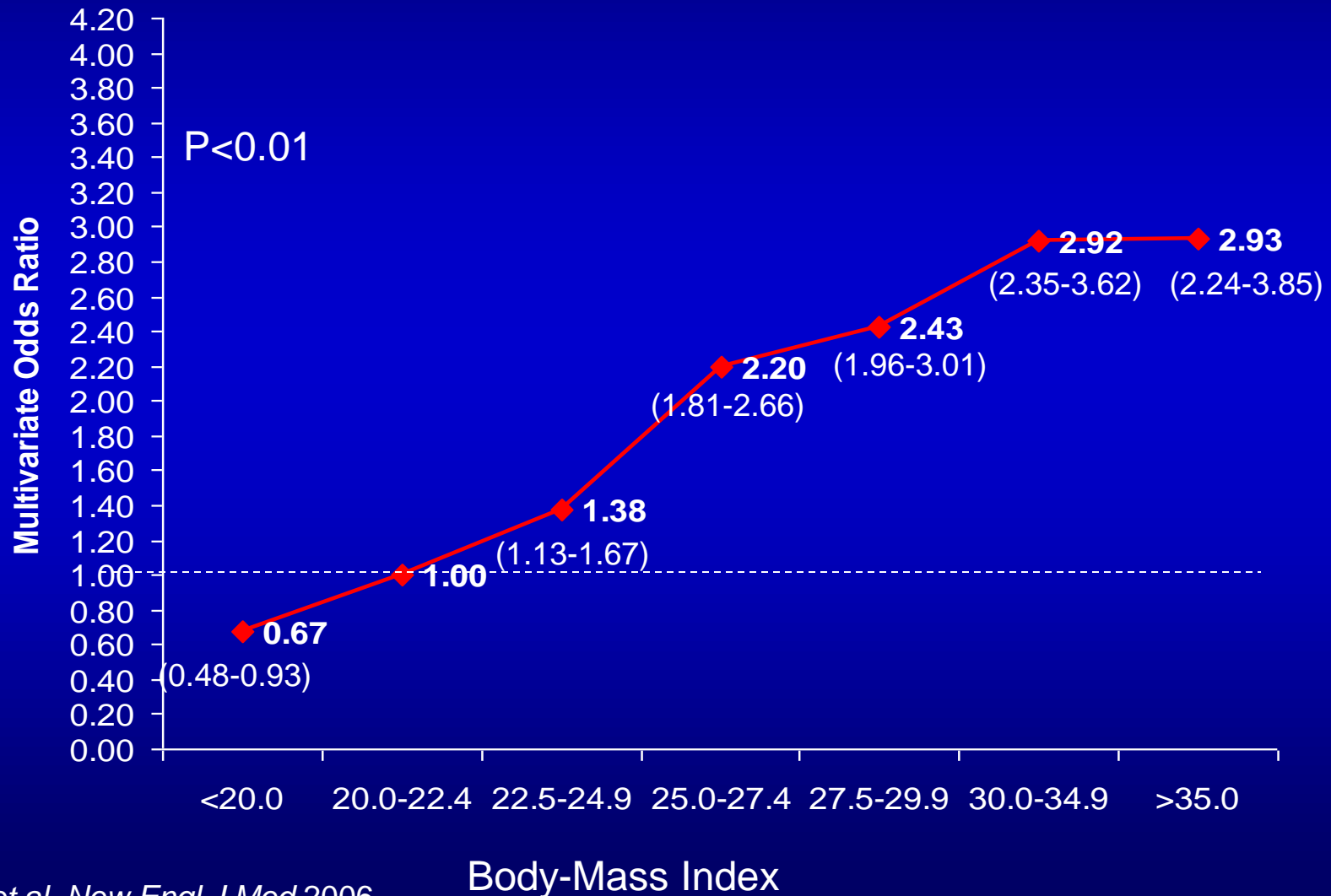
<http://www.cartoonbank.com>



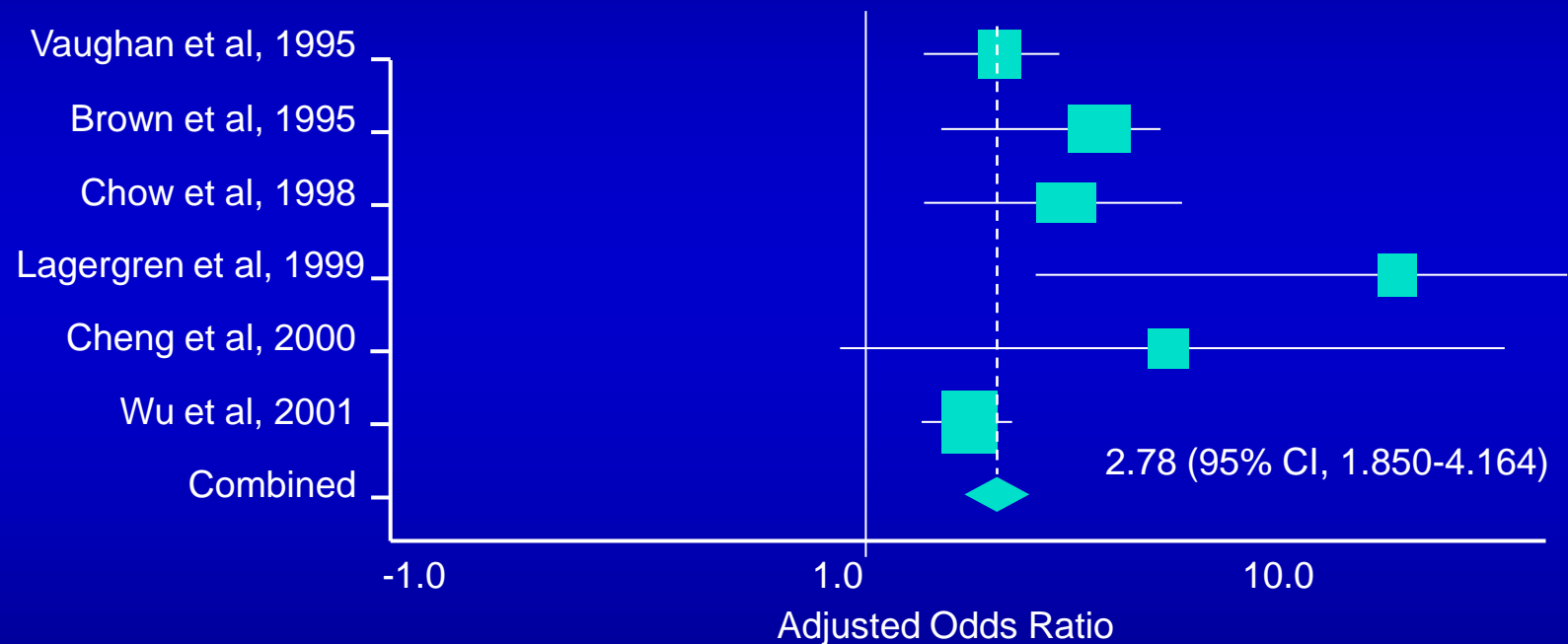
"According to an article in the upcoming issue of 'The New England Journal of Medicine,' all your fears are well founded."

“According to an article in the upcoming issue of “New England Journal of Medicine”, all your fears are well founded

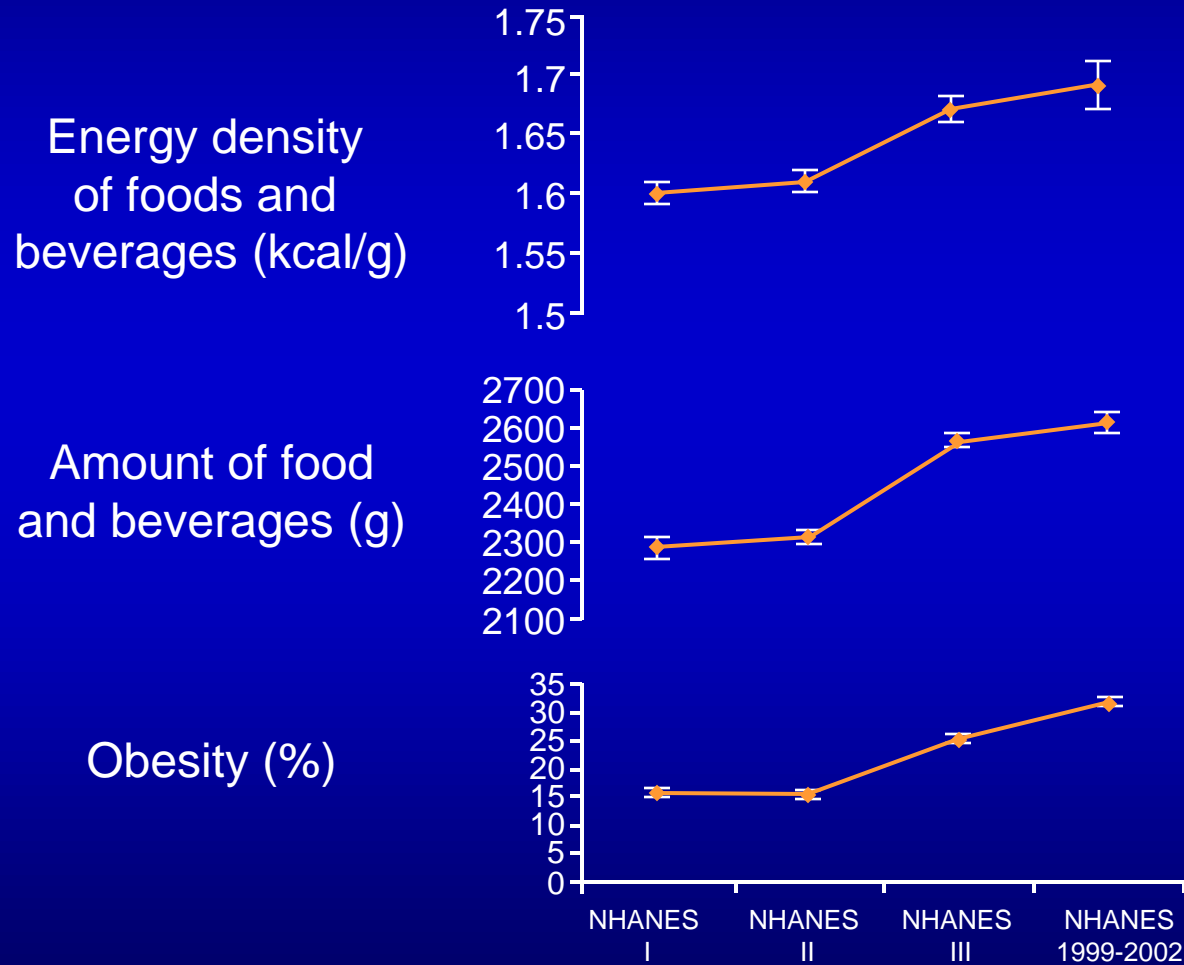
Association Between Body-Mass Index and the Risk of Frequent Symptoms of Gastroesophageal Reflux Disease (N=10,545, women)



Obesity and Risk of Esophageal Adenocarcinoma



Ecological Evidence for Gluttony



Gastroesophageal Reflux Disease

Obesity vs Diet

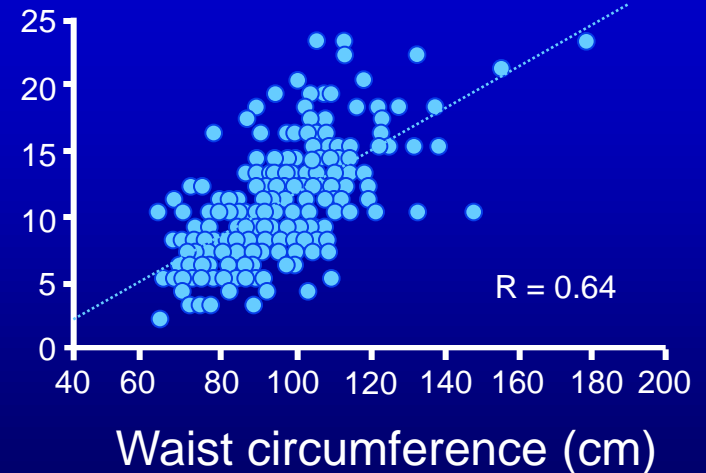
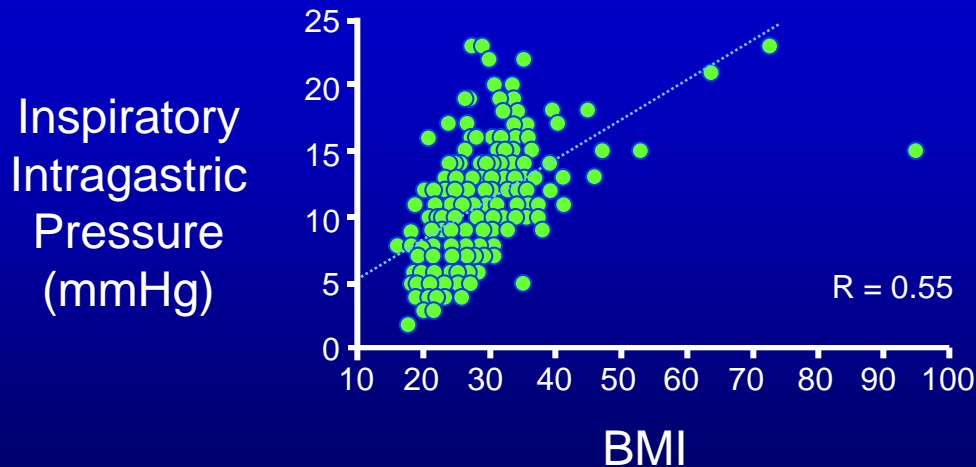
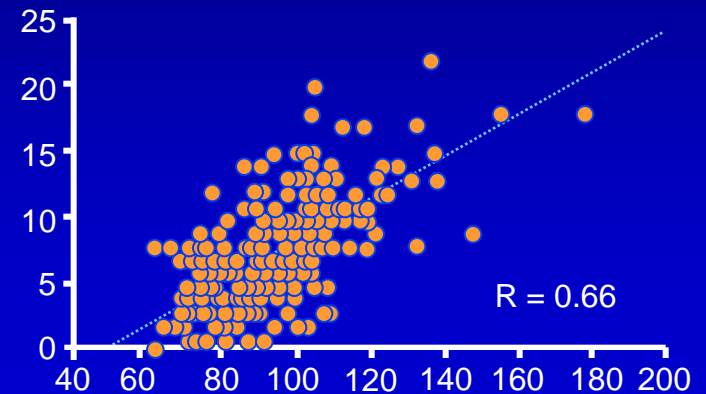
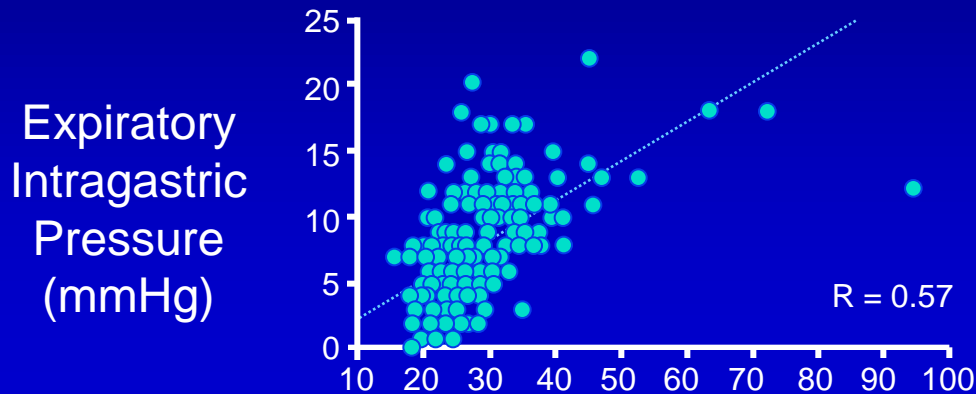
- No consistent association of dietary fat with
 - GERD
 - Esophageal adenocarcinoma



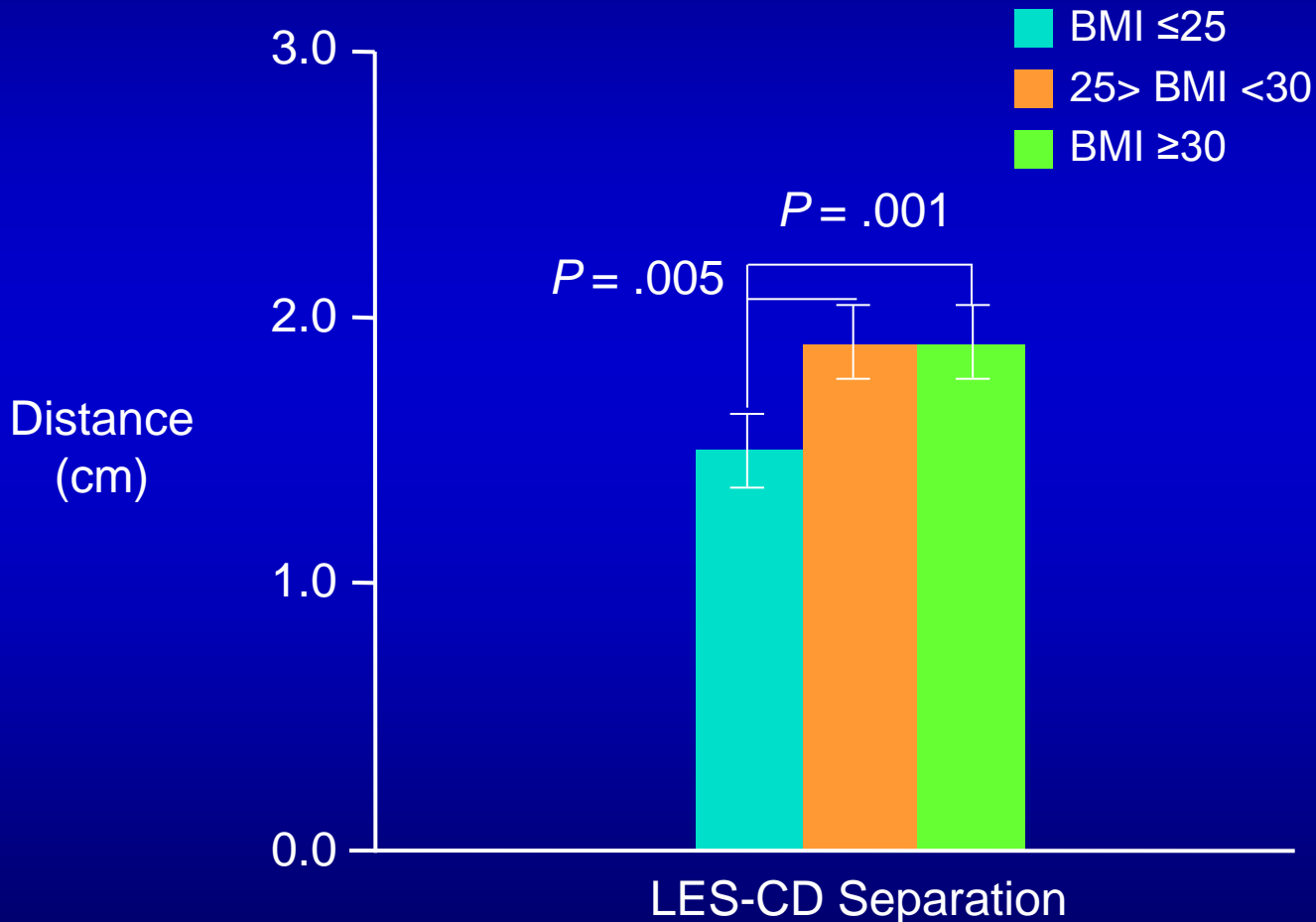
Denny's Beer Barrel Pub

- 6 pounds of beef
- 1 large onion
- 2 tomatoes
- 1/2 head of lettuce
- 1 1/4 pounds of cheese
- 1 cup of mayonnaise
- 1 cup of pickles

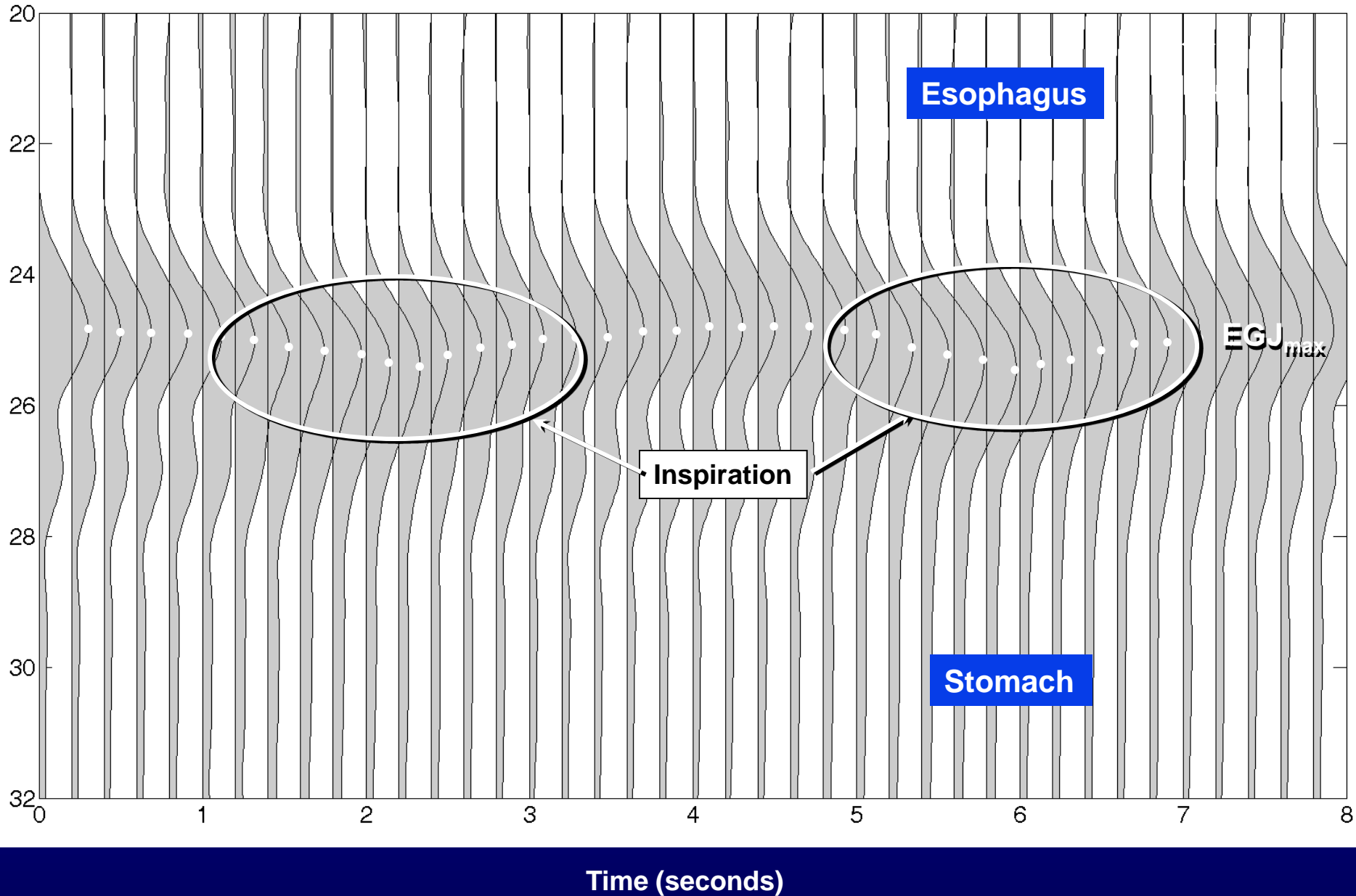
Intragastric Pressure Increased by Higher BMI/Waist Circumference



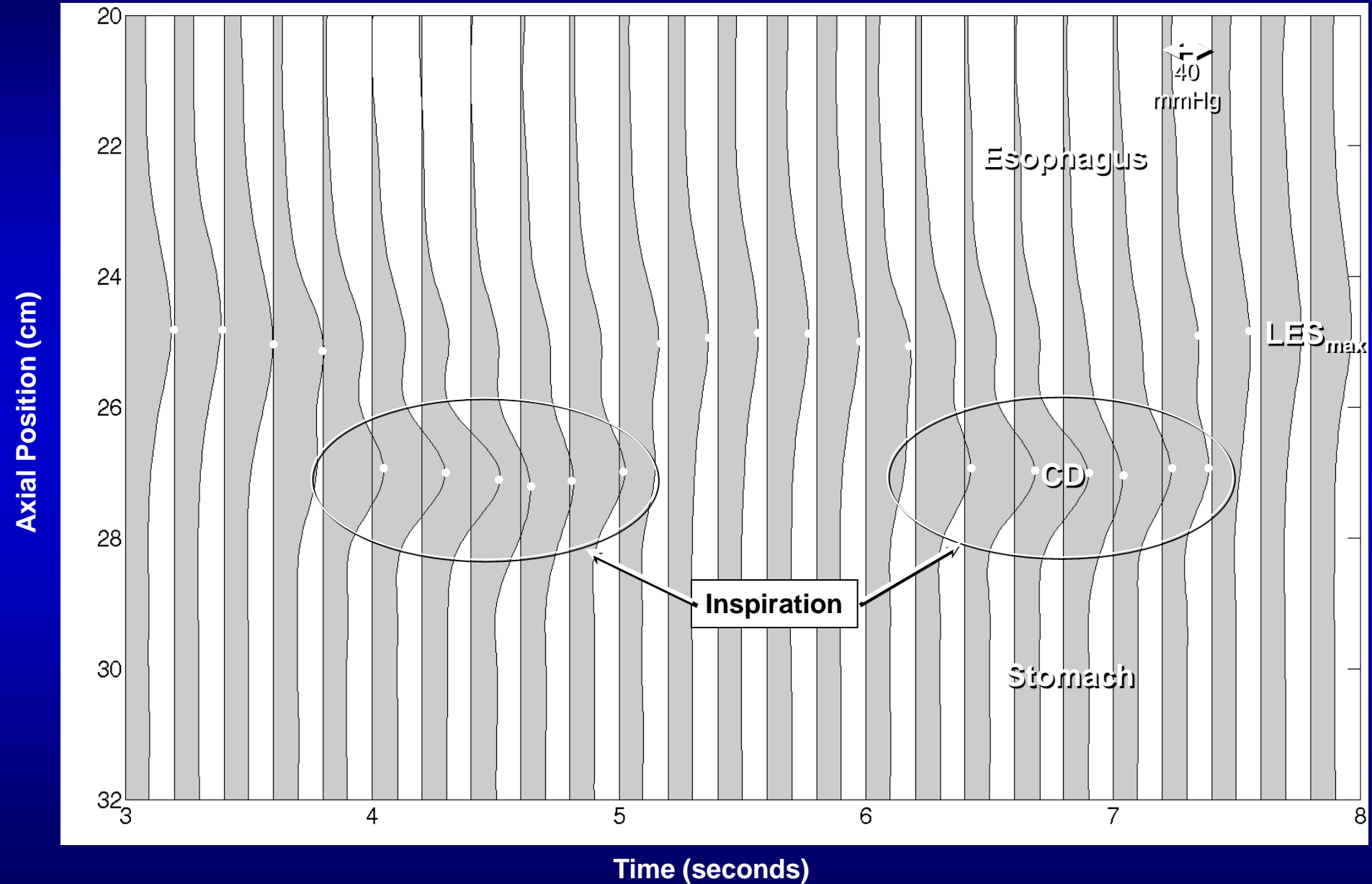
LES-Crural Diaphragm Separation Increases With Higher BMI



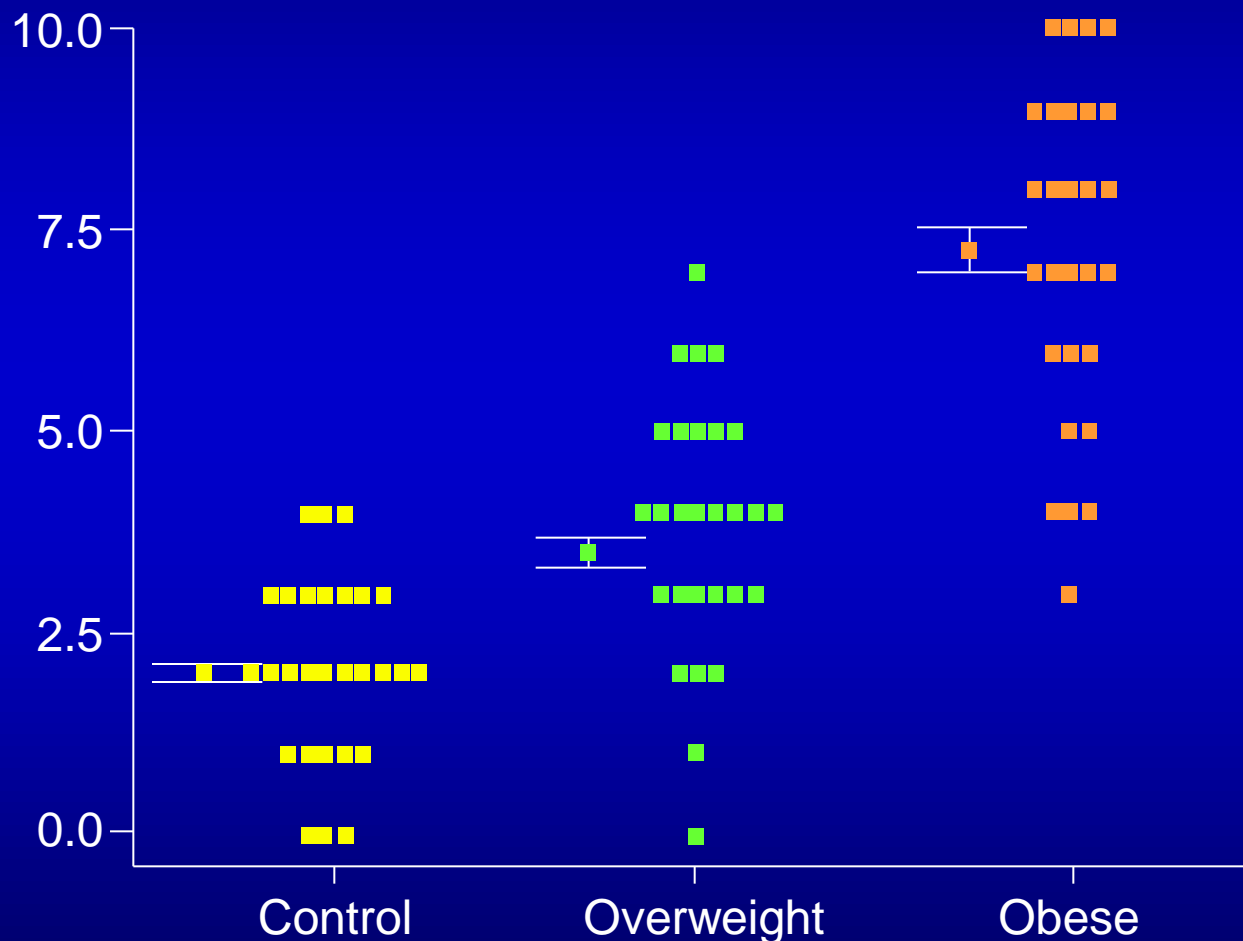
Normal anatomy, completely overlapping LES and CD



Obese subject with partially overlapping LES and CD



Total Number of TLOSr in 2 Hours in Normal Weight Controls and Overweight and Obese Groups



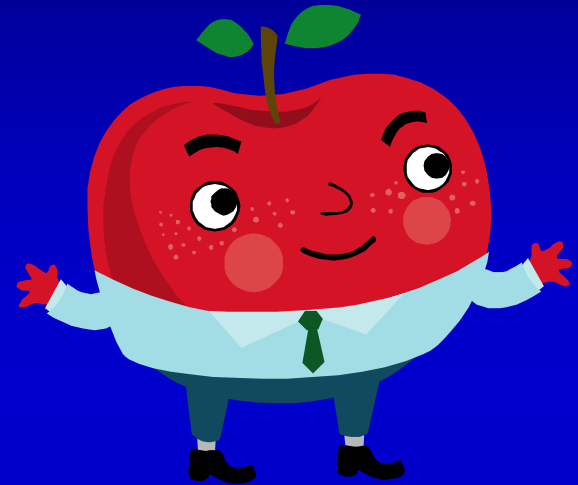
CAUTION: HAZARDOUS WAIST



A hazardous belly can be a good one too. It's the stress fat packed around your middle. Fat that increases your risk of heart disease and other serious diseases, such as diabetes. Good news is that **a better fitness program** can help.

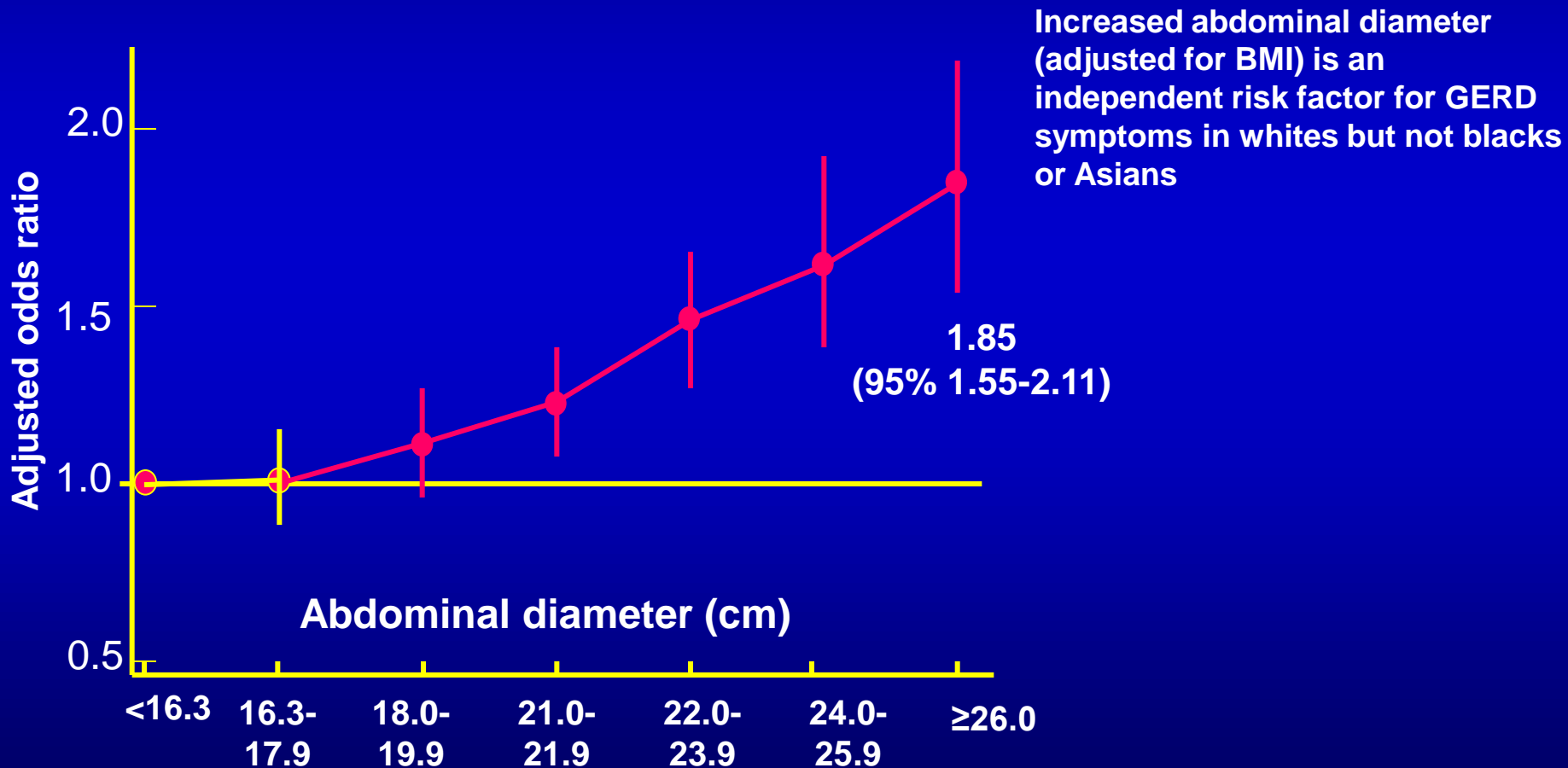
Does it make “epidemiological” sense?

- Both obesity and GERD are increasing in parallel
- Abdominal obesity more likely
 - Caucasians more than African Americans
 - Men more than women



Abdominal obesity, ethnicity and GERD: A cross-sectional study

80,110 members of the Kaiser Permanente check-up cohort:

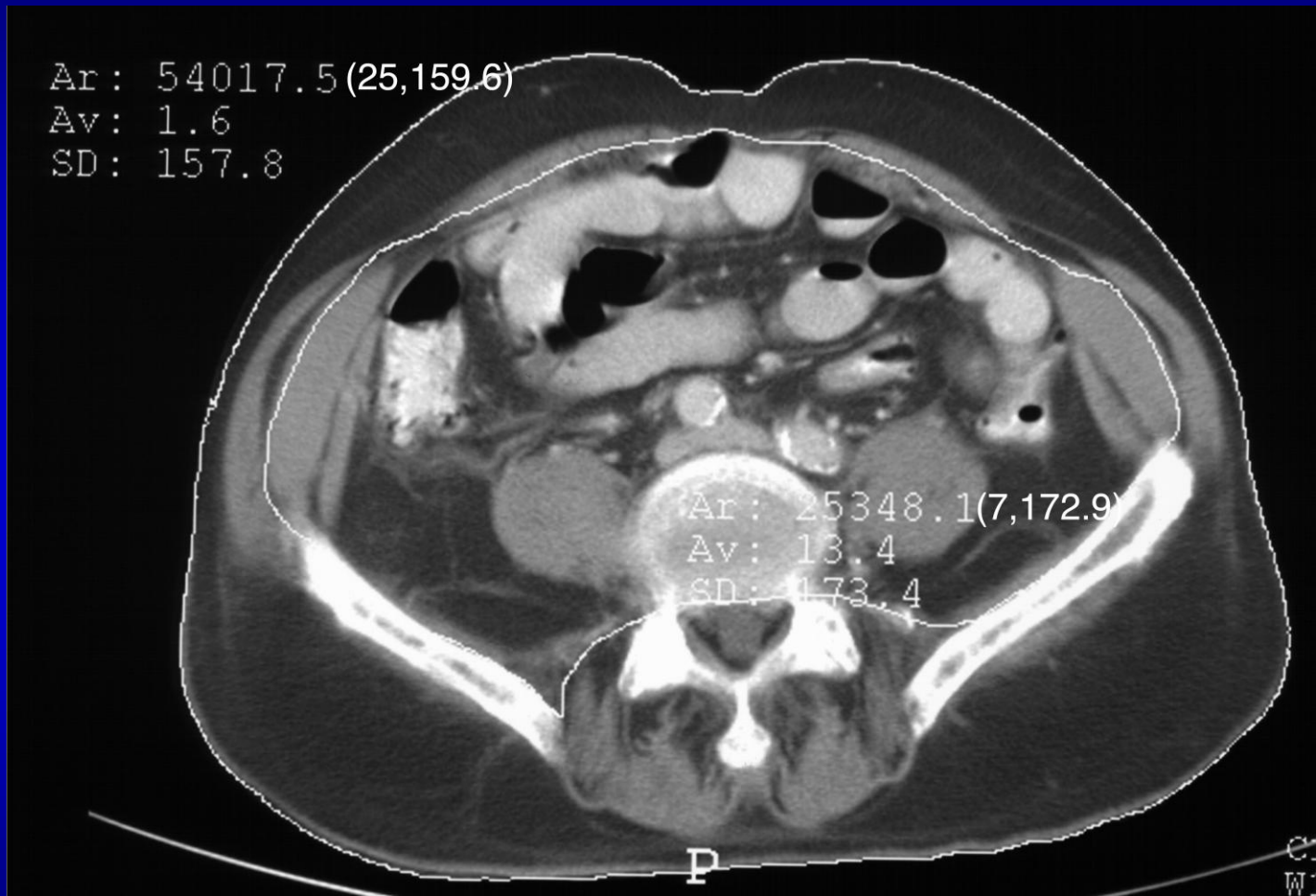


Ar : 54017.5 (25,159.6)
Av : 1.6
SD : 157.8

Ar : 25348.1 (7,172.9)
Av : 13.4
SD : 473.4

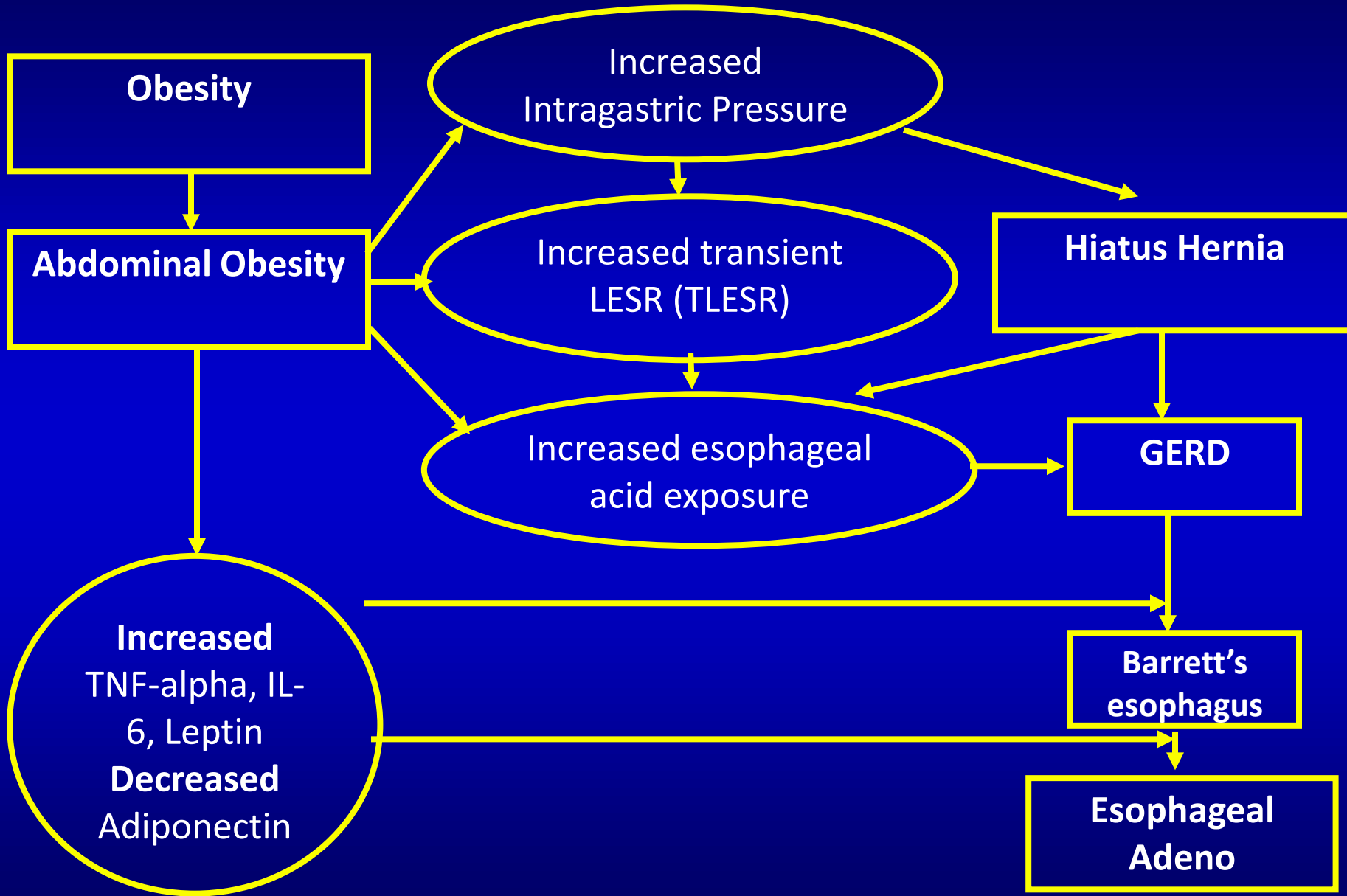
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Obesity and Barrett's Esophagus

- Two recent case-control studies of BE
 - Corley et al. Gastroenterology 2007
 - Edelstein ZR et al. Gastroenterology 2007
- No or weak association with BMI
- Consistent association with waist circumference



Stories Behind the Trend

Story IV

Proton Pump Inhibitors (PPI)

- Population-based case-control study
 - *Garcia Rodriguez LA et al, Gut 2006*
- 287 EAC, 327 GCA, 10,000 controls

Exposure	Control s	Esophageal adenocarcinoma		Gastric cardia adenocarcinoma	
	N (%)	%	OR (95% CI)	%	OR (95% CI)
Use of PPI					
Never	93.9	92.3	1.00 reference	88.7	1.00 reference
Past	2.1	1.7	0.81 (0.33 to 1.99)	4.1	1.96 (0.94 to 4.07)

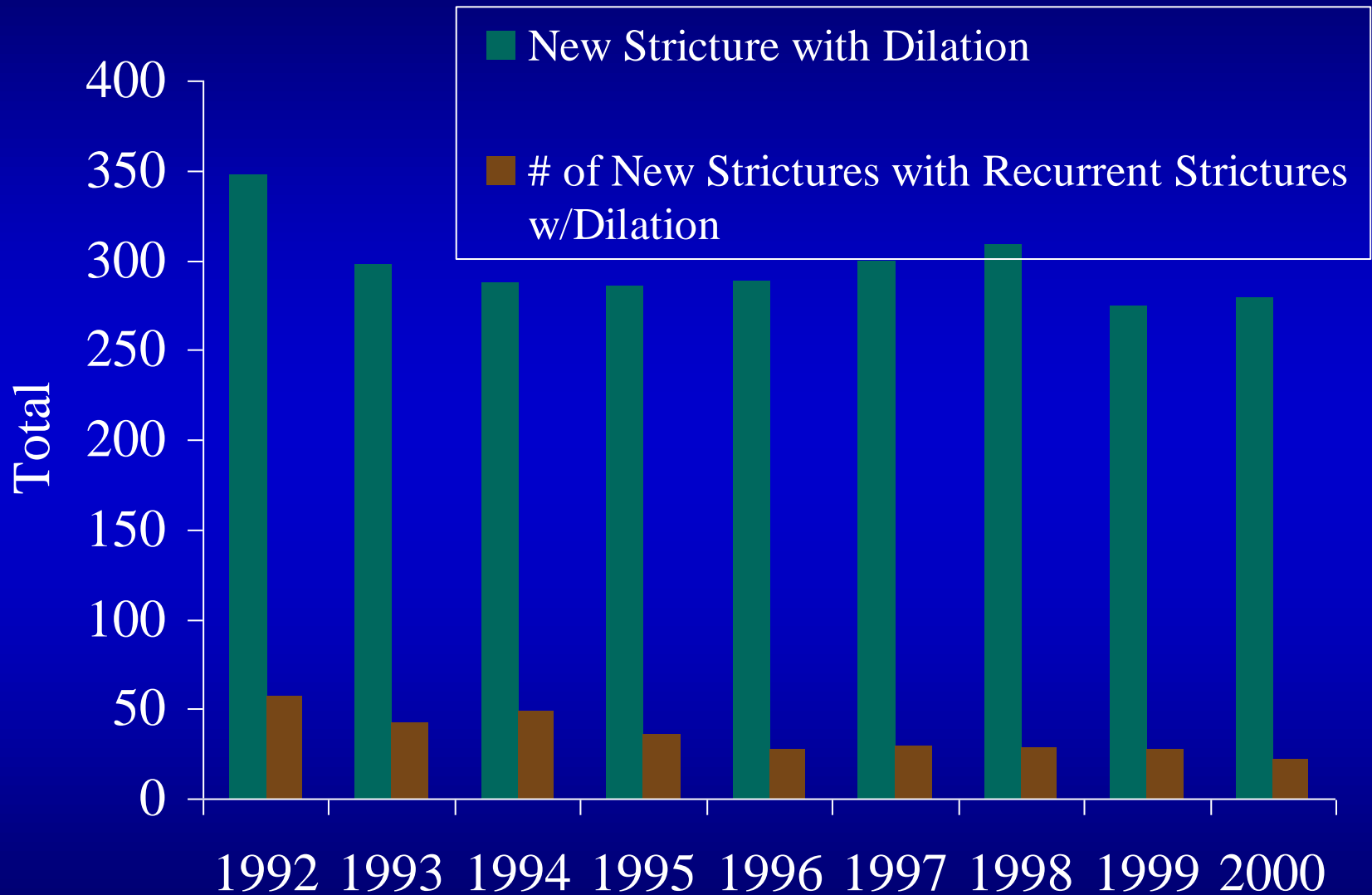
PPI

Exposure	Controls N (%)	Esophageal adenocarcinoma		Gastric cardia adenocarcinoma	
		N (%)	OR (95% CI)	N (%)	OR (95% CI)
Current < 1 year	2.5	2.4	1.05 (0.49 -2.25) 0.64 (.28 -1.42) †	5.6	2.51 (1.34- 4.71) 1.42 (.72 -.81) †
Current 1-3 years	1.2	2.8	2.34 (1.12 - 4.89) 1.22 (.55 - .72) †	1.5	1.31 (0.41 -4.21) .72 (.22 -2.42) †
Current > 3 years	0.4	0.7	1.78 (.42 - 7.56) * 0.87 (.20 - 3.87) †	0.0	N.A.

† adjusted for GERD and dyspepsia

Garcia Rodriguez LA et al, Gut 2006

Esophageal Strictures in Medicare Population



Summary

- The Trends:
 - Progressive ↑ esophageal adenocarcinoma in the US
 - These trends only partly reflect increased recognition
- Stories behind the trend include
 - Earlier onset of GERD
 - Decline in the frequency of *Hp* and/or a change in the pattern of *Hp* gastritis
 - Rising obesity
 - ? PPI
- If any/all explanations mentioned above, further increase is expected