

# **GERD and Sleep – An Eye Opening Experience**

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# Health-Related Consequences of Sleep Deprivation

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**Accidents**

**Psychiatric disorders**

**Short attention span**

**Heart disease**

**Memory impairment**

**Reduced immune response**

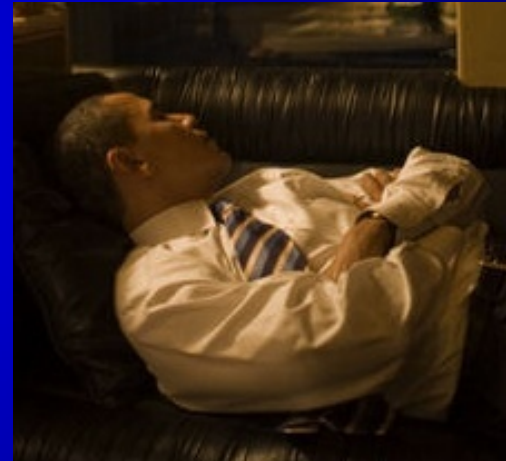
**Obesity**

**Dementia**

**Limited comprehension**

# Sleep Is One of the Three Pillars of Health

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**Regular Naps Prevent Old Age...**

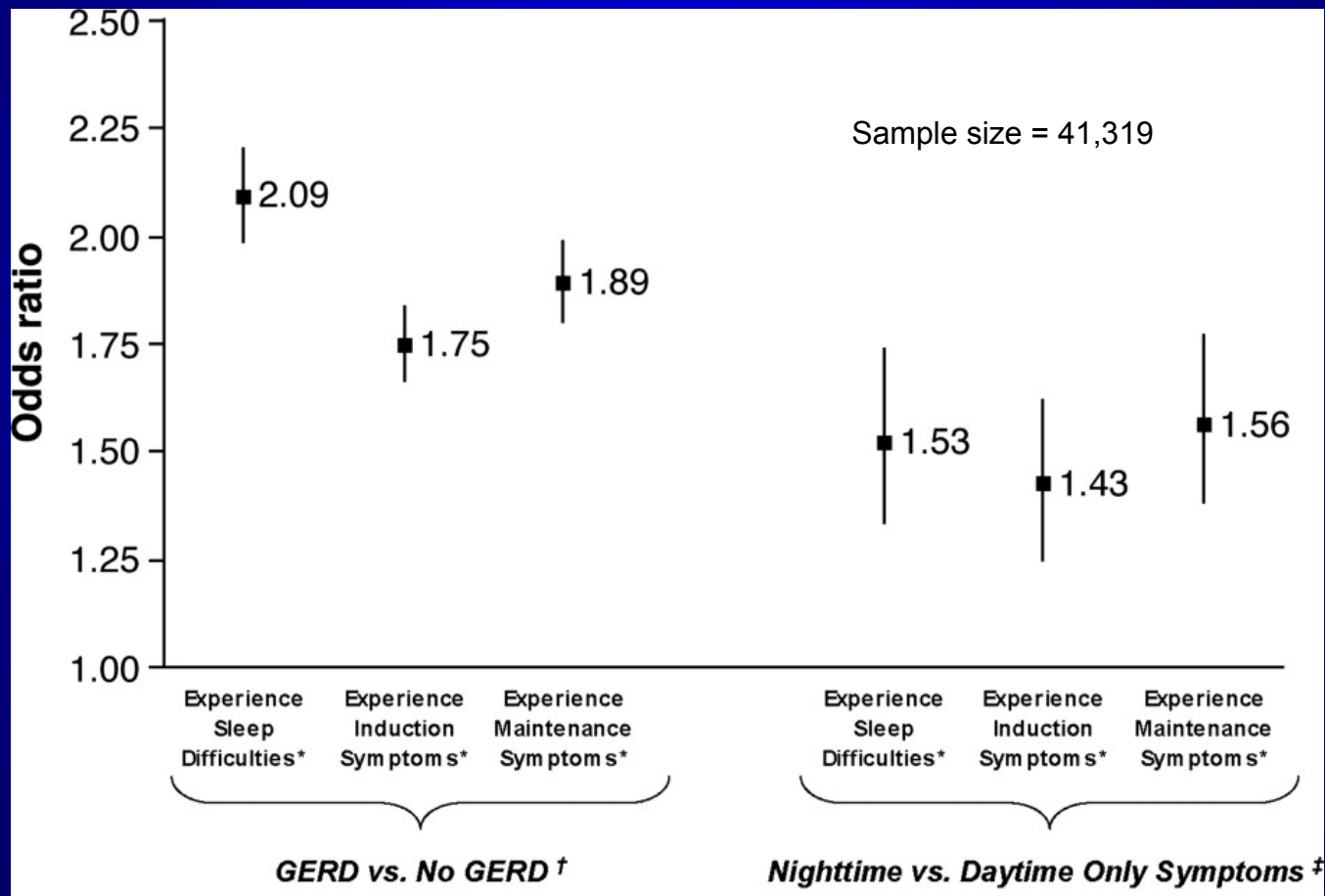
***...Especially If You Take Them While Driving!***



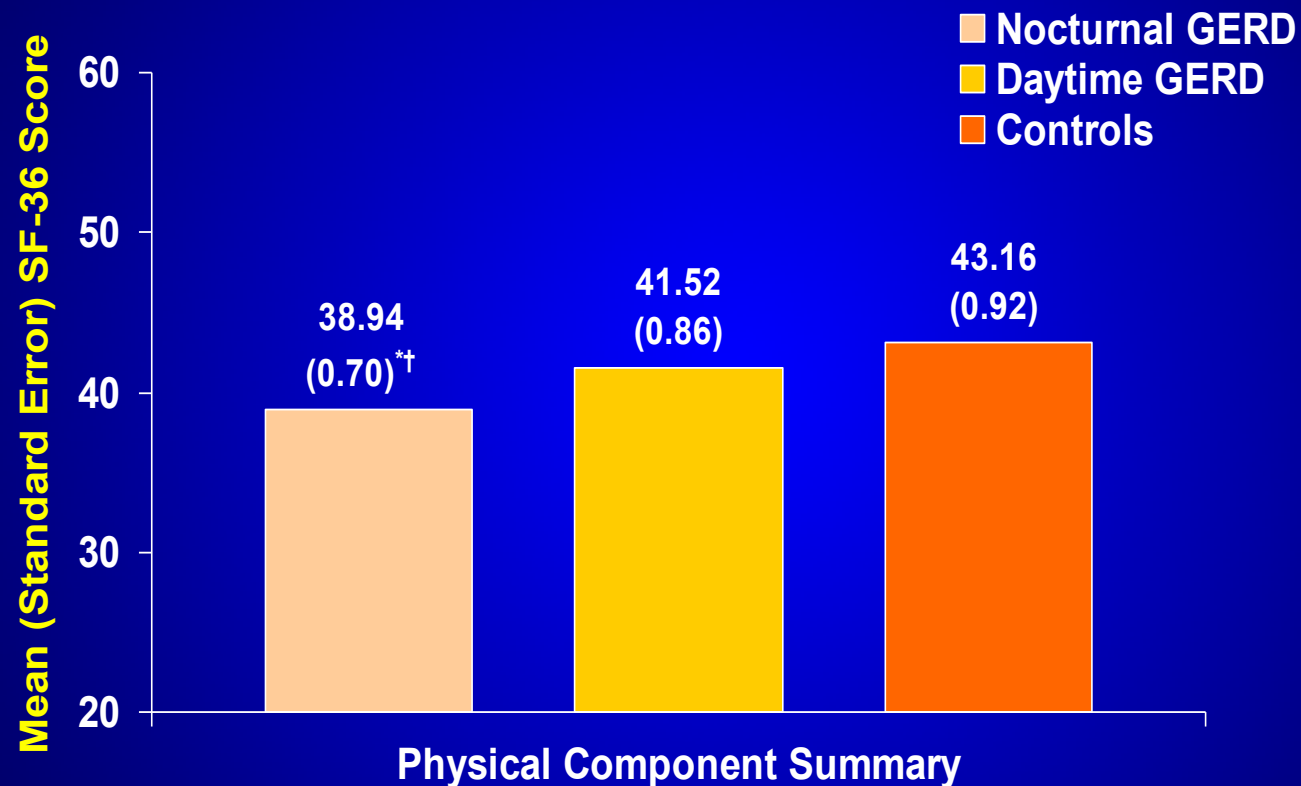
## Associations with Nocturnal GERD and Associated Evidence Ratings

Parameter	Studies cited	Evidence rating	Causality?
Nighttime awakening	3	B	Yes
Next day functioning	2	B	Yes
Difficulty falling asleep	1	B	Yes
Poor sleep quality	4	B	Yes
Decreased quality of life	2	B	Yes
Supine reflux on pH monitoring			
More likely 1 <sup>st</sup> half night	1	B	Yes
Greater frequency in EE (C-D) & BE	4	B	Yes
Late evening meals	3	B	No
Asthma	2	B	No
OSA	4	B	No
HOB elevation	4	A (1), B(3)	Yes
Right lateral decubitus position	2	B	No

# Adjusted Effects of GERD and Nighttime Symptoms on Sleep Difficulties



# Impact of Nocturnal and Daytime GERD Symptoms on QOL



N = 1,552.

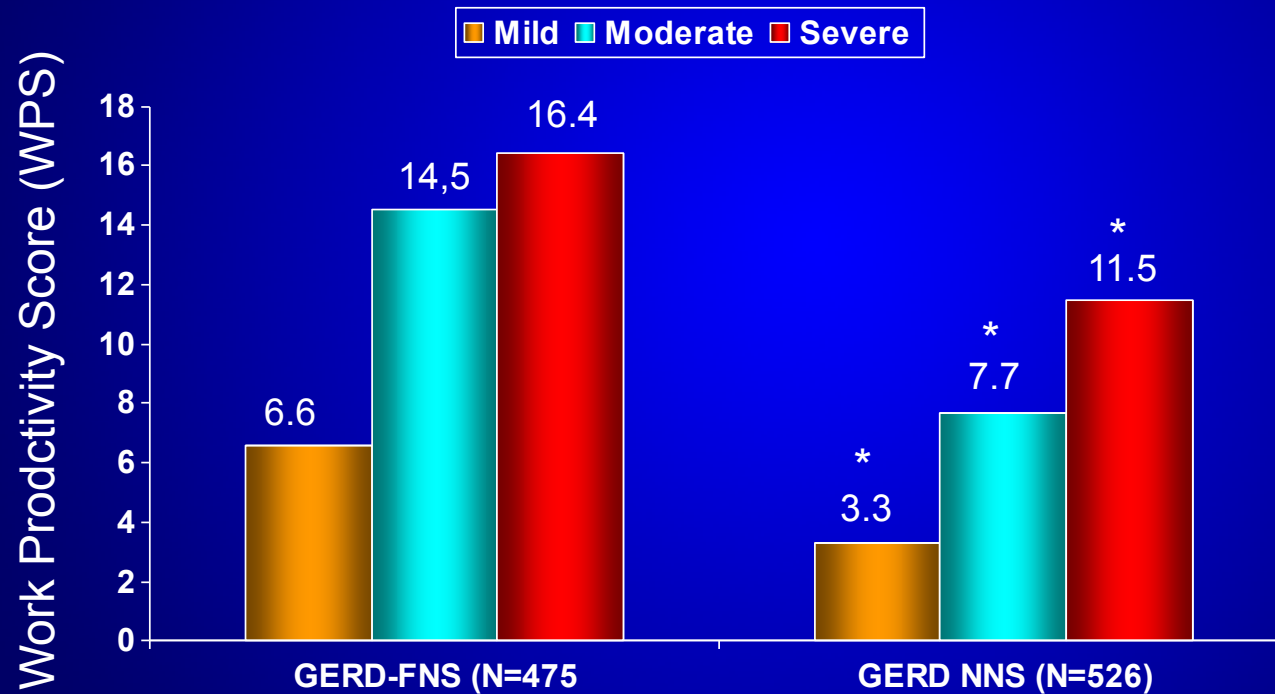
SF-36 - Mean Medical Outcomes Study Short-Form 36 Health Survey.

\* $P < 0.001$  vs daytime GERD.

† $P < 0.001$  vs controls.

Farup et al. *Arch Intern Med.* 2001;161:45-52.

# GERD-Specific Total Work Loss Among GERD-FNS and GERD-NNS Cases by Severity of Symptoms During the Previous Week

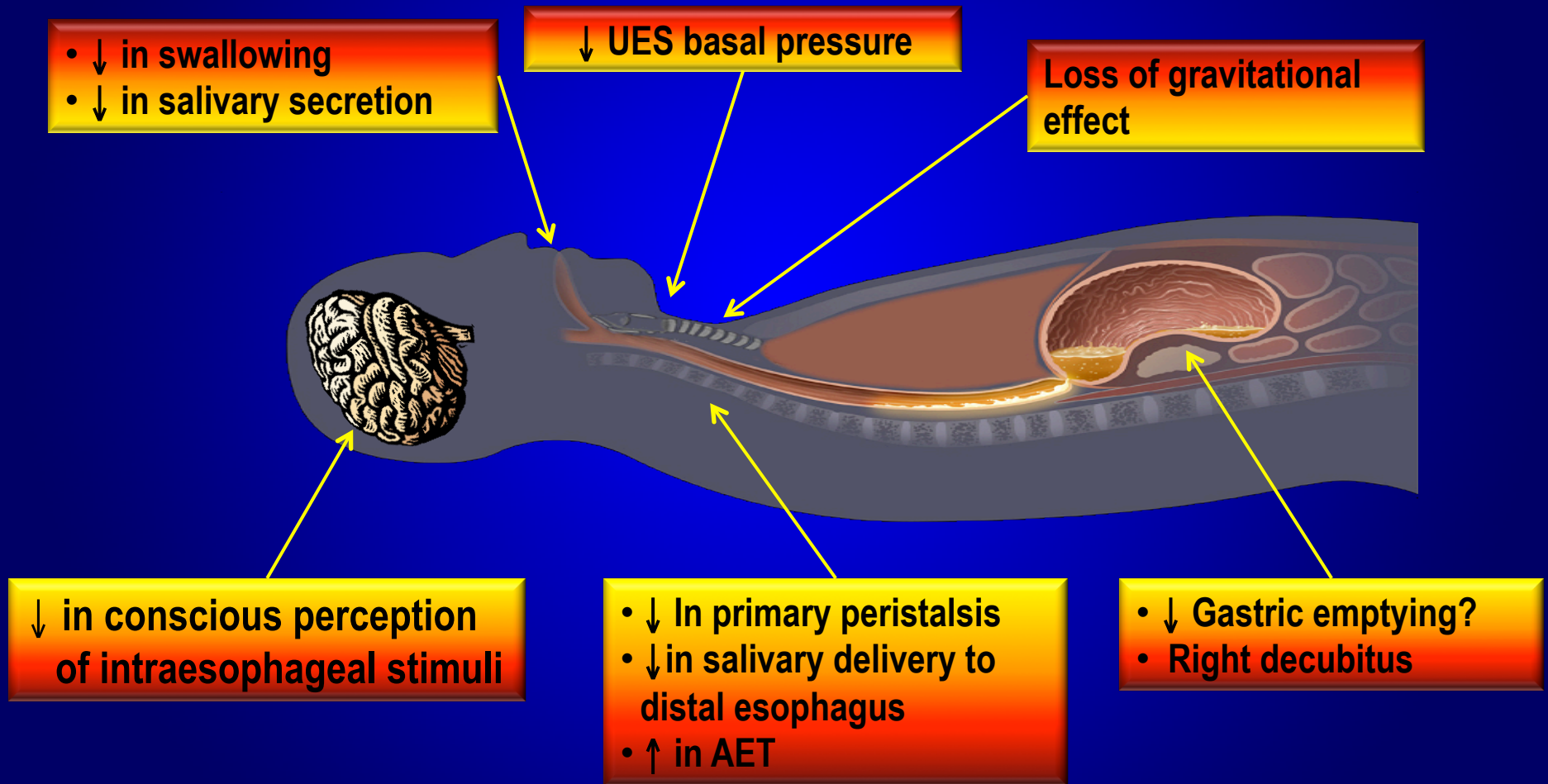


FNS – Frequent nocturnal symptoms  
NNS – No nocturnal symptoms

\*p<0.01



# Alterations in Esophageal Function During Sleep



# Nighttime Reflux Increases Risks of GERD Complications

## Esophageal Disease Progression

- Erosive esophagitis<sup>1</sup>
- Complicated erosive esophagitis<sup>2</sup>
  - Ulceration
  - Strictures
  - Barrett's esophagus
- Adenocarcinoma<sup>3</sup>

## Extra-esophageal Manifestations

Asthma<sup>4</sup>  
Aspiration pneumonia  
Chronic cough  
Hoarseness

## Other Symptoms

Sleep deprivation<sup>4</sup>

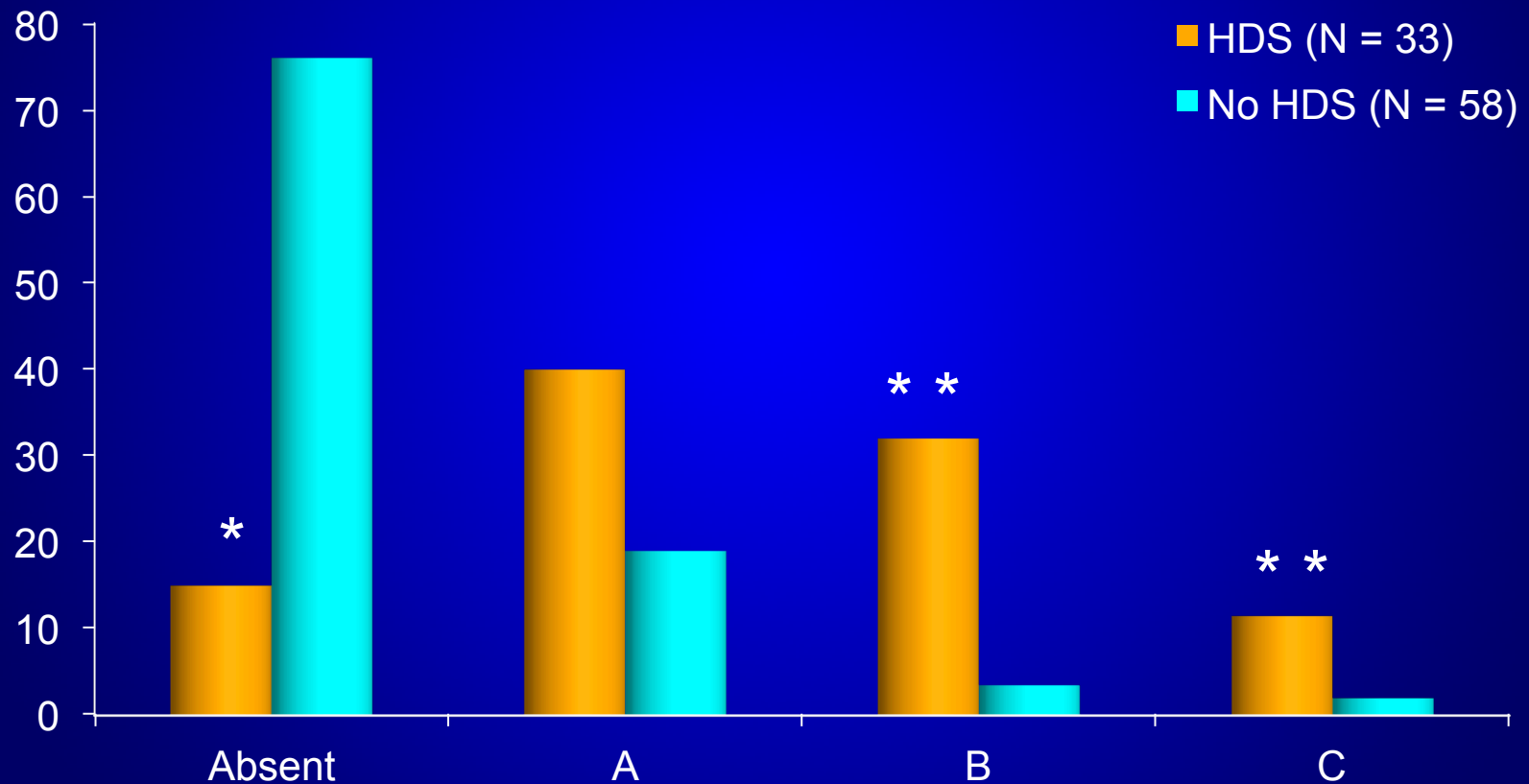
<sup>1</sup>Orr *et al.* *Am J Gastroenterol.* 1994;89:509–512.

<sup>2</sup>Robertson *et al.* *Gut.* 1987;28:1484–1488.

<sup>3</sup>Lagergren *et al.* *N Engl J Med.* 1999;340:825–831.

<sup>4</sup>Gislason *et al.* *Chest.* 2002;121:158–163.

# Presence and Grade of Reflux Esophagitis in Patients with and without Heartburn during Sleep (HDS)



# Is Nighttime GERD a Separate Entity From Daytime GERD?

- “Nighttime heartburn and GOR represent a distinct clinical entity which deserves specific attention in the diagnosis and optimal treatment of GERD” (Orr WC APT 2010)

»**FDA – No!**

# Data Analysis of Esophageal Function

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Body position (upright and recumbent)

*versus*

State of consciousness (awake and asleep)

# Comparison of Acid Reflux Characteristics Among Upright, Recumbent-Awake and Recumbent-Asleep Periods (N=64)

	Upright	Recumbent- awake	Recumbent- asleep
Frequency/hour	7.04	7.16	1.86*
% Total time	8.5	12.86	1.43*
# Sensed reflux events / hour	0.13	0.8	0.01*

**\*P < 0.0001**

# Integrative Actigraphy and pH Testing Technology and the FRIM™ Analysis

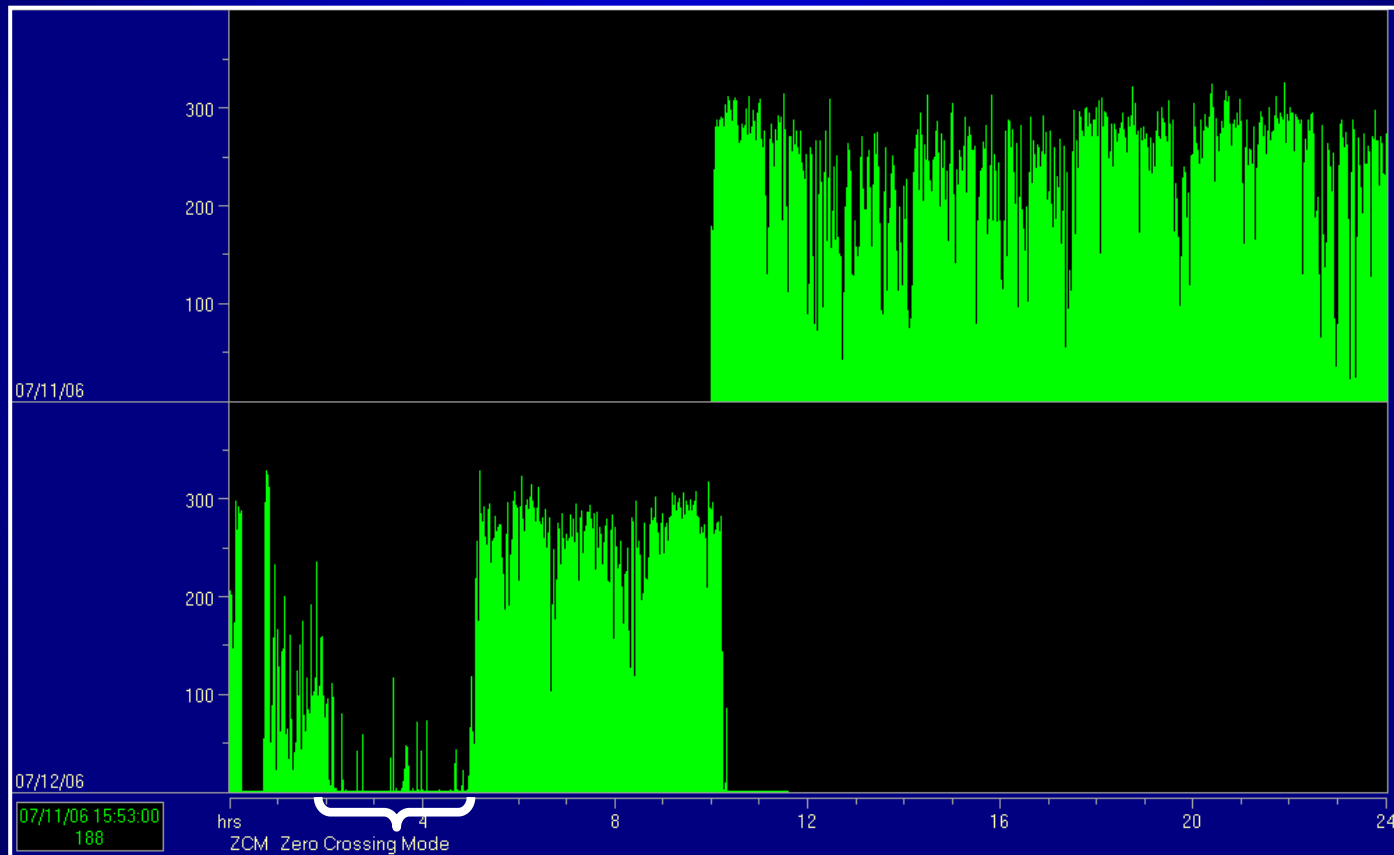
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The actigraph is a watch-like device, which is worn on the nondominant wrist, to record motion with accelerometers.

A novel technique superimposes actigraphy raw data over pH monitoring-collected data, matched by time.

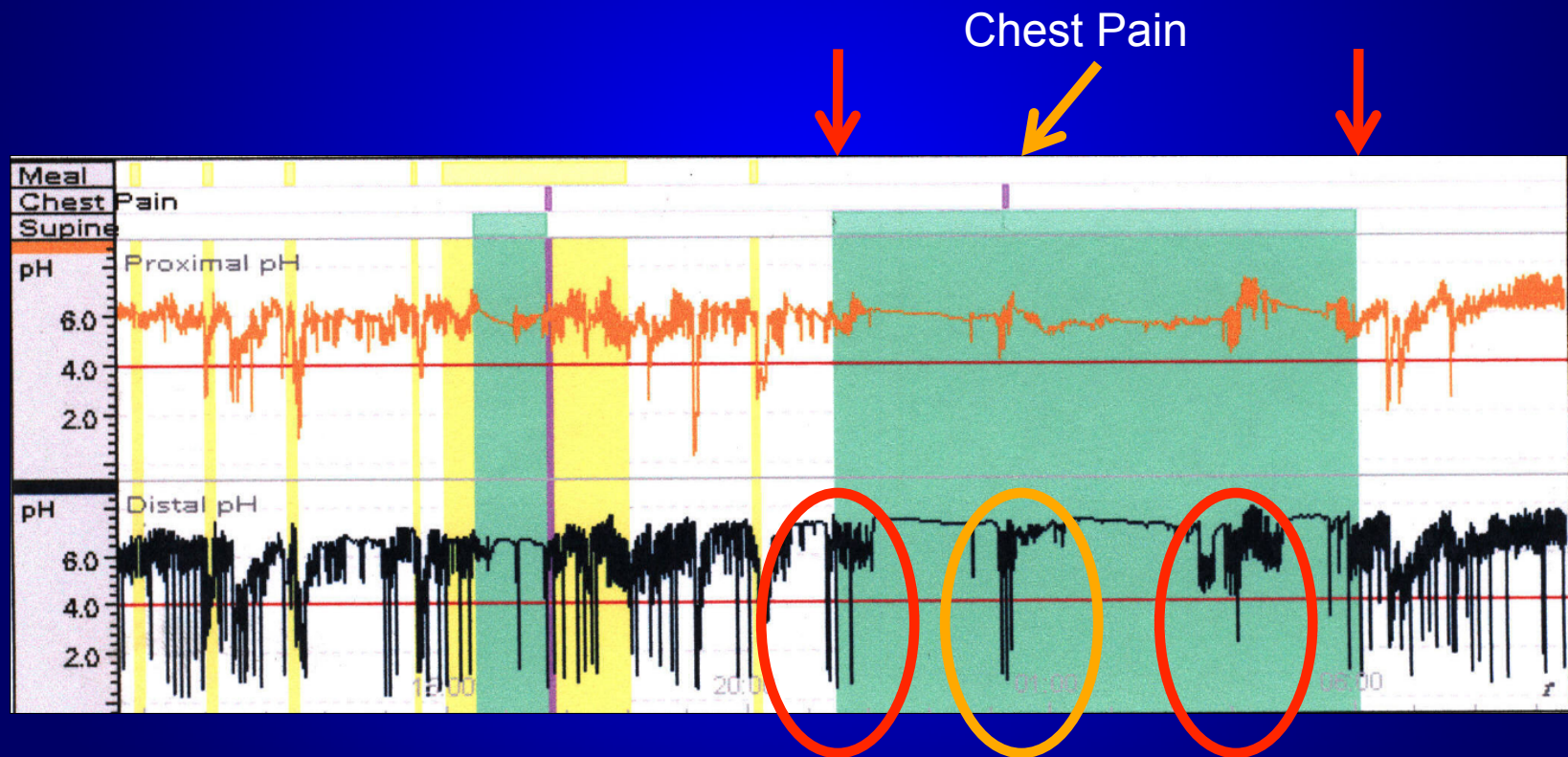


# Actigraph Recordings

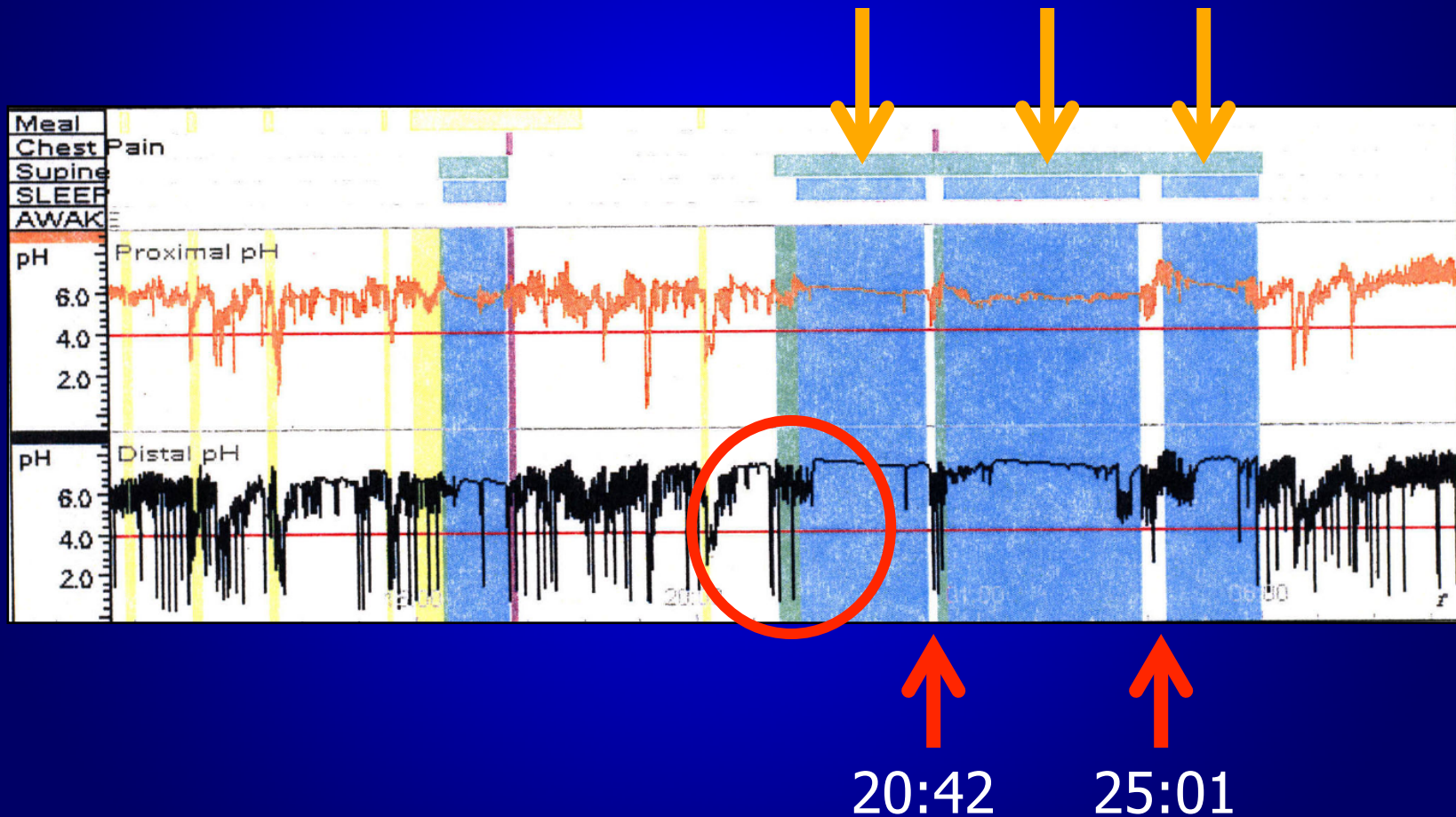




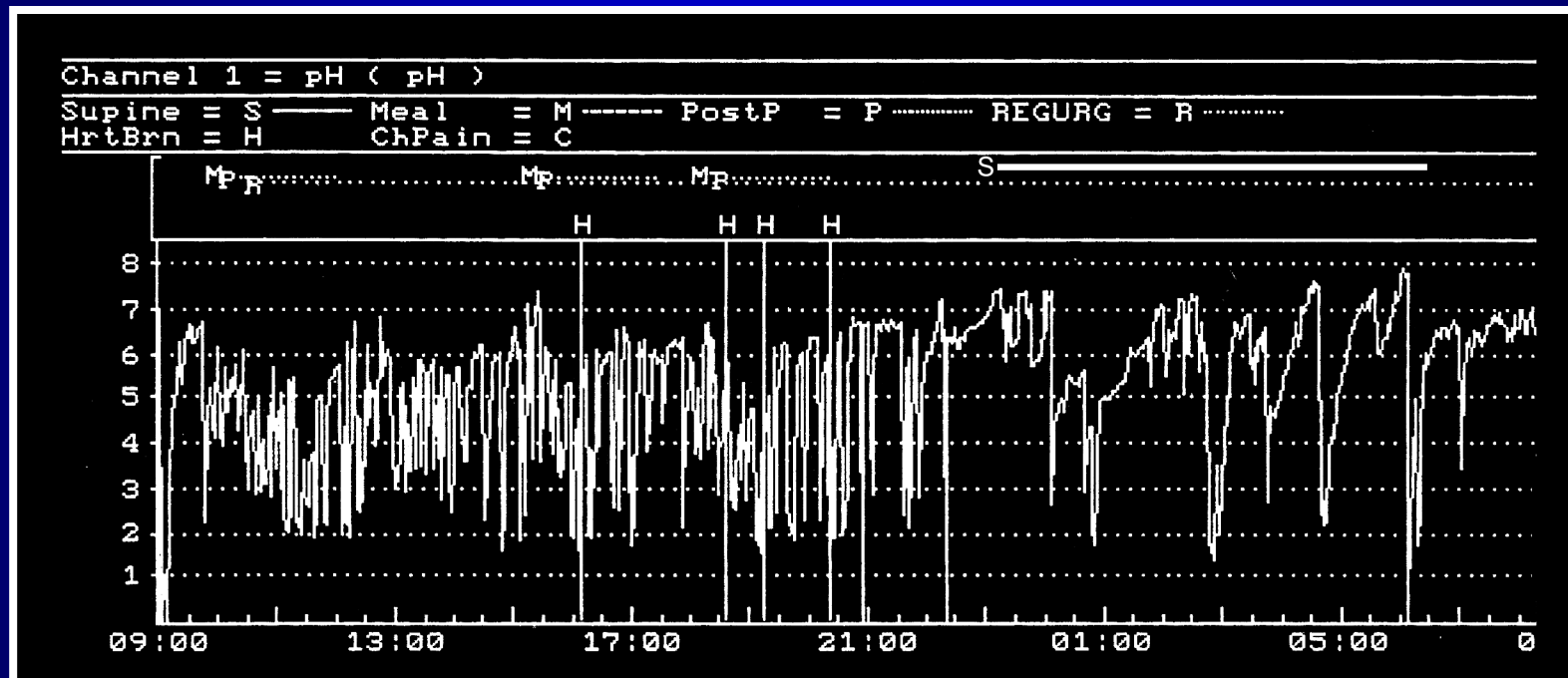
# Regular pH Testing



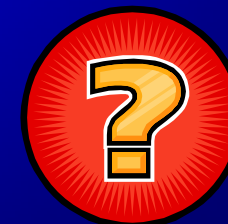
# pH Strip Using the FRIM™ Sleep-Reflux Integrative Program



# Duration of an Acid Reflux Event During Sleep and Awake Periods



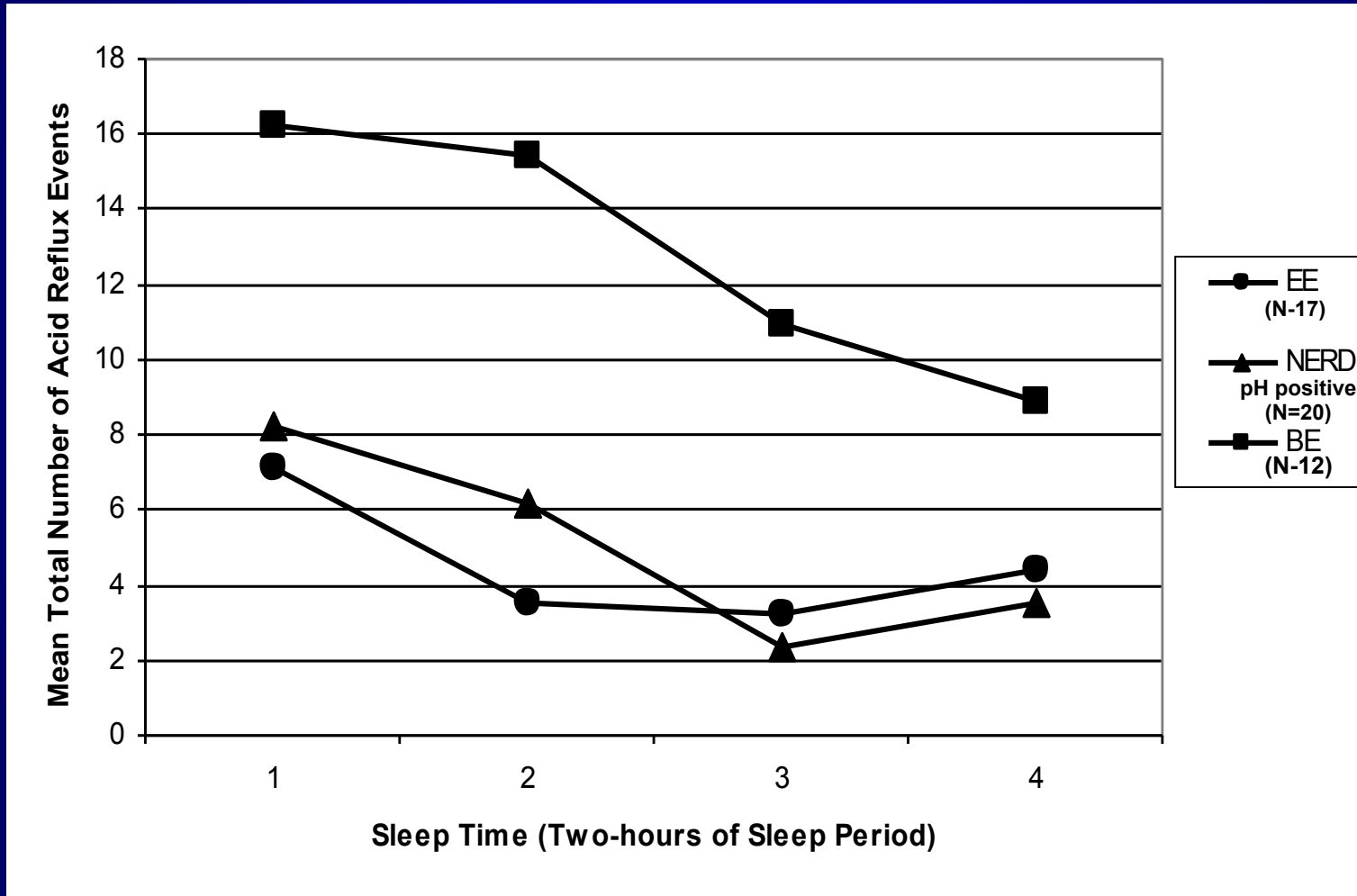
Upright -  $0.87 \pm 0.09$   
Recumbent awake -  $1.12 \pm 0.34$      $P = NS$   
Recumbent asleep -  $1.28 \pm 0.24$



# Impact of Supine-Awake and Conscious Awakening Periods on Acid Reflux Characteristics



# Mean Total Number of Acid Reflux Events During Sleep in Patients with EE, NERD and BE.

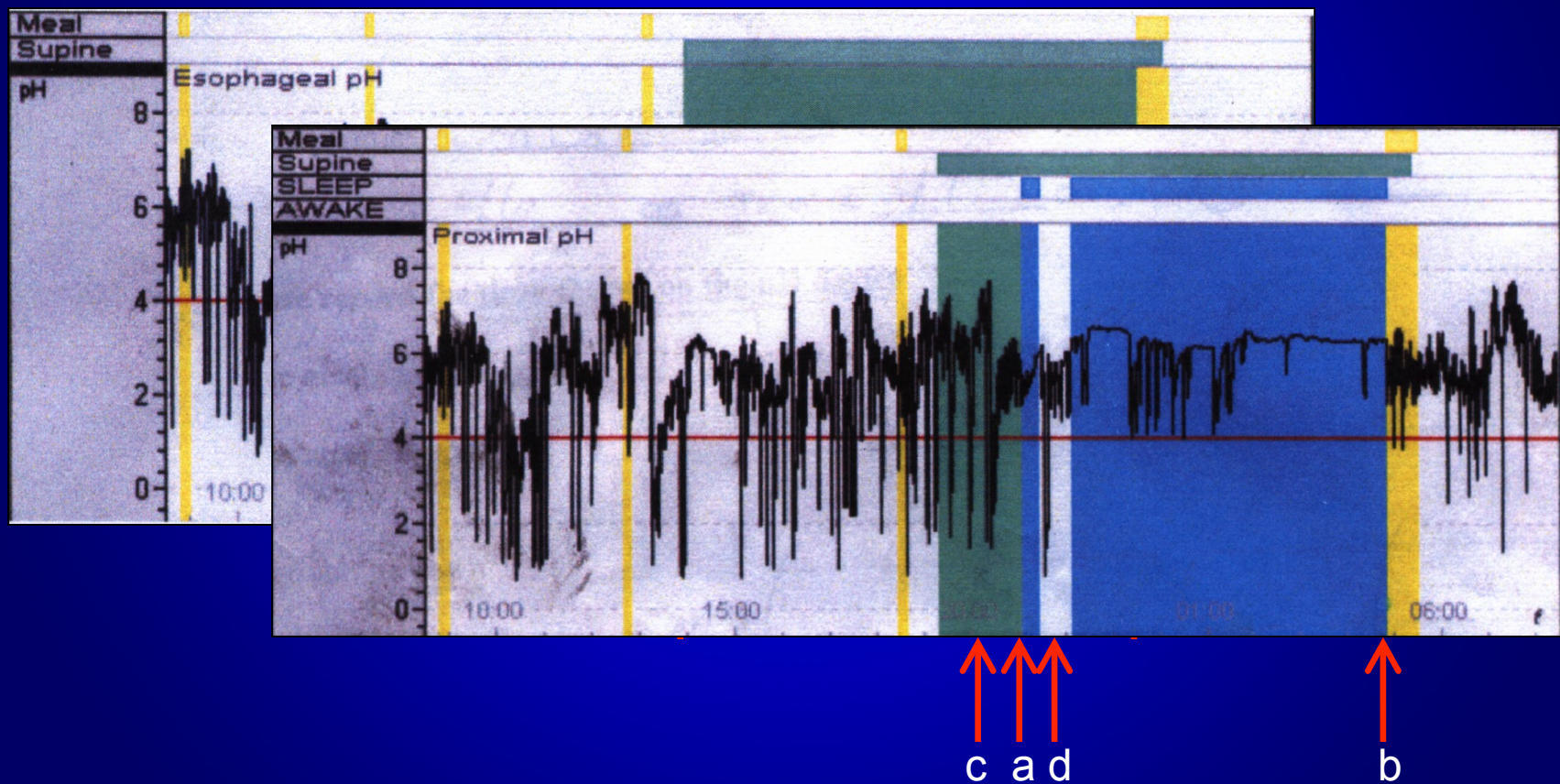


# Comparison of Acid Reflux Characteristics Between Recumbent-Awake and Corresponding Recumbent-Asleep Period

N = 39	Recumbent-awake (± SE)	Recumbent-asleep (± SE)
# of acid reflux events	195	55*
Mean # of acid reflux events	8.13 ± 4.36	3.24 ± 1.5*
Mean duration of acid reflux events (seconds)	55.67 ± 7.66	186.38 ± 120.22*
% associated with symptoms	36.41%	3.7%*

\* P<0.05

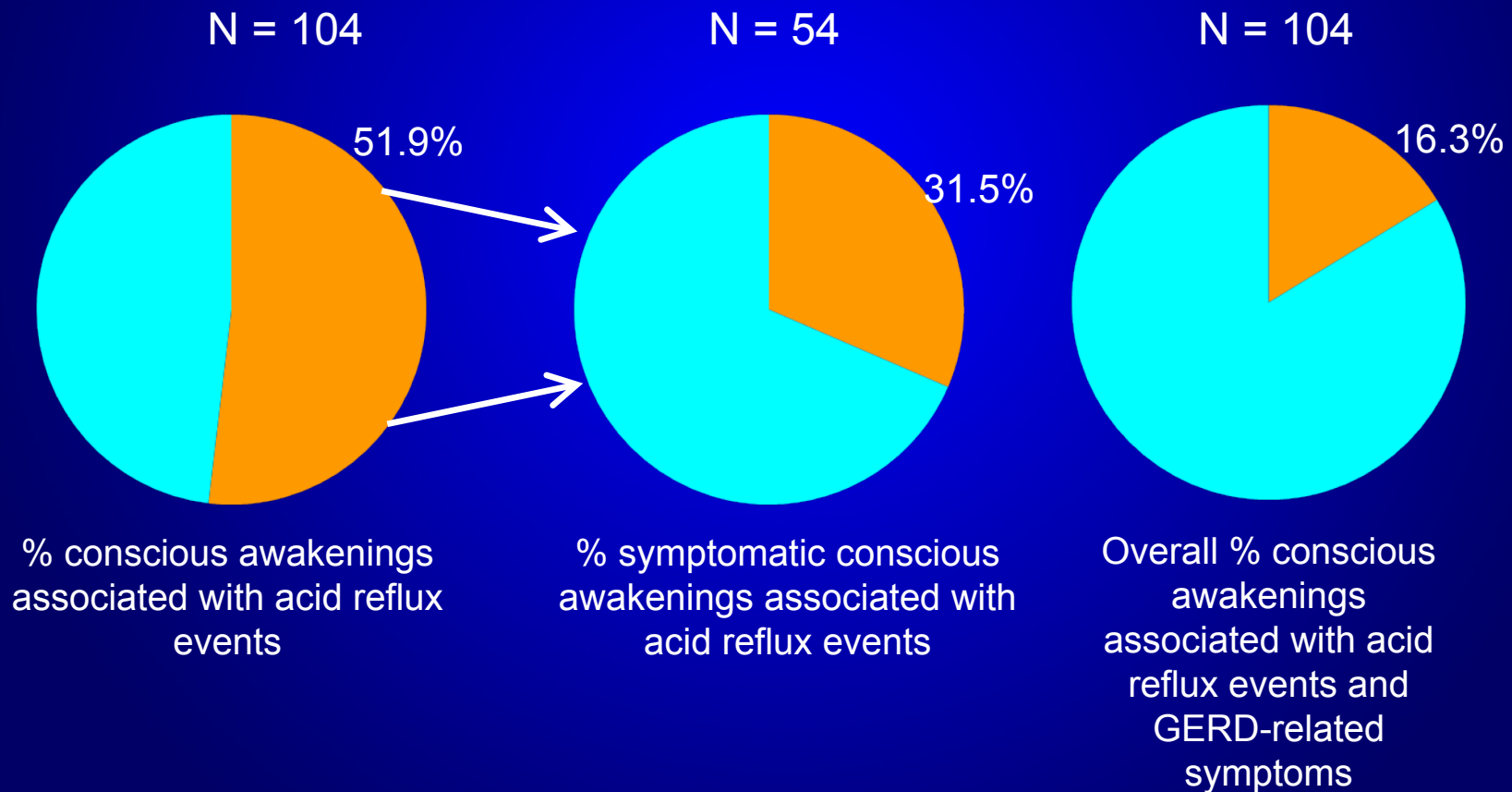
# Acid Reflux Events at the Beginning of Sleep Are Primarily a Sleep-Awake Phenomenon



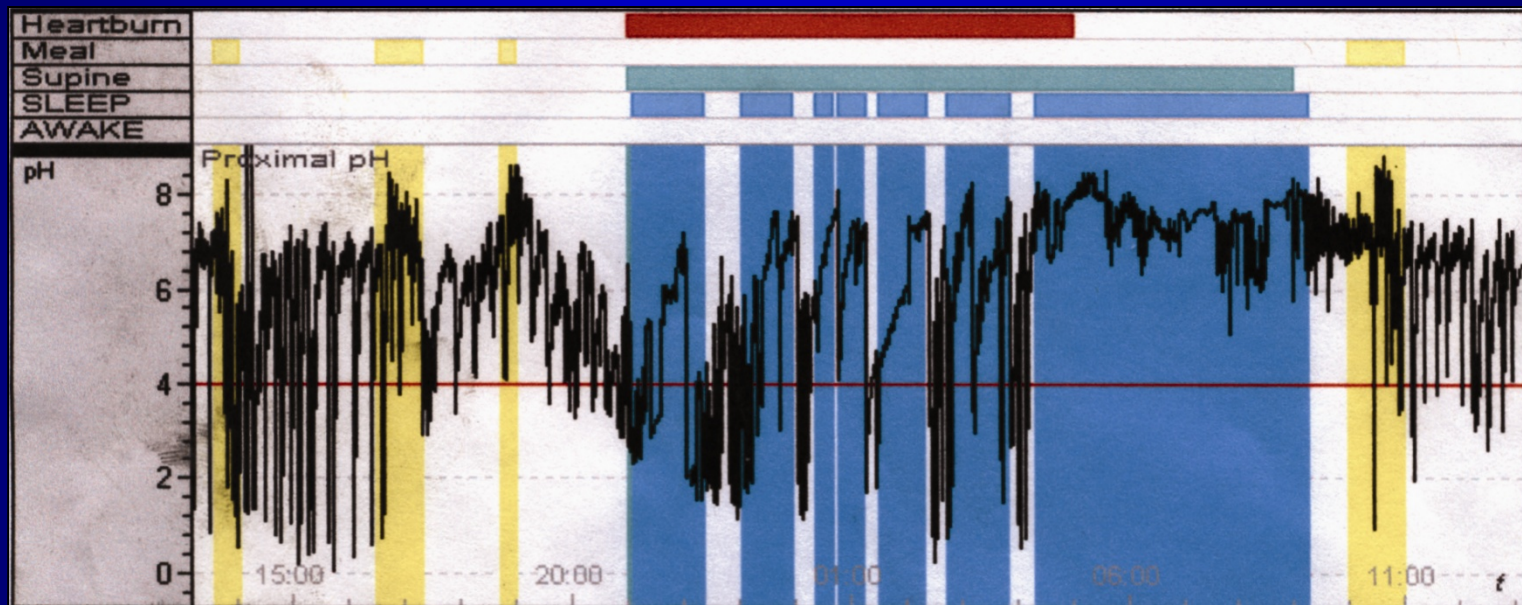
**What Is the Relationship Between  
Conscious Awakenings and Acid  
Reflux Events and Symptoms?**



# The Relationship Between Conscious Awakenings and Acid Reflux Events as well as GERD-Related Symptoms (N = 39)



# The “Devastating” Impact of Conscious Awakenings (>2 min) During Sleep

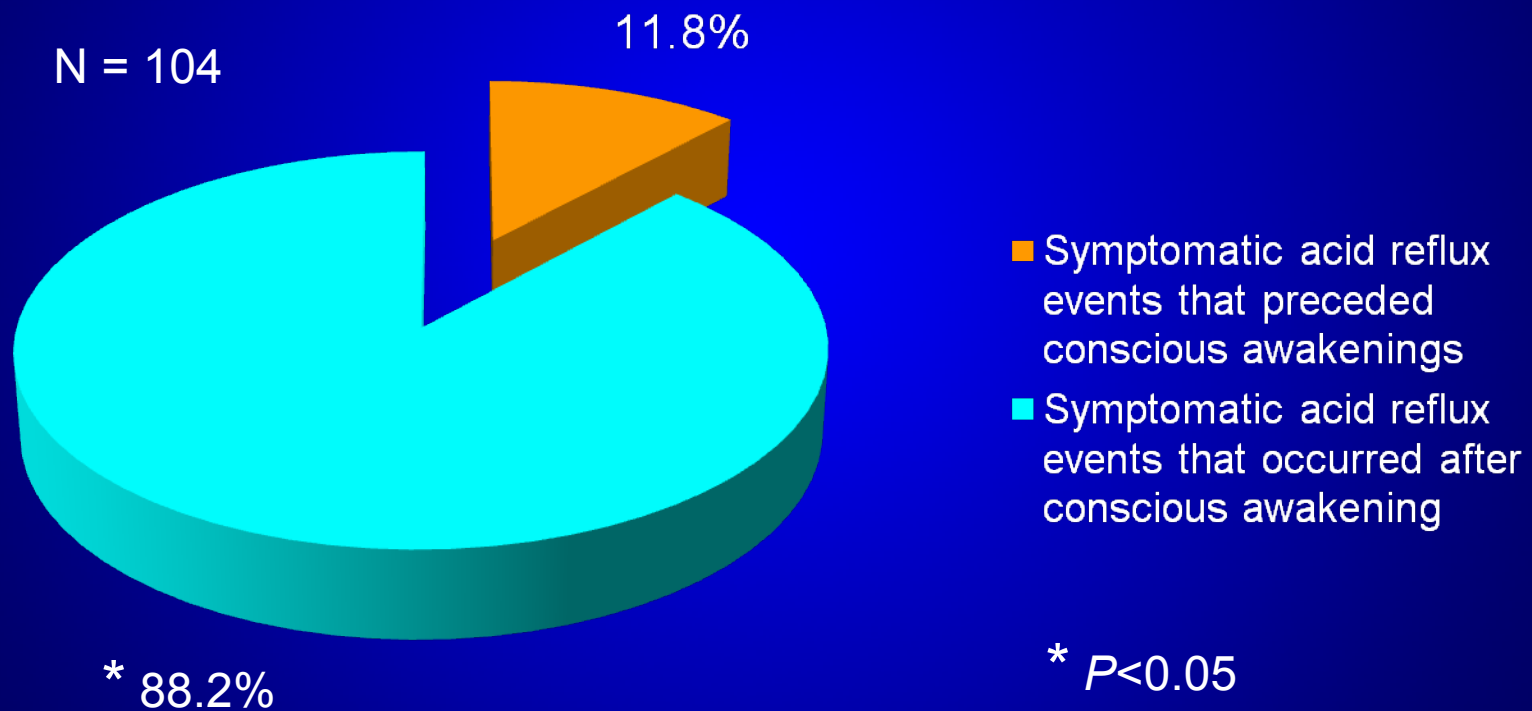


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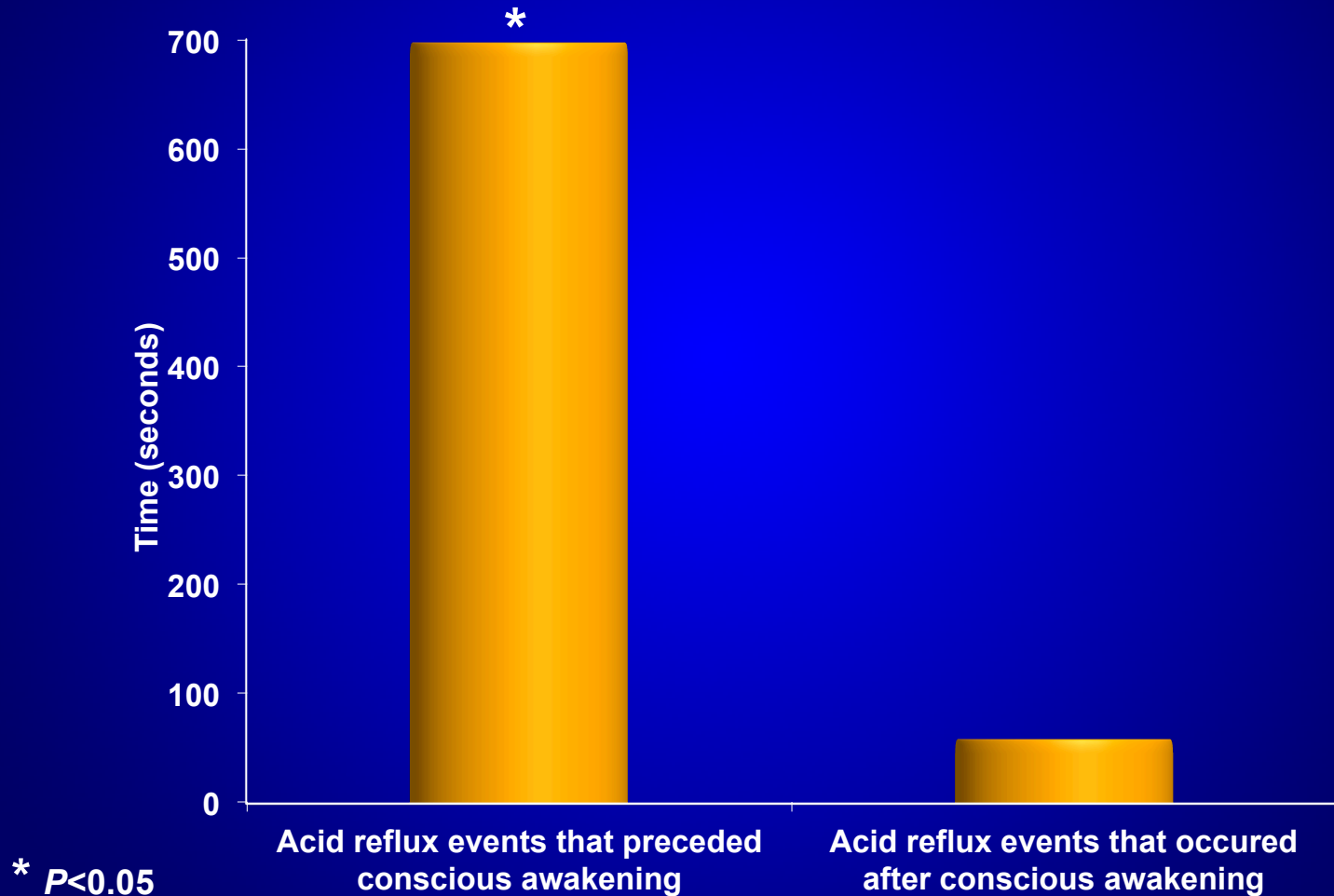
a   
 b c d   
 e   
 f

a = 38 min    b = 21 min  
 c = 4 min    d = 12 min  
 e = 20 min    f = 25 min

# The Temporal Relationship Between Conscious awakenings and Acid Reflux Events Using the FRIM Analysis

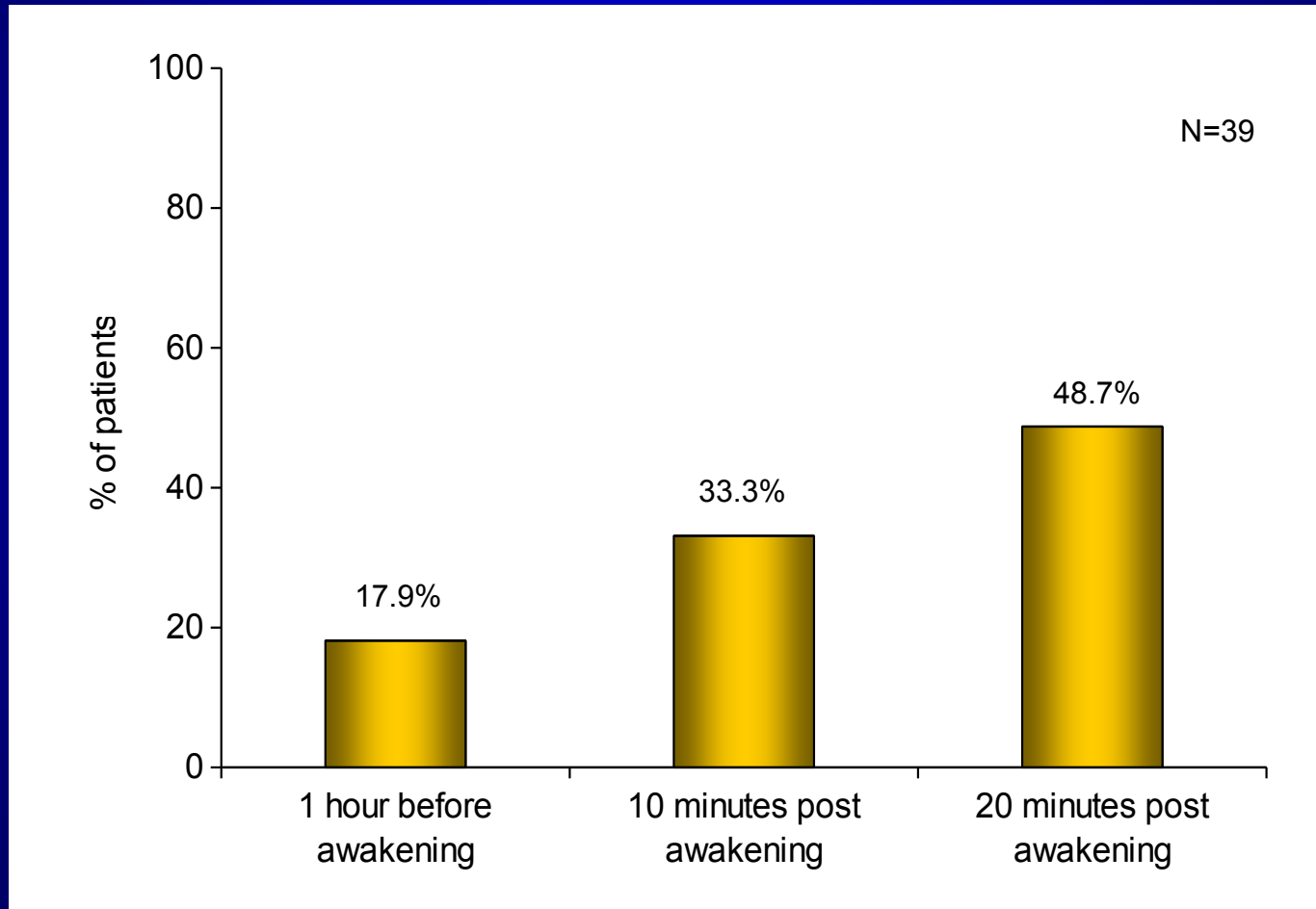


# Comparison of the Mean Duration of Acid Reflux Events that Preceded Conscious Awakening versus Those that Occurred After Conscious Awakening

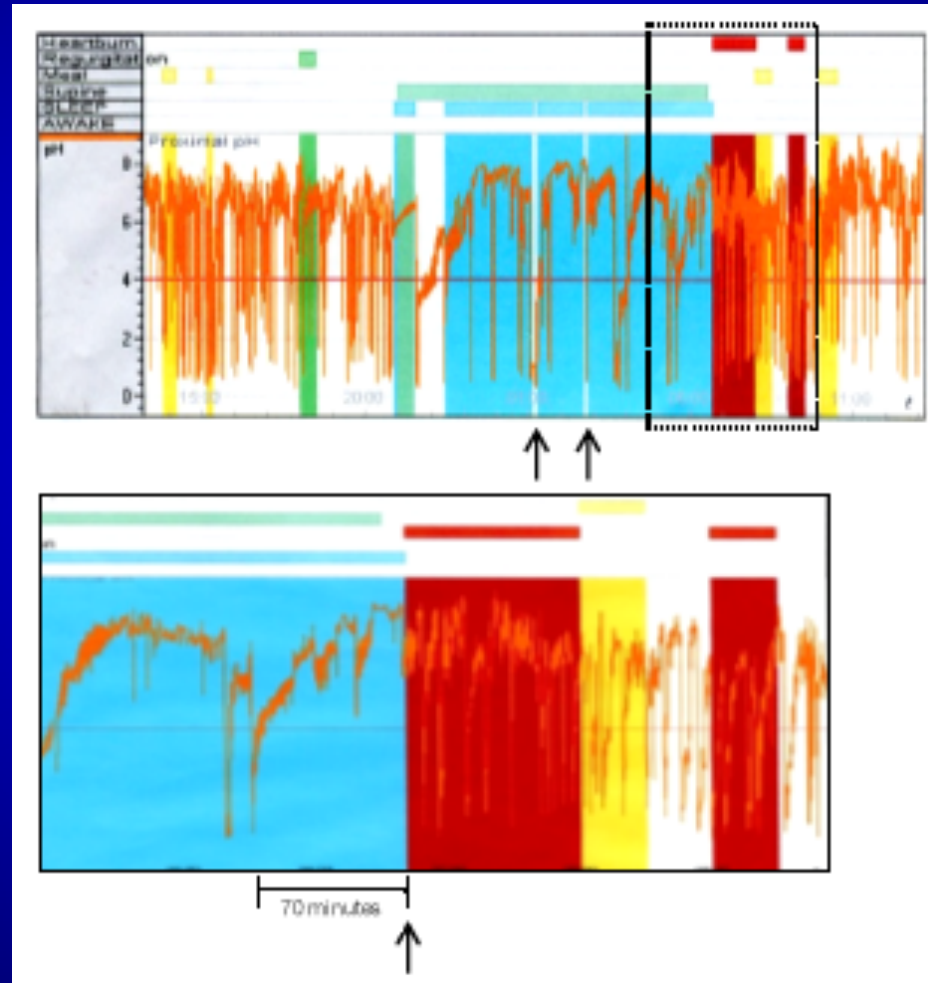


# Riser's Reflux

## *An Eye-Opening Experience*



# Integrated Actigraph and pH Data Demonstrating Riser's Reflux that is Symptomatic

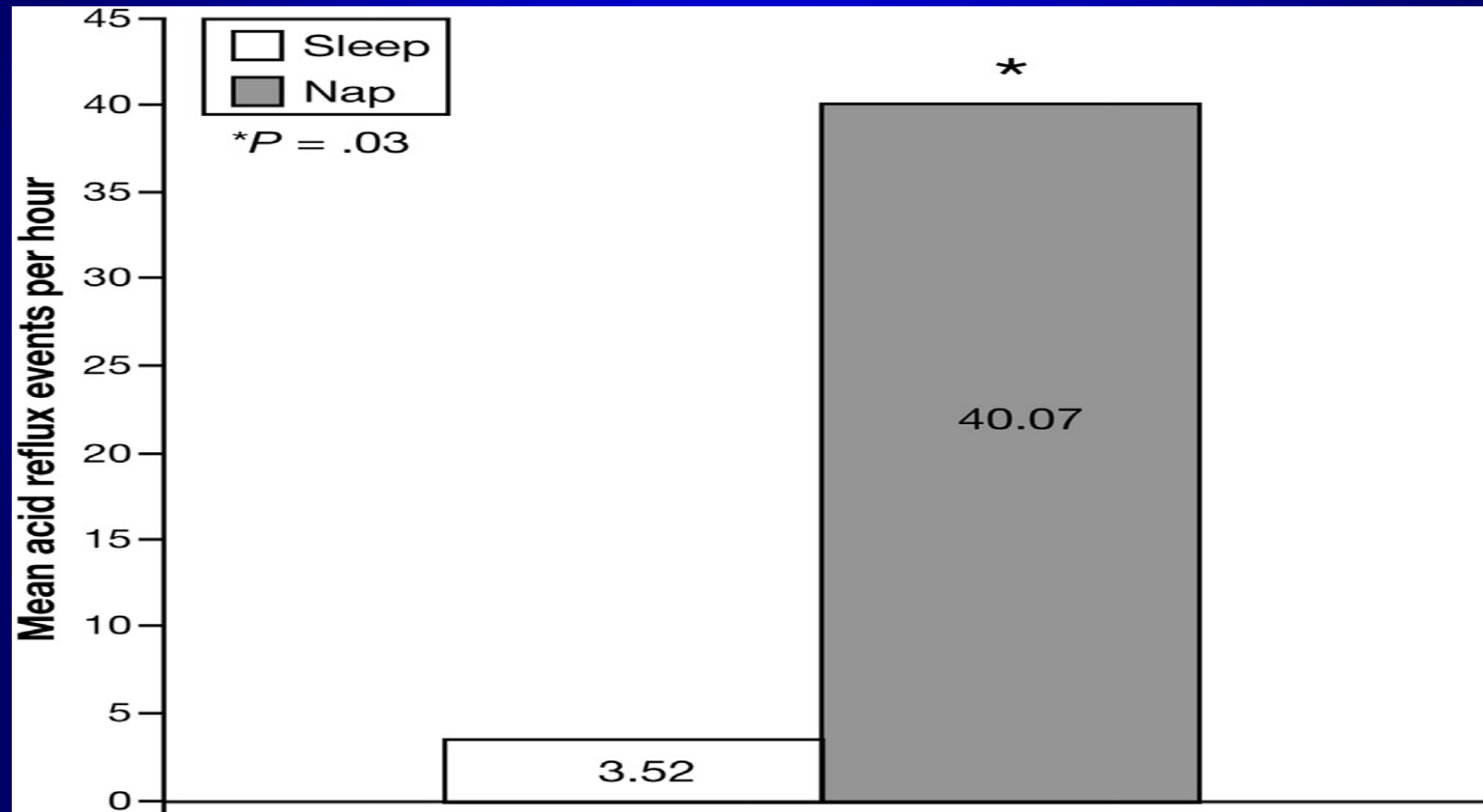


Poh CH *et al. Neurogastroenterol Motil* 2010;22:387-394

# Napping

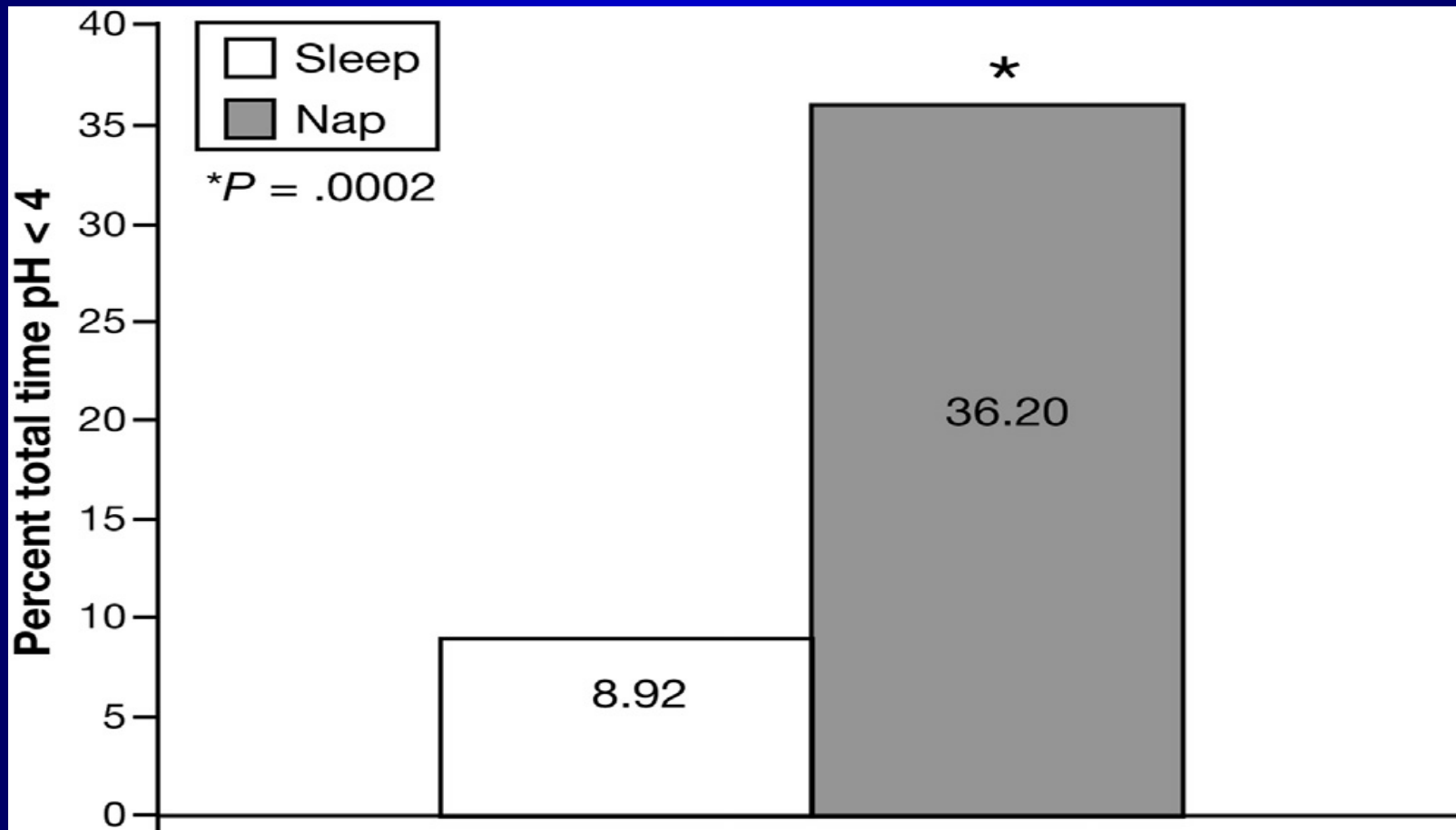


# Reflux Events Per Hour are More Common During Naps as Compared to Sleep Time



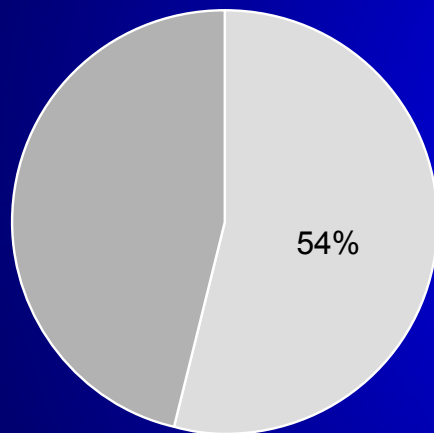


# Percent Time pH<4 is Greater During Naps as Compared to Nighttime Sleep



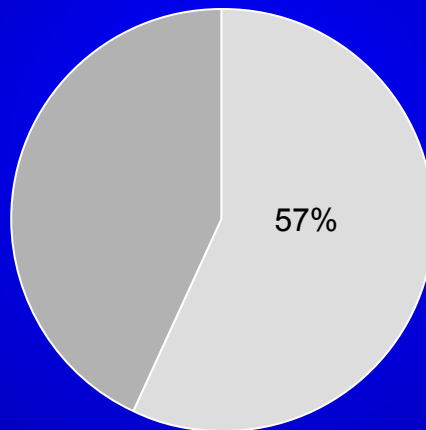
# Heartburn that Awakens Patients from Sleep

Among GERD Patients



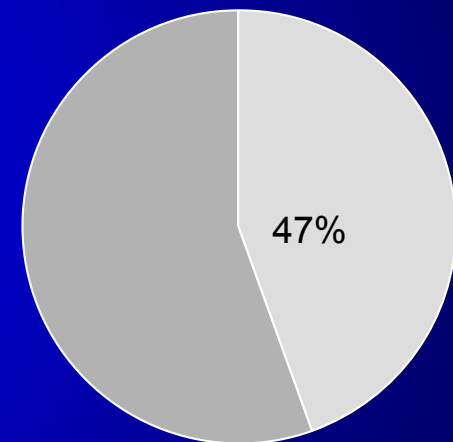
\*N = 1284

Among GERD Patients with Weekly Symptoms



\*\*N = 1000

Among GERD Patients



\*\*\*N = 2200

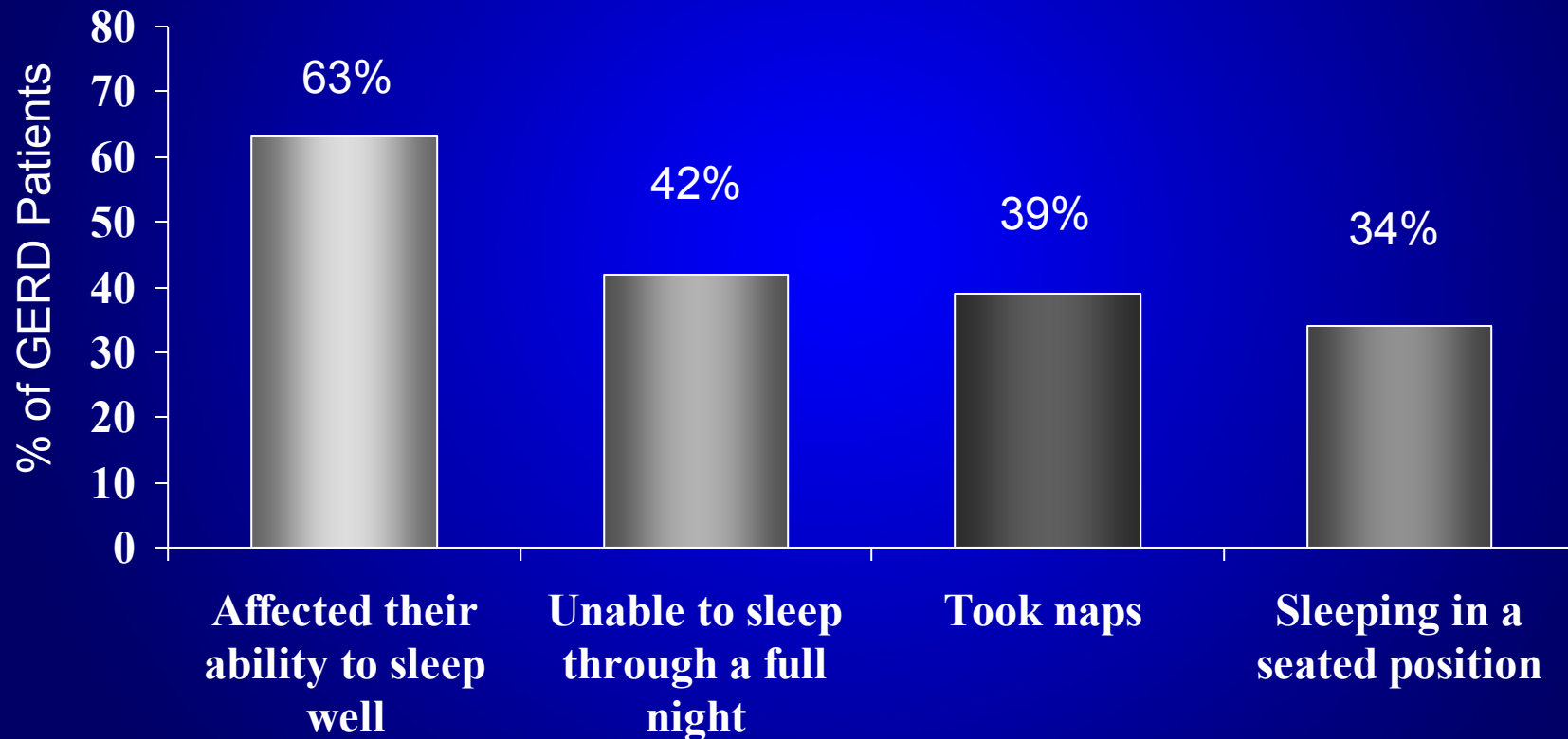
□ Reported  
■ Not Reported

\*Farup et al. *Arch Intern Med.* 2001;161:45-52.

\*\*Shaker et al. *Am J Gastroenterol.* 2003;98:1487-1493.

\*\*\*Locke et al. *Gastroenterology.* 1997;112:1448-1456.

# Nighttime Heartburn and Its Effect on Sleep



**27% Reported that Their Heartburn-  
Induced Sleep Disturbances Kept Their  
Spouses from Having a Good Night's Sleep**



**Shaker et al. *Am J Gastroenterol.* 2003;98-1487-1493.**

# Factors that Affect Reports of Heartburn that Awaken Patients from Sleep

	OR	95% LCL	95% UCL	P value
College education	0.74	0.64	0.86	<0.0001
Snoring and sleepy	2.16	1.77	2.63	<0.0001
BMI	1.17	1.07	1.29	0.00
Insomnia	2.05	1.73	2.44	<0.0001
Benzodiazepines	1.5	1.13	1.98	0.00
Carbonated soft drinks	1.24	1.07	1.45	0.01
Hypertension	1.27	1.10	1.47	0.00
Asthma	1.31	1.03	1.68	0.03

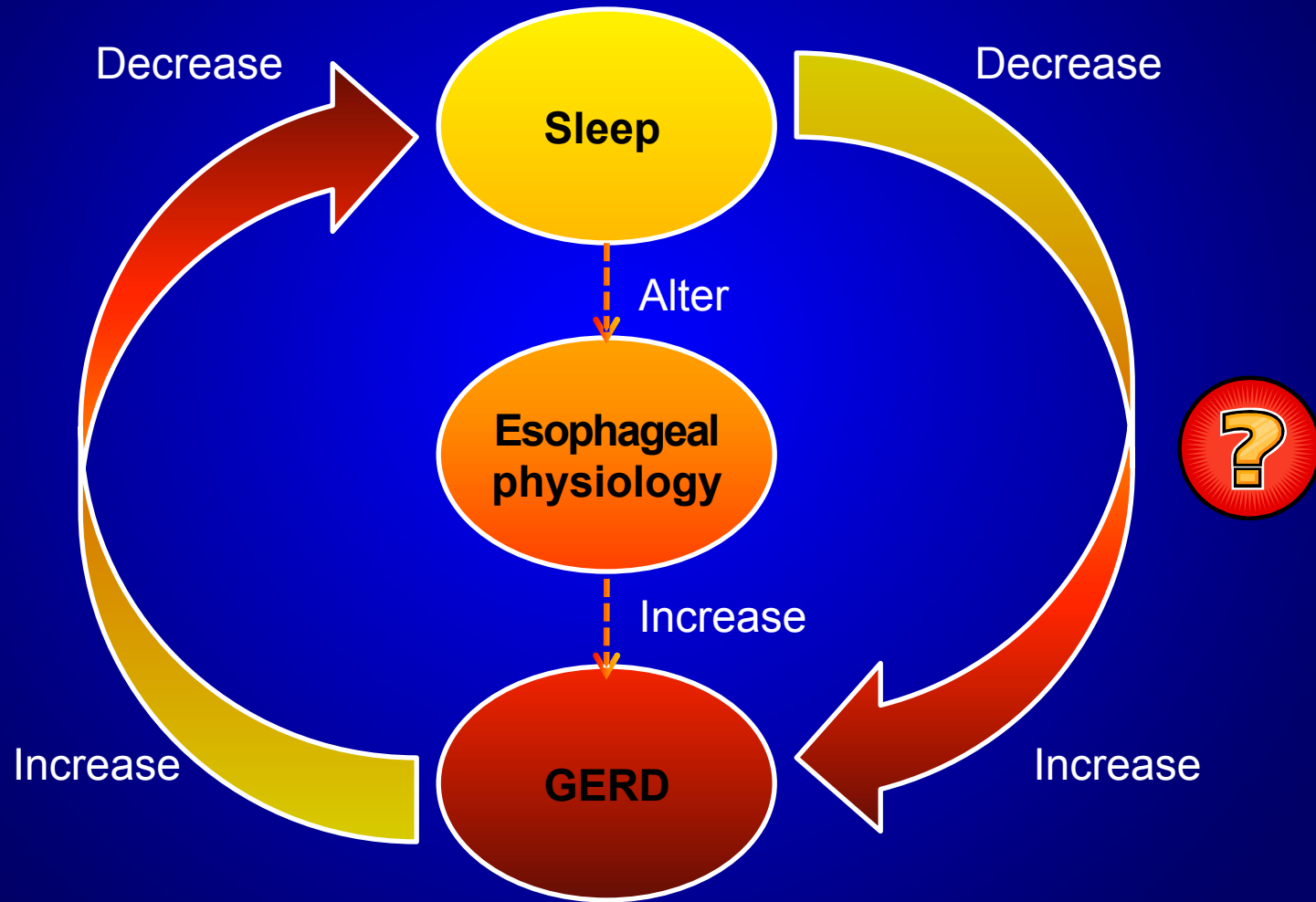
**Forward Stepwise, Multi-Variate Models**

# Amnestic Short Arousals In GERD Patients

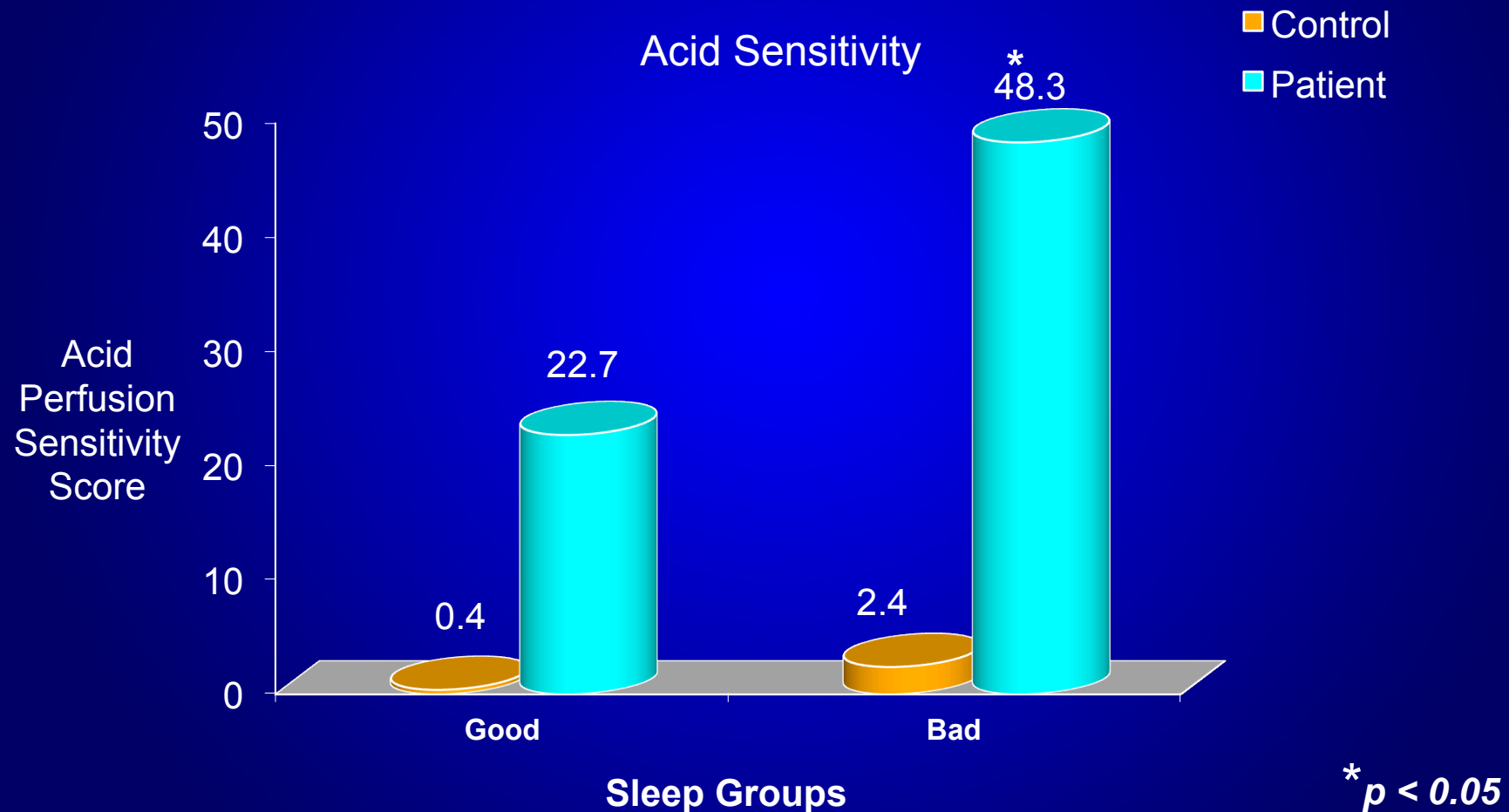
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- 90% of acid reflux events were associated with a short awakenings from sleep.
- Most patients awoke for an epoch (30 seconds) after an acid reflux event.
- There were significantly more spontaneous arousals during pH drops than during comparison periods.

# The Sleep and Acid Reflux Model



# The Relationship Between Acid Perfusion Sensitivity Score and Sleep Deprivation During an Acid Perfusion Test 0.1 N HCl 10 cc/min





# The Differential Effect of Sleep Deprivation versus Good Sleep on Esophageal Acid Exposure in Normal Subjects (N=11)

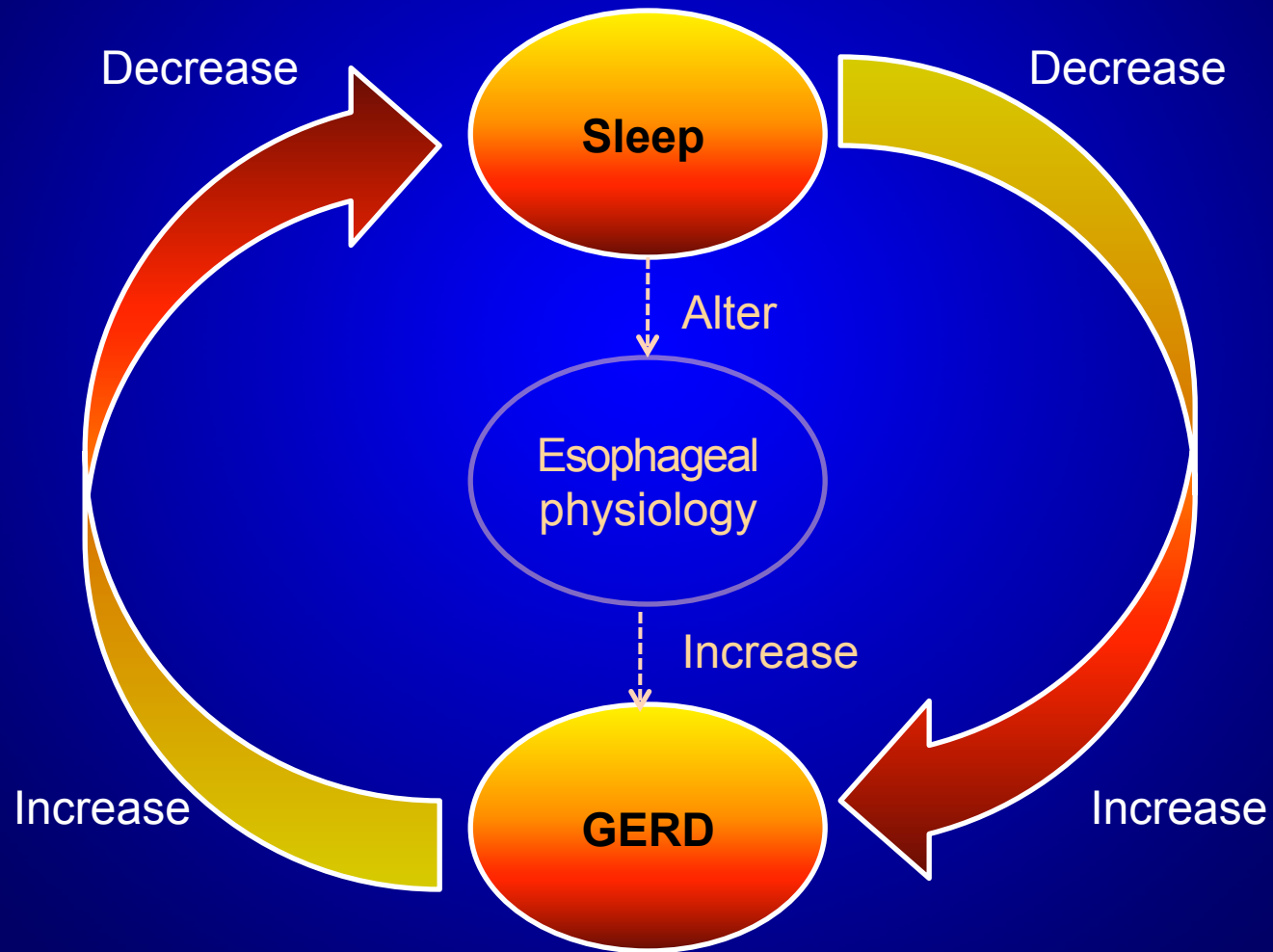


45.5% of subjects developed an abnormal pH test after sleep deprivation.

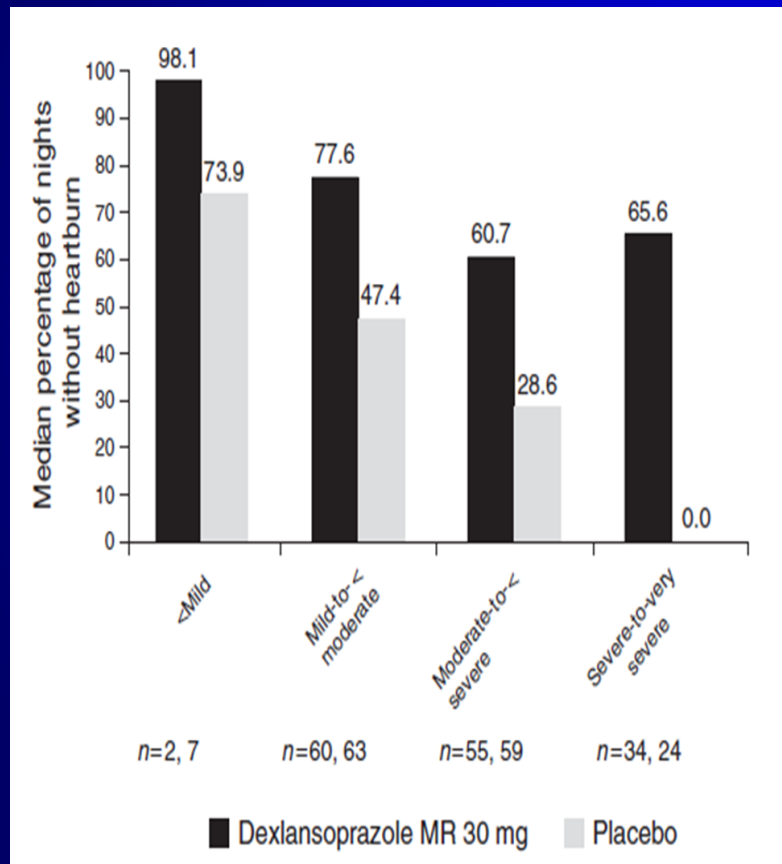
\* Good sleep = At least 7 hours on 2 consecutive nights

\*\* Bad sleep = 4 hours or less on 2 consecutive nights

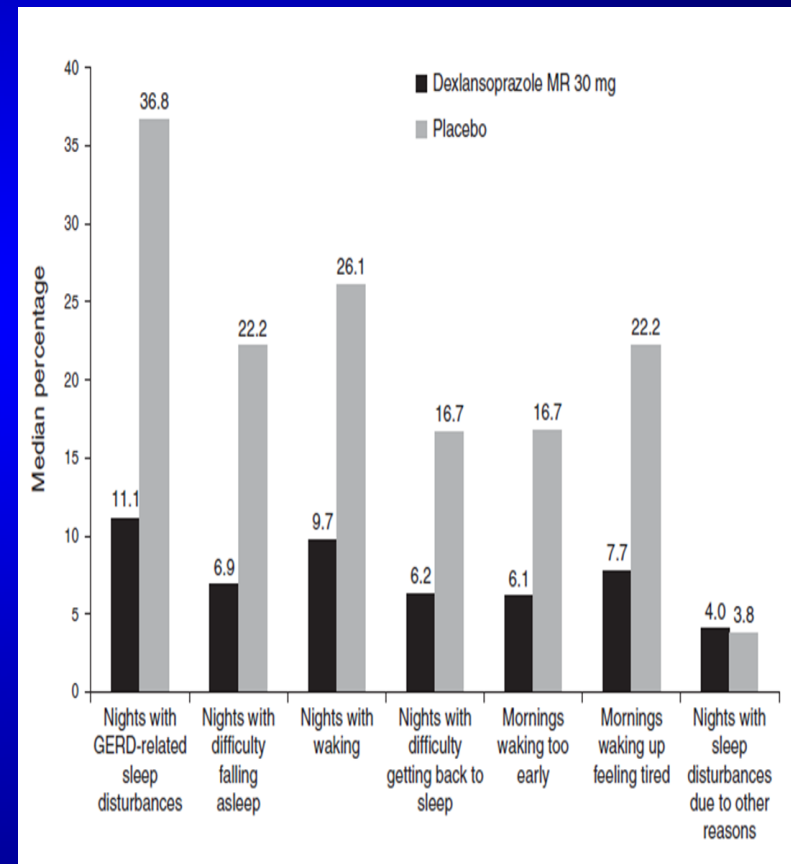
# The Bidirectional Relationship Between Sleep and GERD



# The Effect Of Anti-Reflux Treatment On Nighttime GERD And Sleep Disturbances

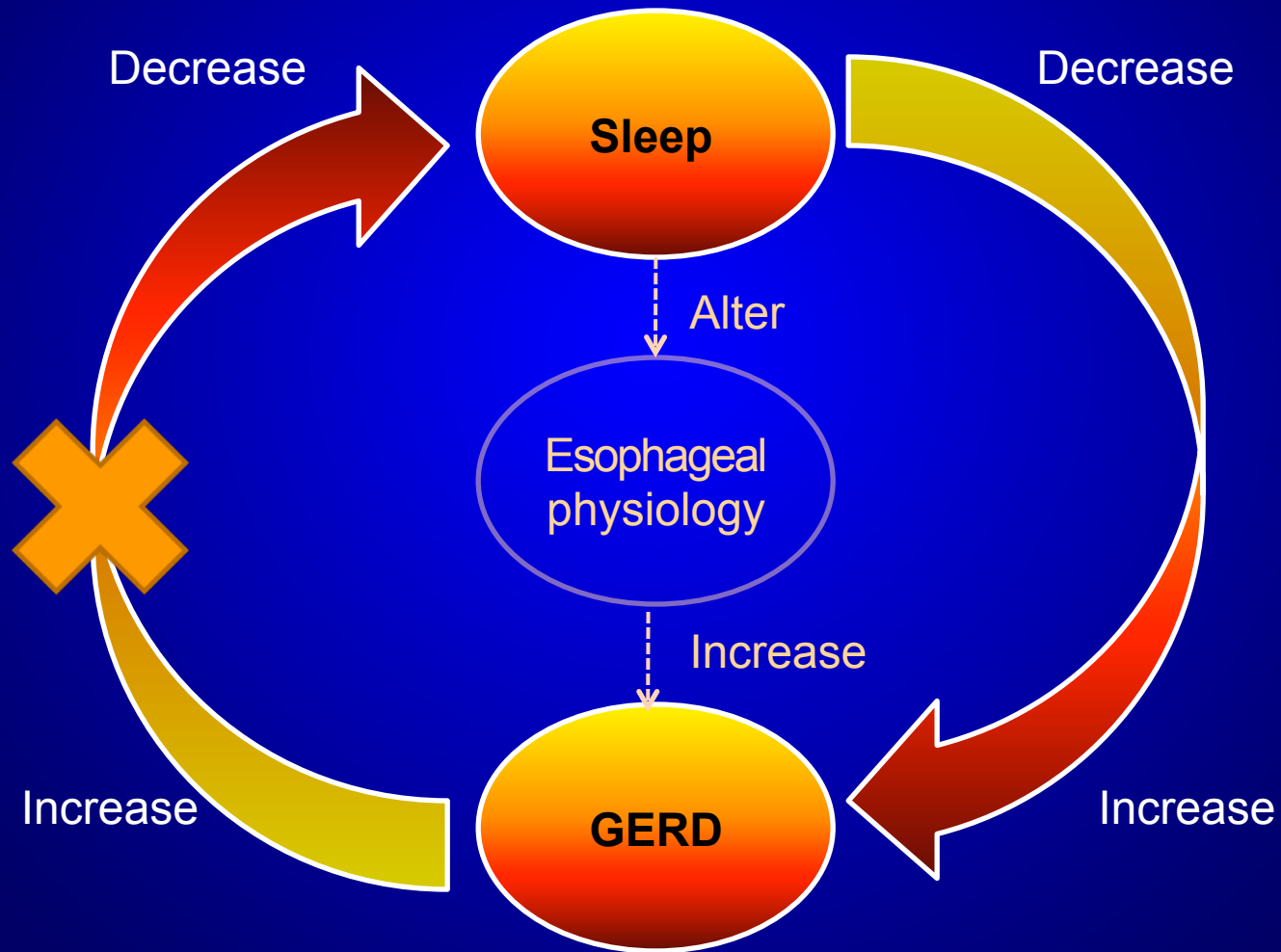


Sleep Disturbances

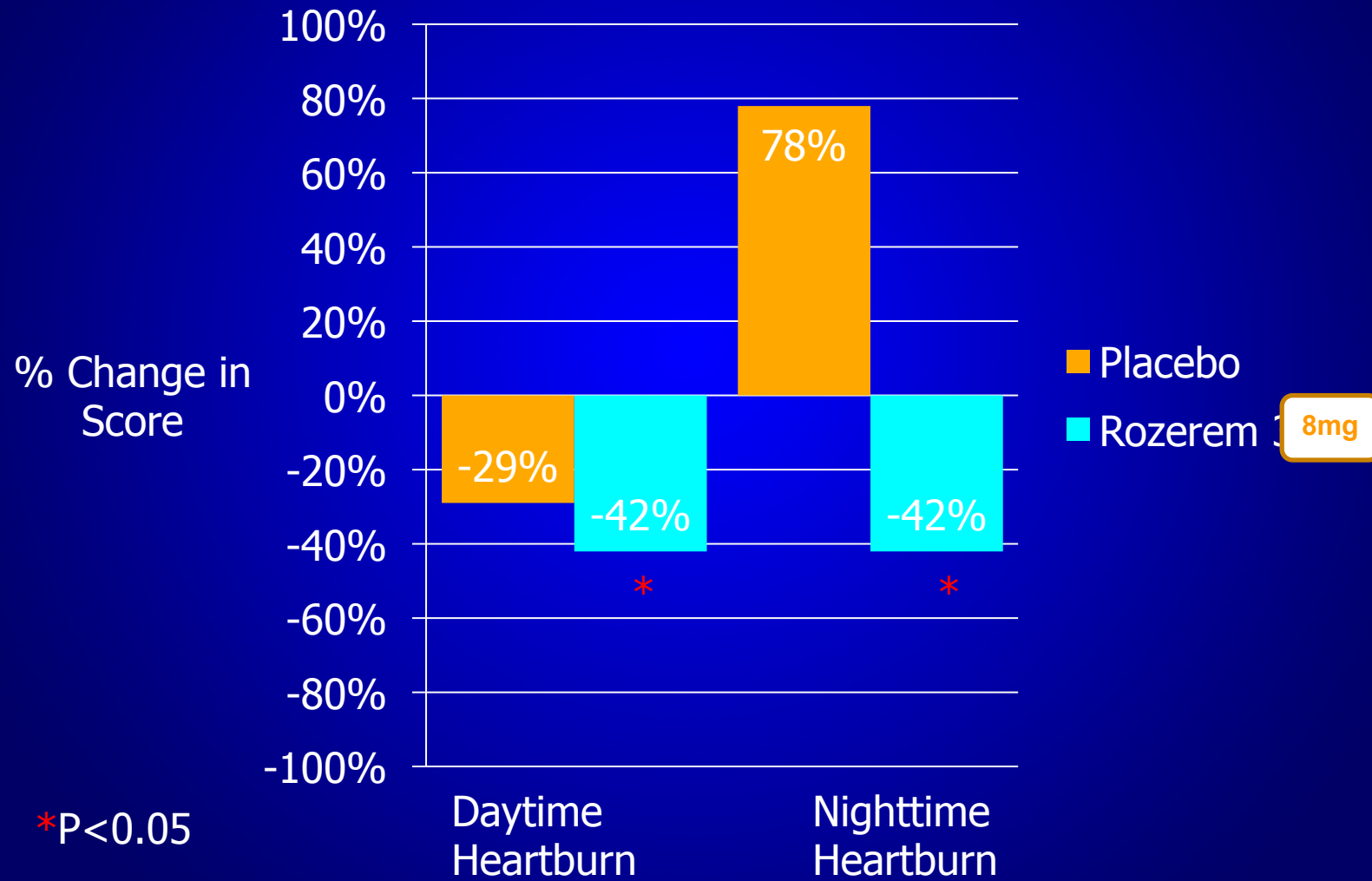


Nighttime GERD

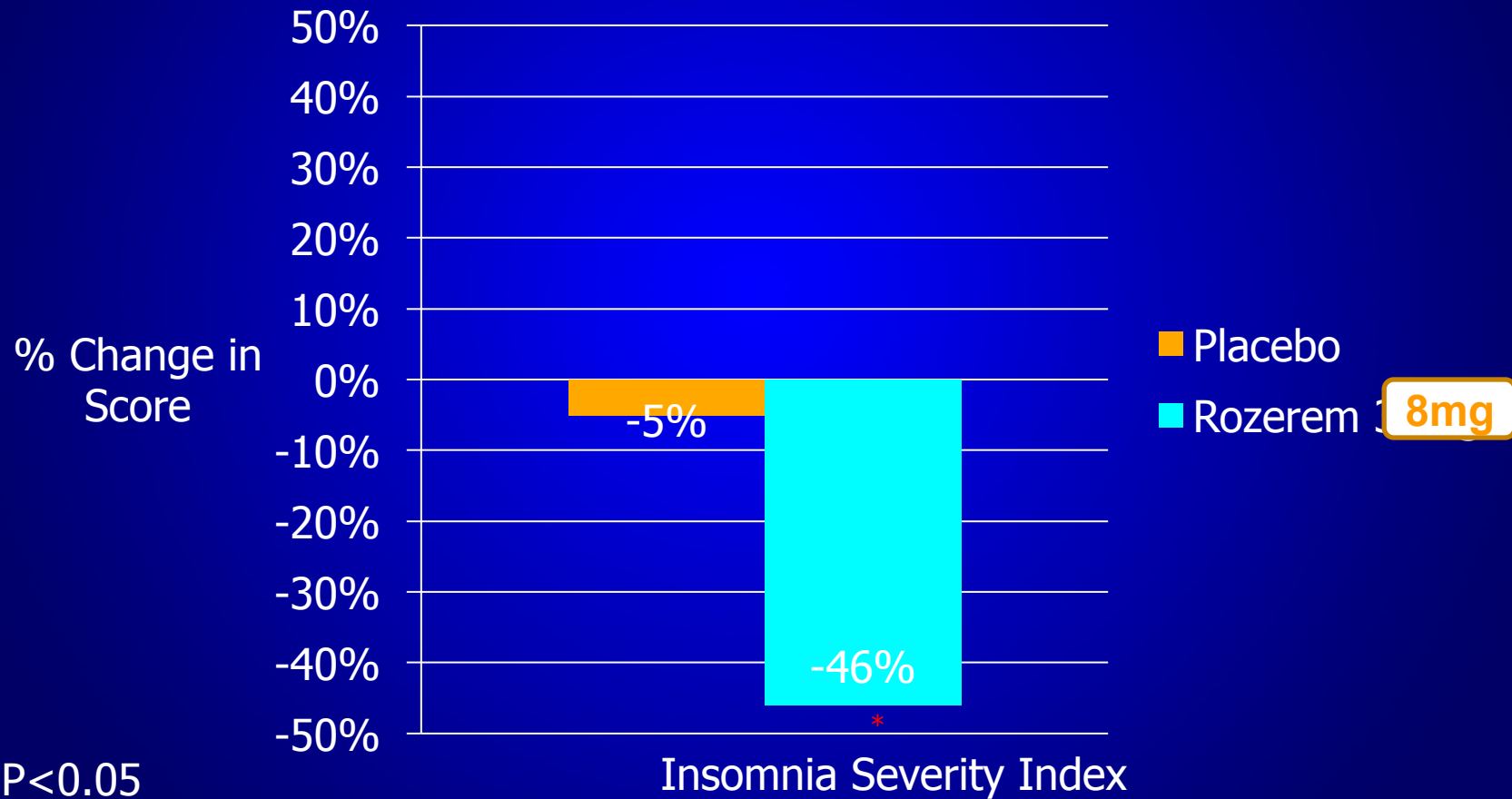
# The Bidirectional Relationship Between Sleep and GERD



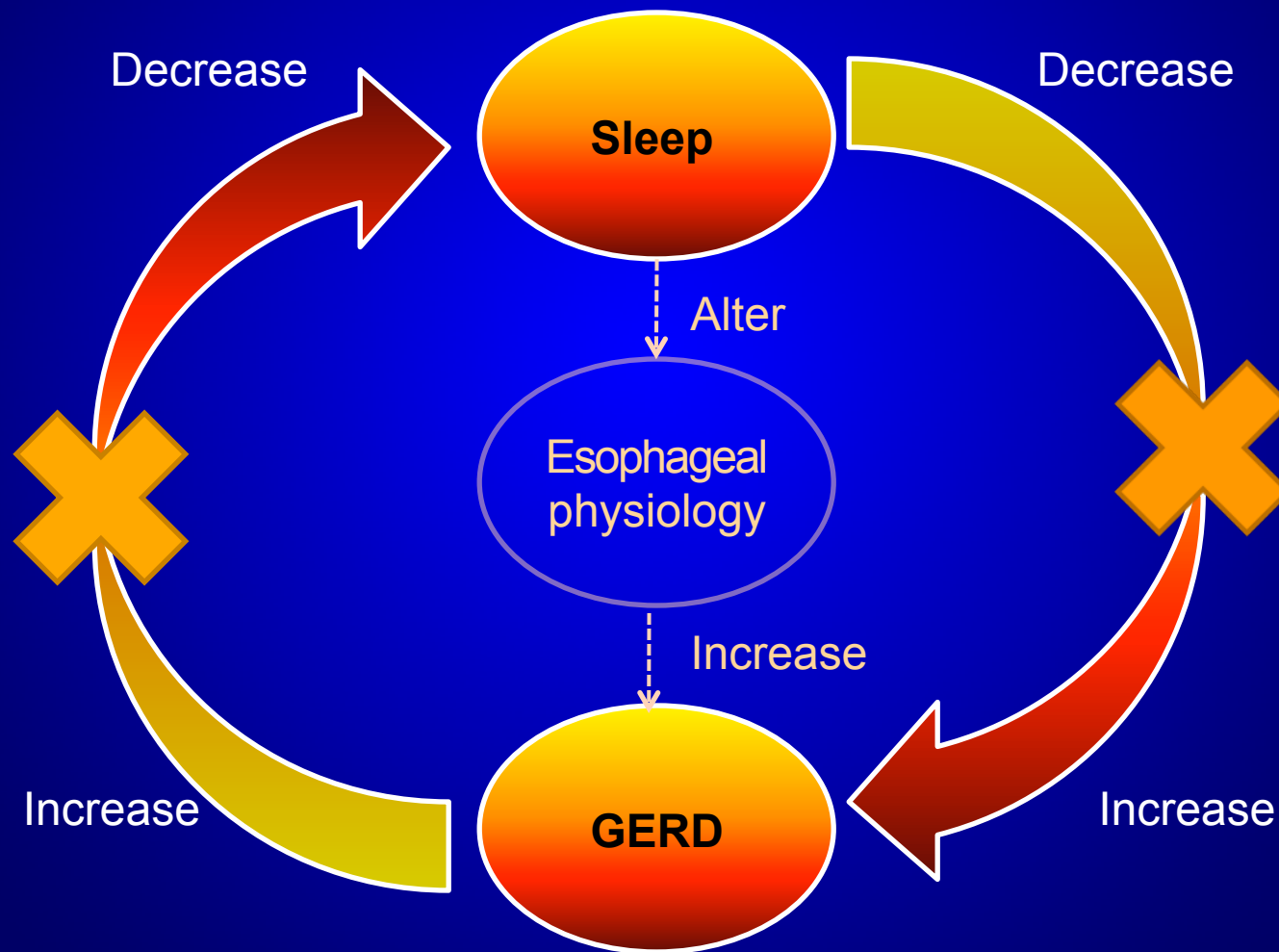
# The Effect of Ramelteon (MT1+MT2 agonist) Versus Placebo Given Over 4 Weeks On GERD-Related Symptoms



# Comparison of changes in Insomnia severity Index after the treatment with Placebo versus Rozerem



# Should We Consider Combined Treatment For GERD?



**Never Give Up On Your Dreams**

**Keep Sleeping**

