Central Apnea

Disclosures

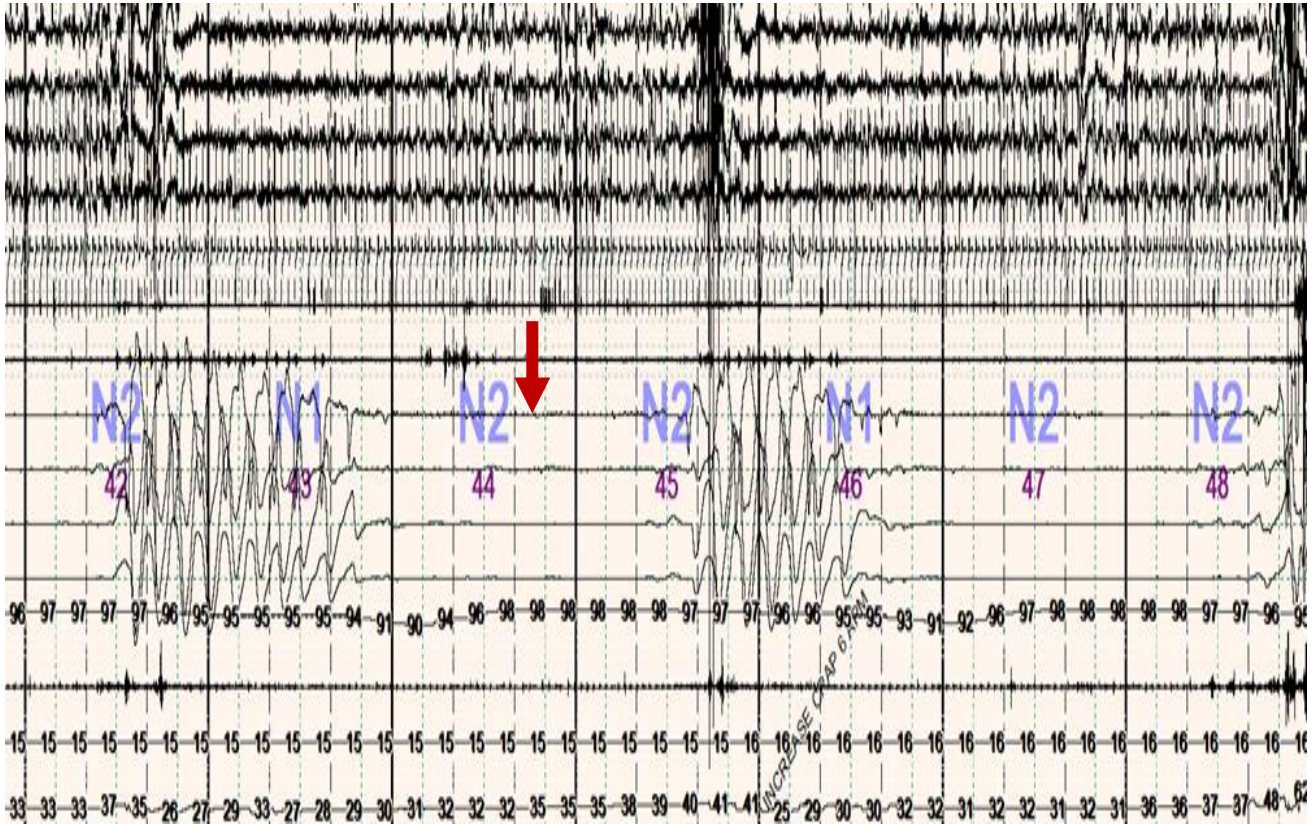
- No financial disclosure
- Past President, American Academy of Sleep Medicine
- Member, ABIM Board of Directors

Objectives

At the end of this presentation, the learner will be able to :

1. Describe the etiology and risk factors of central apnea in different patient population.
2. Describe the relationship between central and obstructive apnea
3. Outline a management approach, including diagnosis and treatment.

- 86 year old male
- Evaluation of snoring, fragmented sleep and dyspnea on exertion.
- Previous smoking history
- PFTs: Poor effort and mild airflow obstruction
- Echocardiography: EF= 40%



Question #1

What is the underlying mechanism of the phenomenon indicated by the arrow?

A. Upper Airway obstruction
B. REM sleep
C. Hypocapnia
D. Diaphragmatic dysfunction

Question # 1

What is the underlying mechanism of the phenomenon indicated by the arrow?

A. Upper Airway obstruction

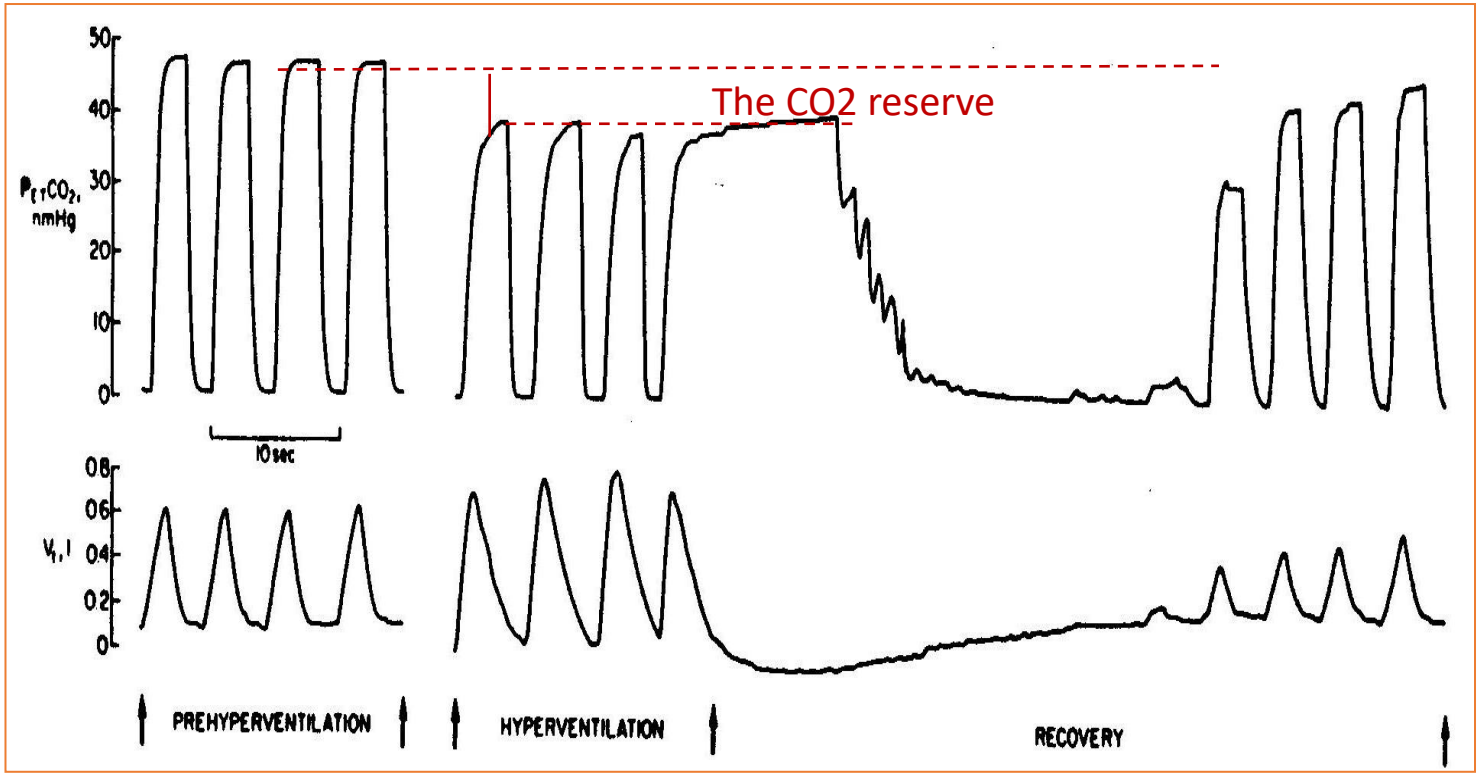
B. REM sleep

C. Hypocapnia

D. Diaphragmatic dysfunction

Effect of NREM sleep on Ventilation

The hypocapnic apneic threshold



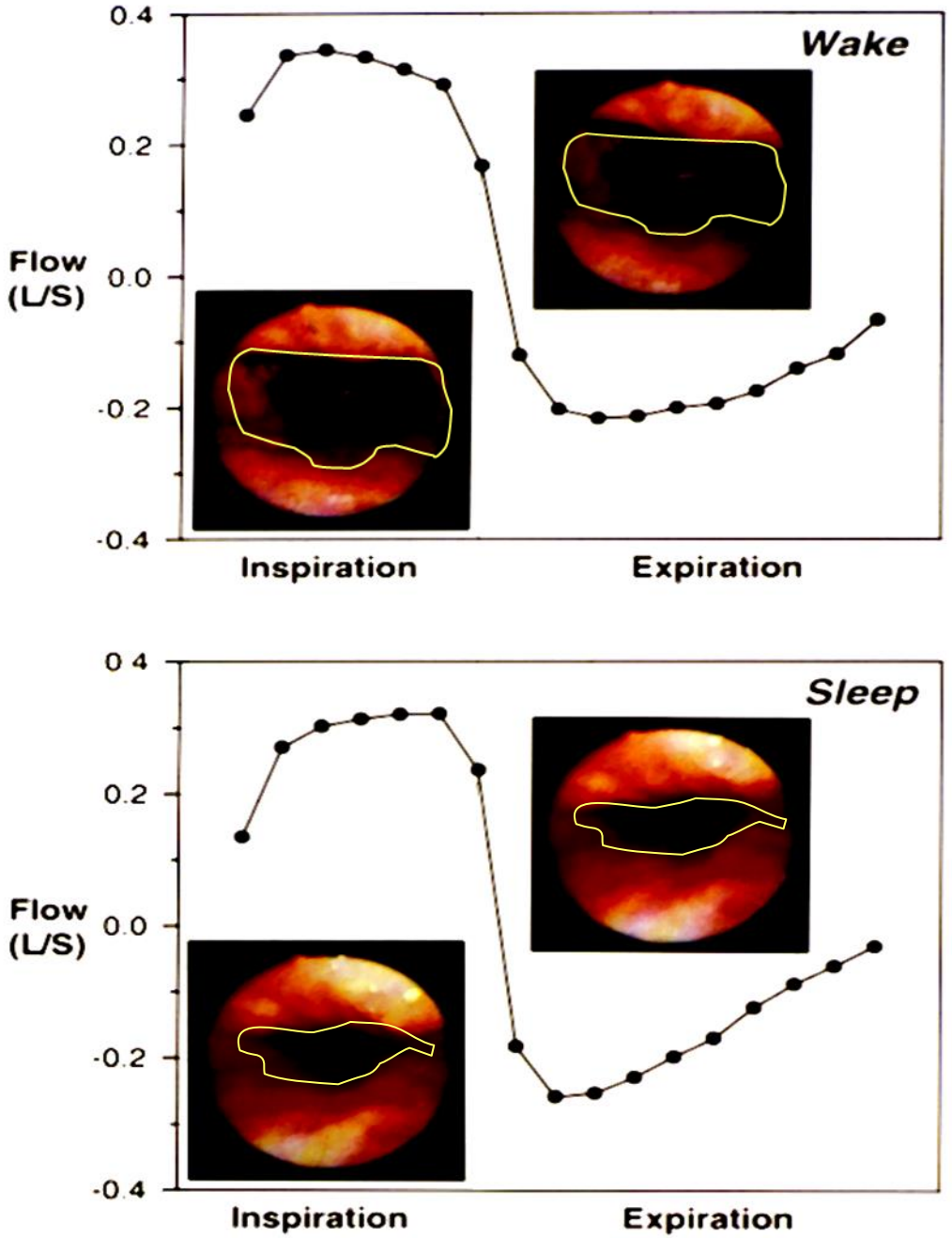
NREM sleep unmasks a reproducible, highly sensitive, hypocapnic apneic threshold

Skatrud et al. JAP. 55:813-22, 1983

Effect of NREM sleep on Ventilation

Upper airway changes

1. Reduced activity of upper airway dilators
2. Loss of load compensation
3. Reduced pharyngeal caliber
4. Reduced tidal volume (V_T)



Classification of Central Apnea

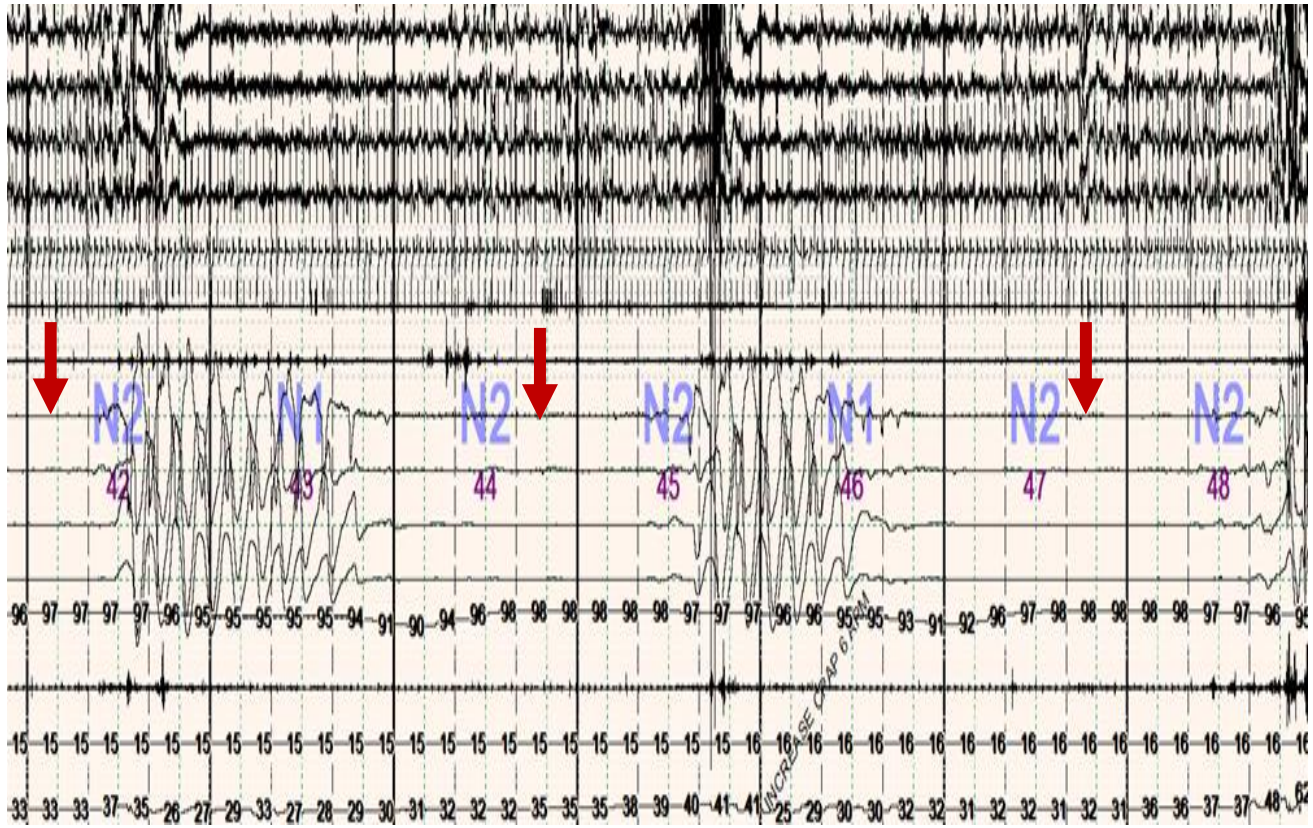
- Central sleep apnea with Cheyne-Stokes breathing
- Central sleep apnea due a medical disorder without Cheyne-Stokes breathing
- Central sleep apnea due to high altitude periodic breathing
- Central sleep apnea due to a medication or substance
- Primary central sleep apnea
- Treatment-emergent central sleep apnea

Central Sleep Apnea Pathophysiologic Classification

- Hypoventilation
  - Sleep related hypoventilation: CNS, neuromuscular or chest wall disease
  - Inadequate ventilatory reserve: hypercapnia not required
  - May not meet the criteria for “central” or apnea”
- Post- hyperventilation
  - No daytime alveolar hypoventilation
  - Hyperventilation
  - The most common type of central apena

- 86 year old male
- Evaluation of snoring, fragmented sleep and dyspnea on exertion.
- Previous smoking history
- PFTs: Poor effort and mild airflow obstruction
- Echocardiography: EF= 40%

- AHI=60/hour of sleep
- CAI= 20/hour of sleep
- ABGs: P_aO_2= 82 torr, P_aCO_2= 34 torr



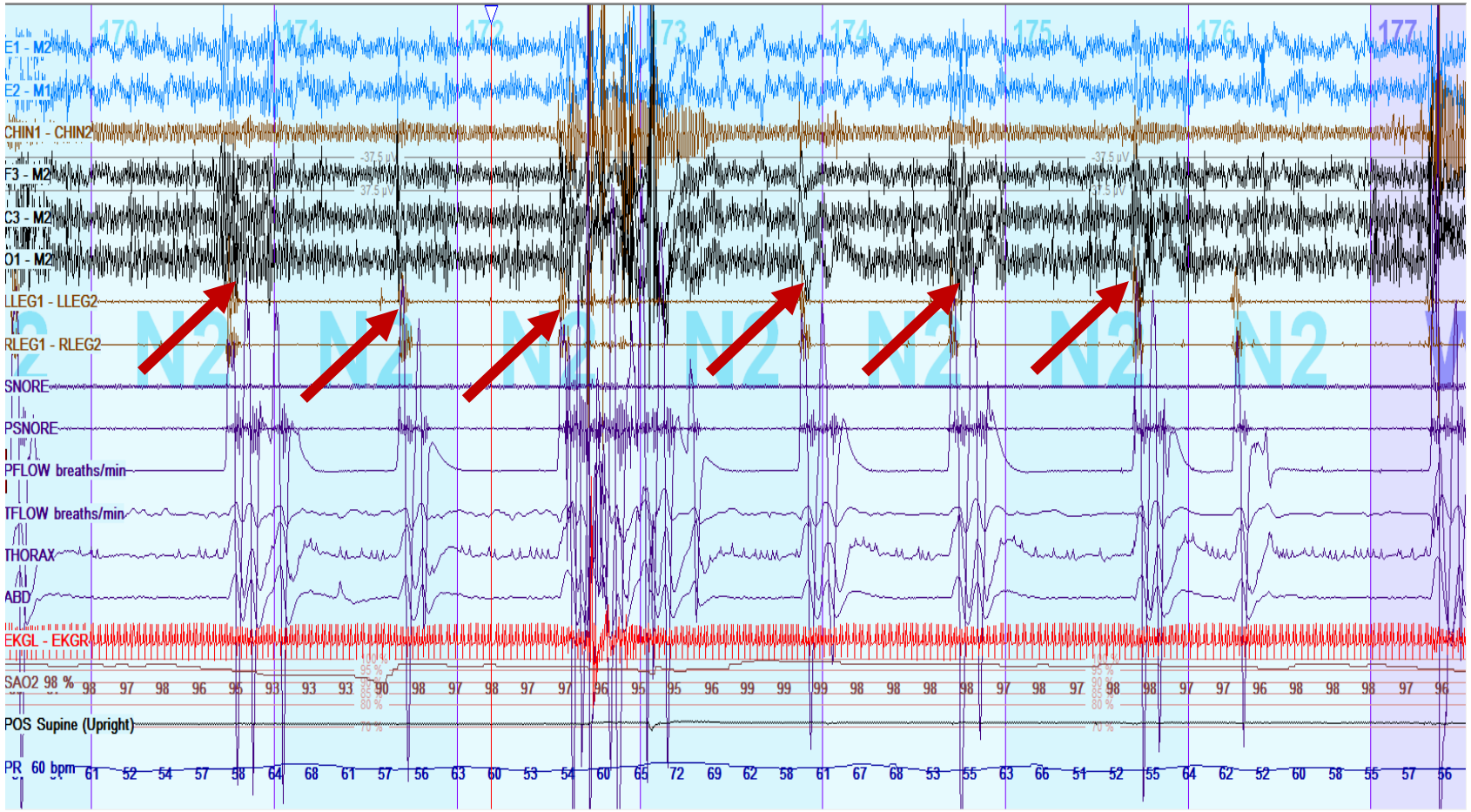
Question # 2

What is/are the potential underlying mechanism (s) of recurrent central apnea?

A. Impaired arousal response
B. Low loop gain
C. Hypercapnia
D. High controller gain

What is/are the potential underlying mechanism (s) of recurrent central apnea?

A. Impaired arousal response
B. Low loop gain
C. Hypercapnia
D. High controller gain

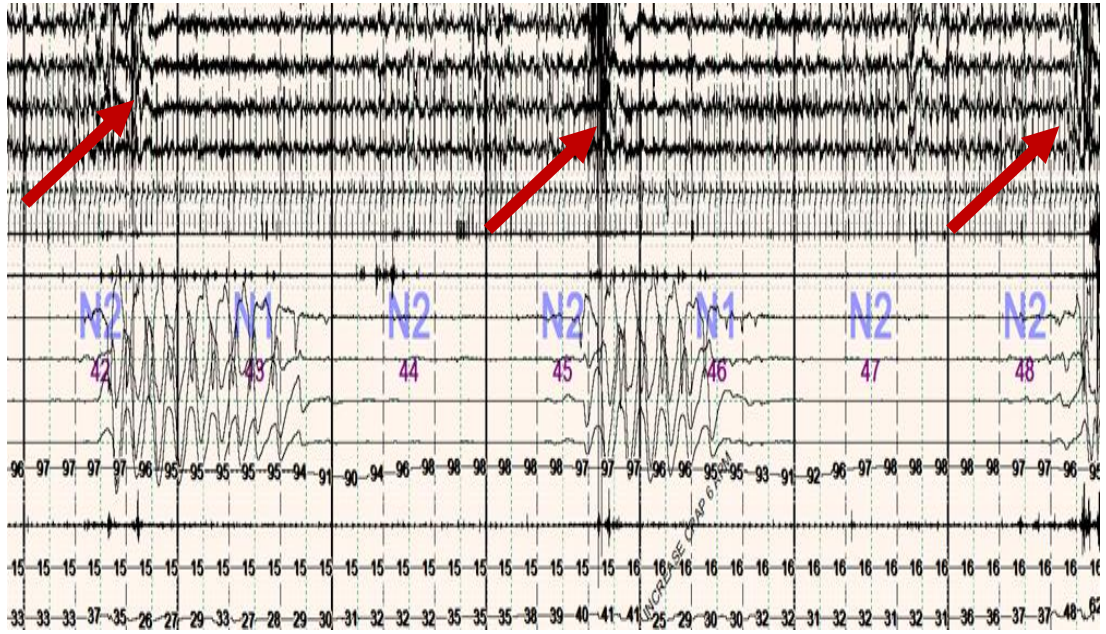


Recurrent Central Apnea: Apnea

Hyperventilation

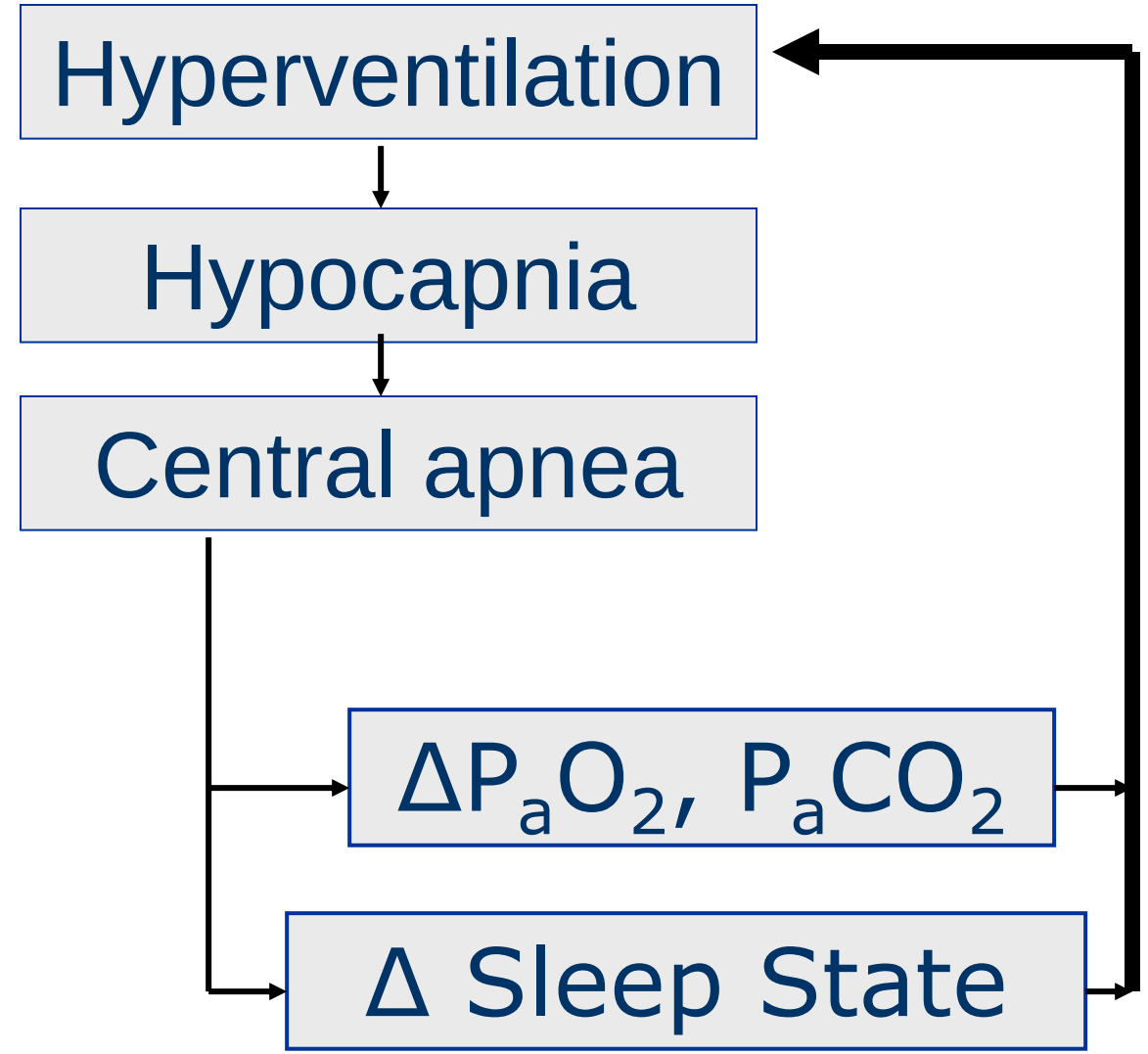
Hypocapnia

Central apnea



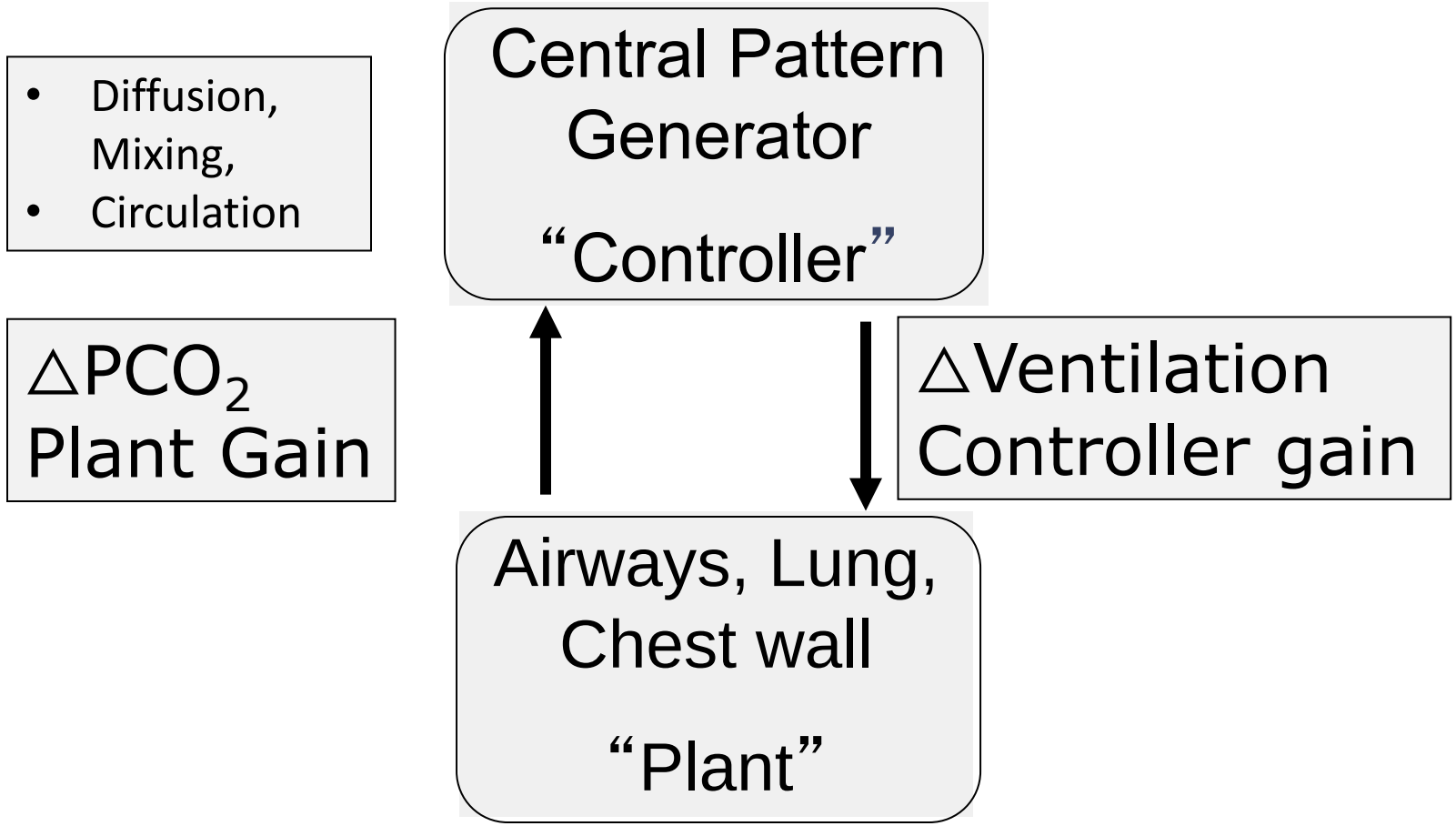
ΔPaO2, PaCO2

Δ Sleep State



Apnea Begets Apnea

The Loop Gain : An engineering Construct



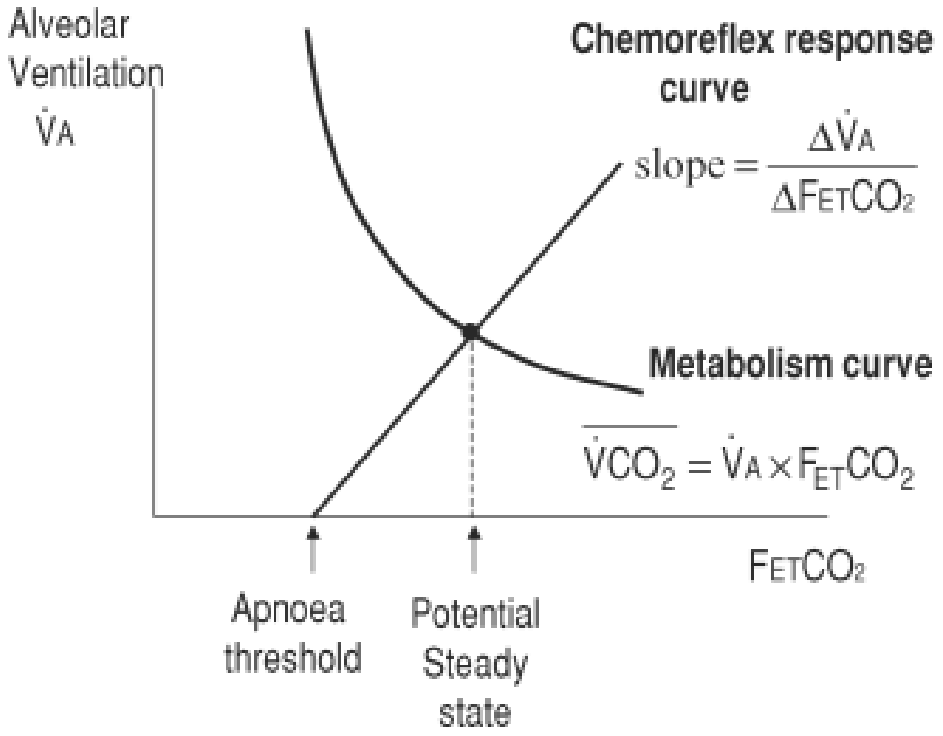
Mechanisms of hypocapnic Central Apnea
Loop Gain

Reducing PCO2
Plant gain

Input = *VE*
Output= *P*aCO2
Plant gain: Δ *P*aCO2 / Δ *V*E

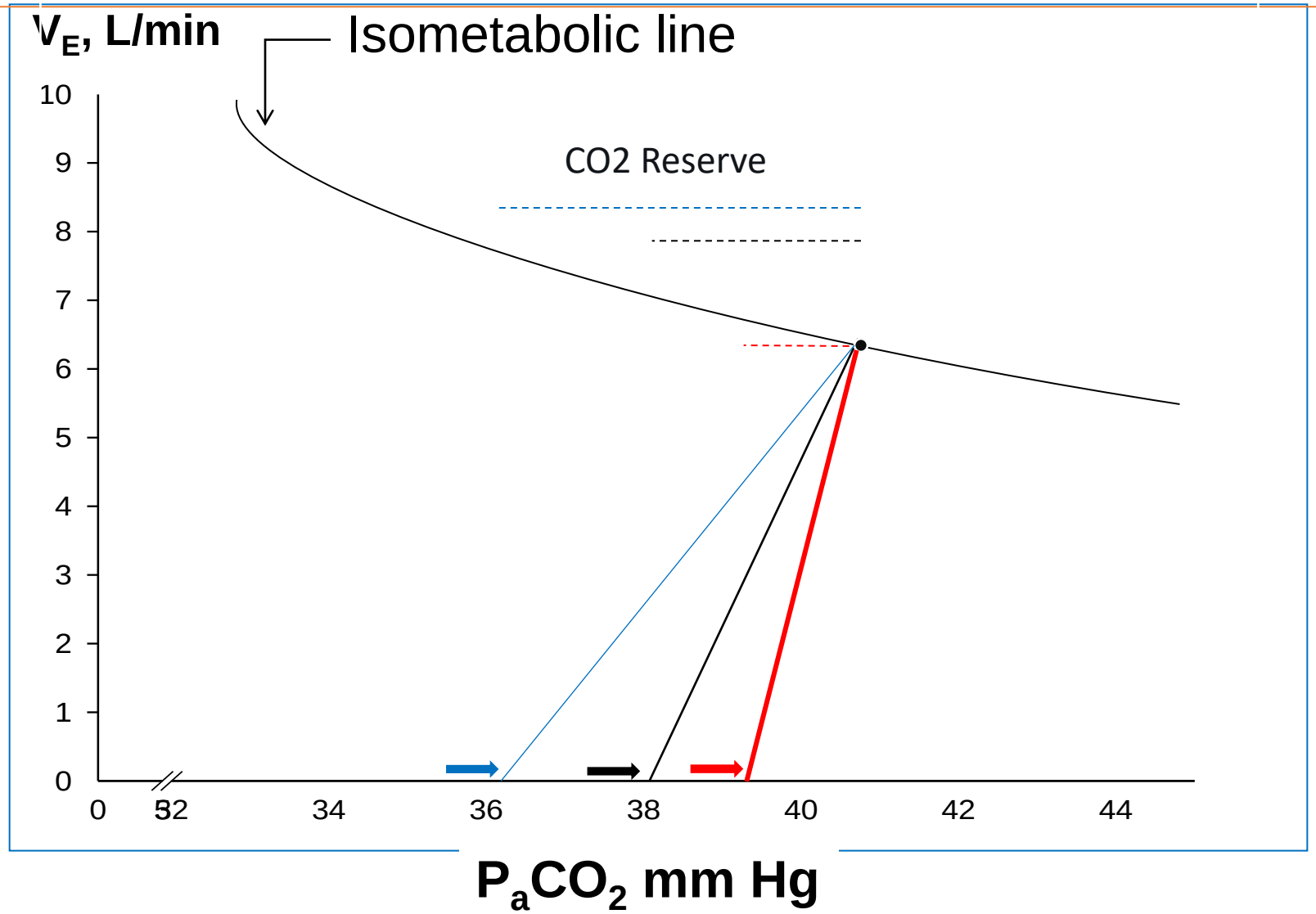
Changing ventilation:
Controller gain (CG) or chemoreflex sensitivity

Input parameter = *PaCO2*
Output parameter= VE
CG= Δ *V*E / Δ *P*aCO2

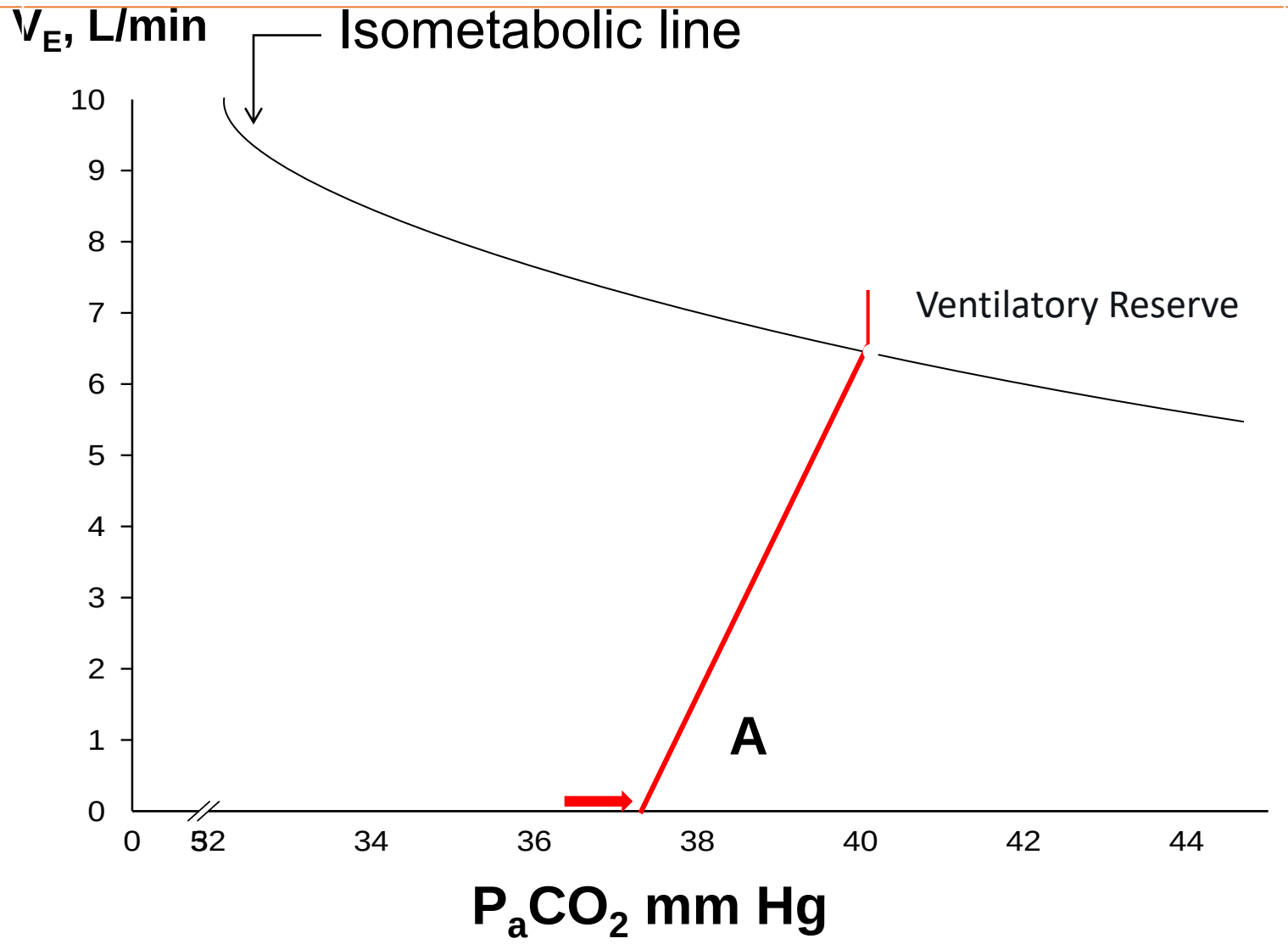


Manisty C. et al. J.Phys. 577. 1: 387-401)

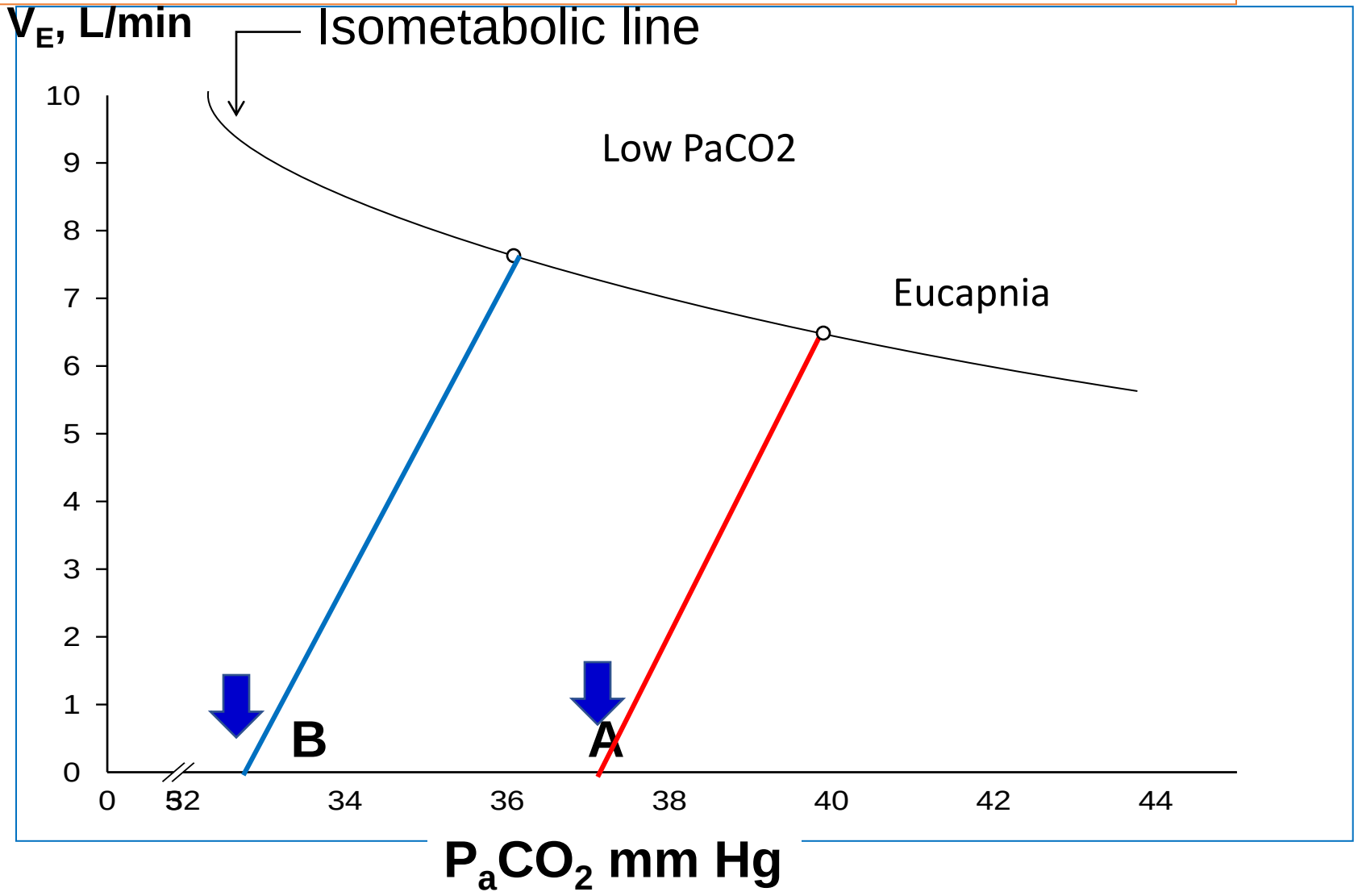
Effect of Chemoreceptor Sensitivity



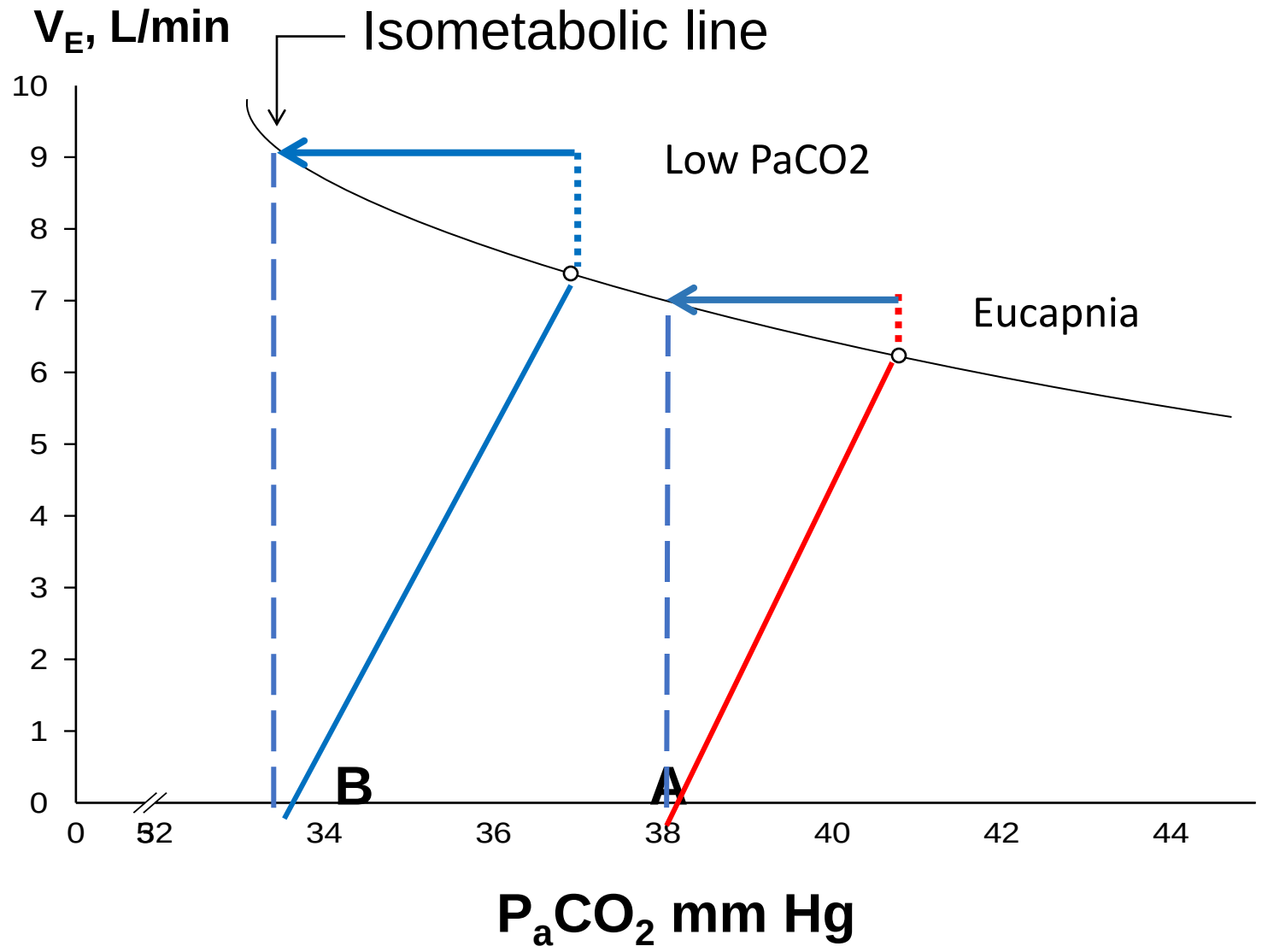
Effect of Prevailing PaCO2



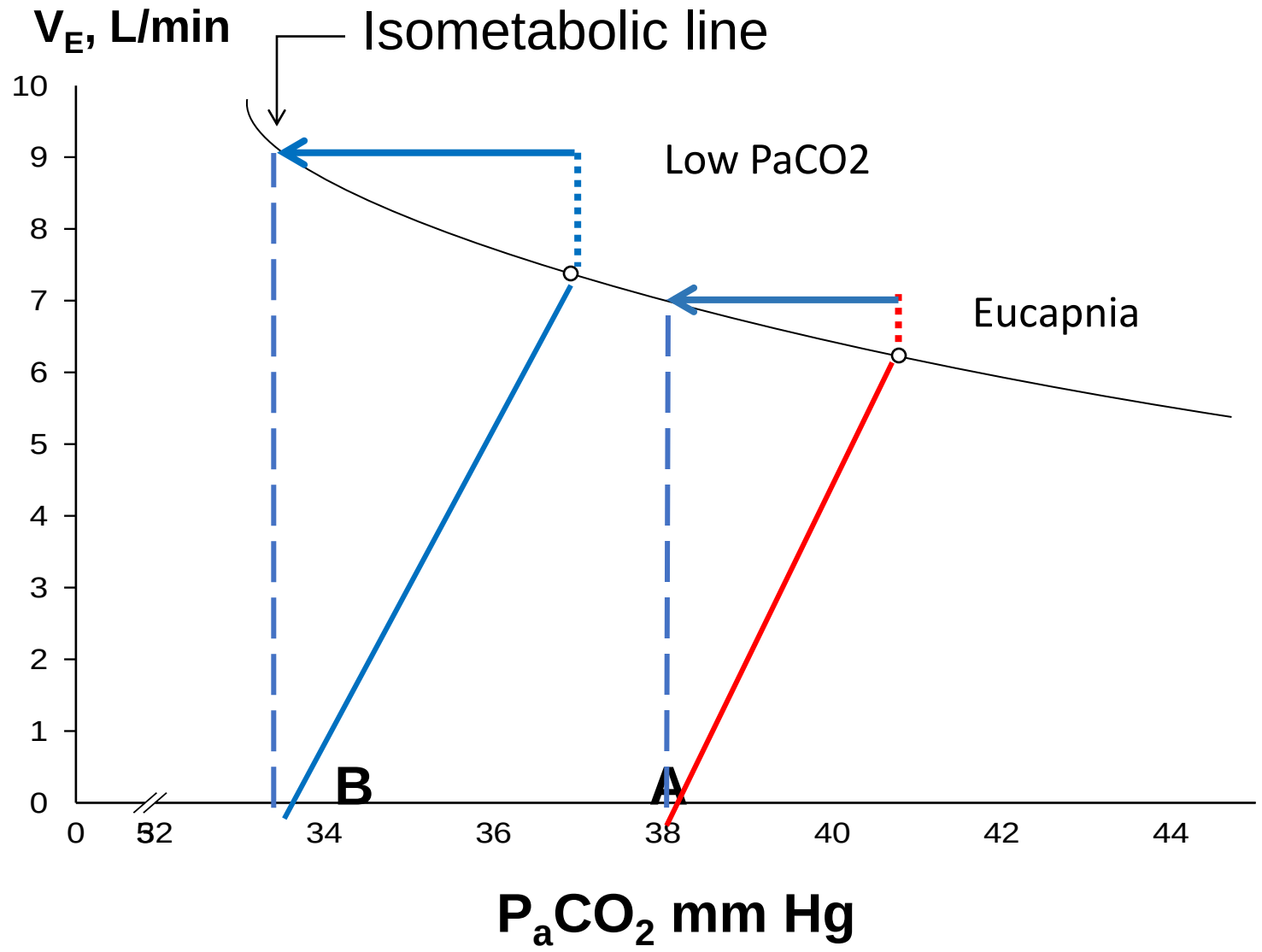
Effect of PrevailingPaCO2



Effect of PrevailingPaCO2



Effect of PrevailingPaCO2



Question # 3

The effect of decreased steady state $PaCO_2$ on susceptibility to central apnea is:

A. No effect- unchanged chemo-sensitivity

B. Increased- $PaCO_2$ closer to the hypocapnic apneic threshold.

C. Decreased- decreased plant gain.

D. Increased- decreased CO2 stores.

Question # 3

The effect of decreased steady state $PaCO_2$ on susceptibility to central apnea is:

A. No effect- unchanged chemo-sensitivity

B. Increased- PaCO2 closer to the hypocapnic apneic threshold.

C. Decreased- decreased plant gain.

D. Increased- decreased CO2 stores.

CENTRAL APNEA RISK FACTORS

- Age, gender and menopause
- Medical Conditions
  - CHF, CVA, Atrial fibrillation ?
  - Narcotics
  - Endocrine: Hypothyroidism, Acromegaly
- Idiopathic central apnea ?

Question # 4:

Which sleep state is least prone to central apnea

A. N1

B. N2

C. N3

D. REM

Question # 4:

Which sleep state is least prone to central apnea

A. N1

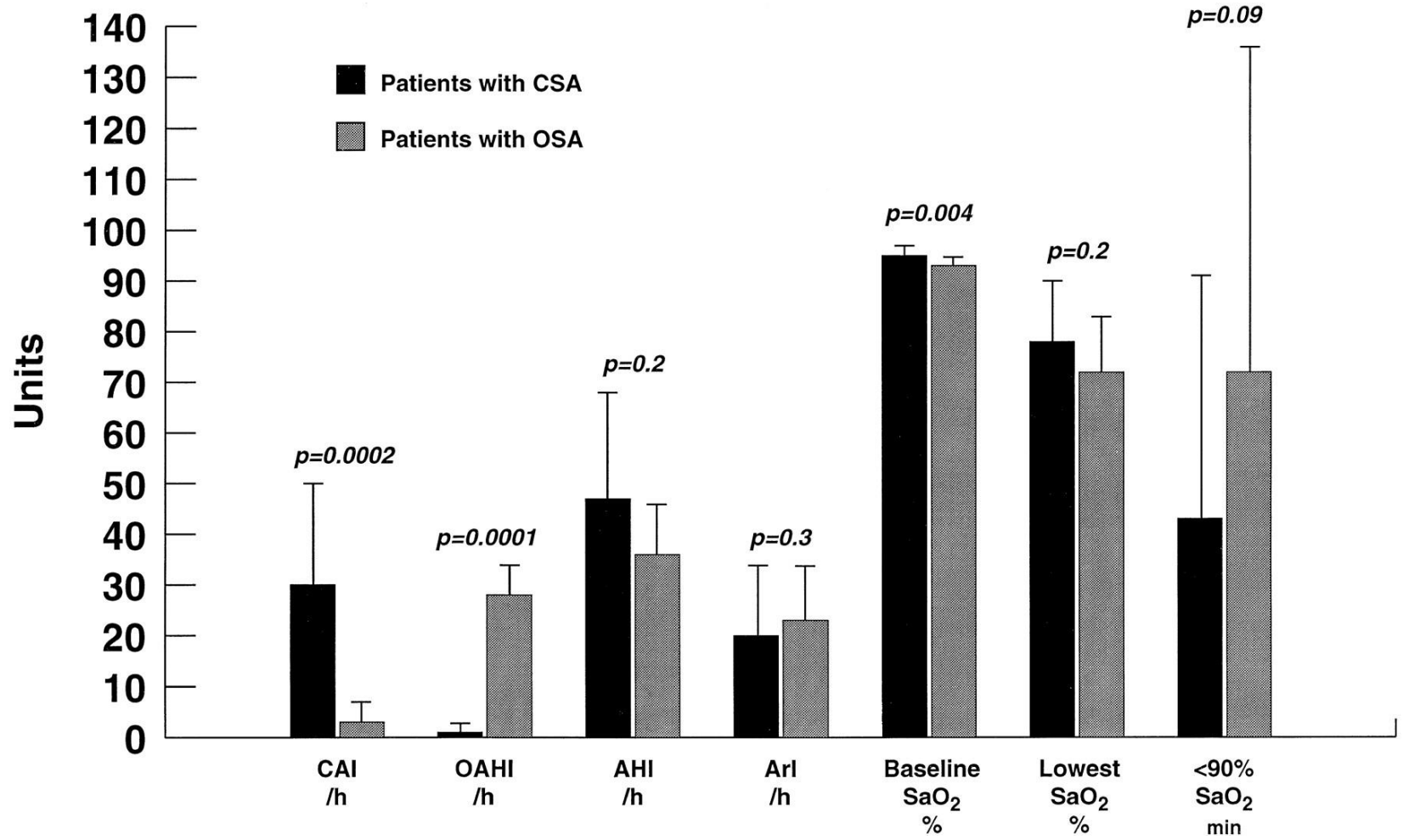
B. N2

C. N3

D. REM

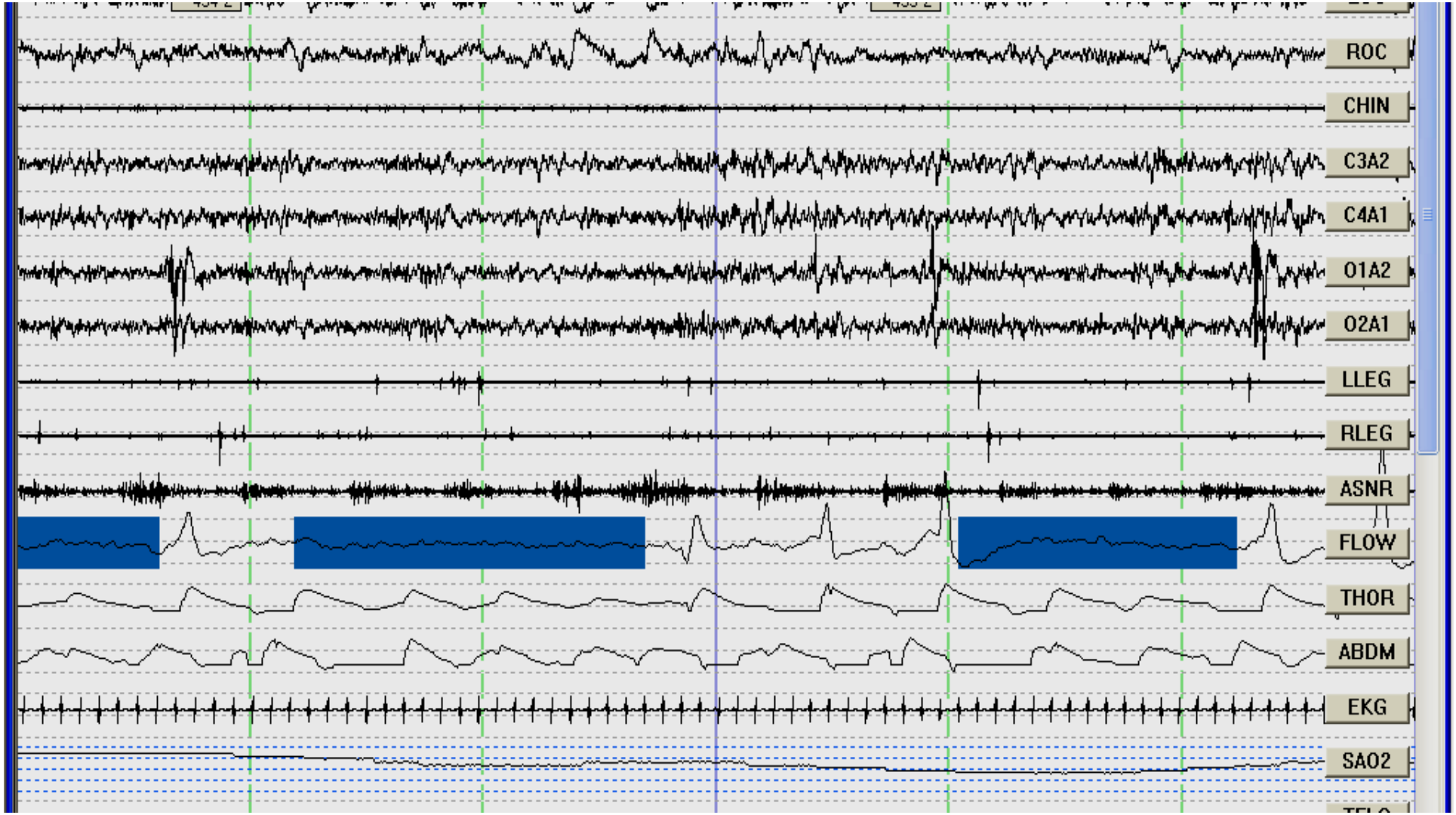
- Congestive Heart Failure
- Opiate analgesics
- Obstructive sleep apnea
  - Treatment-Emergent Central Apnea

Polysomnographic findings in male heart failure patients with either central (CSA) or obstructive (OSA) sleep apnea.

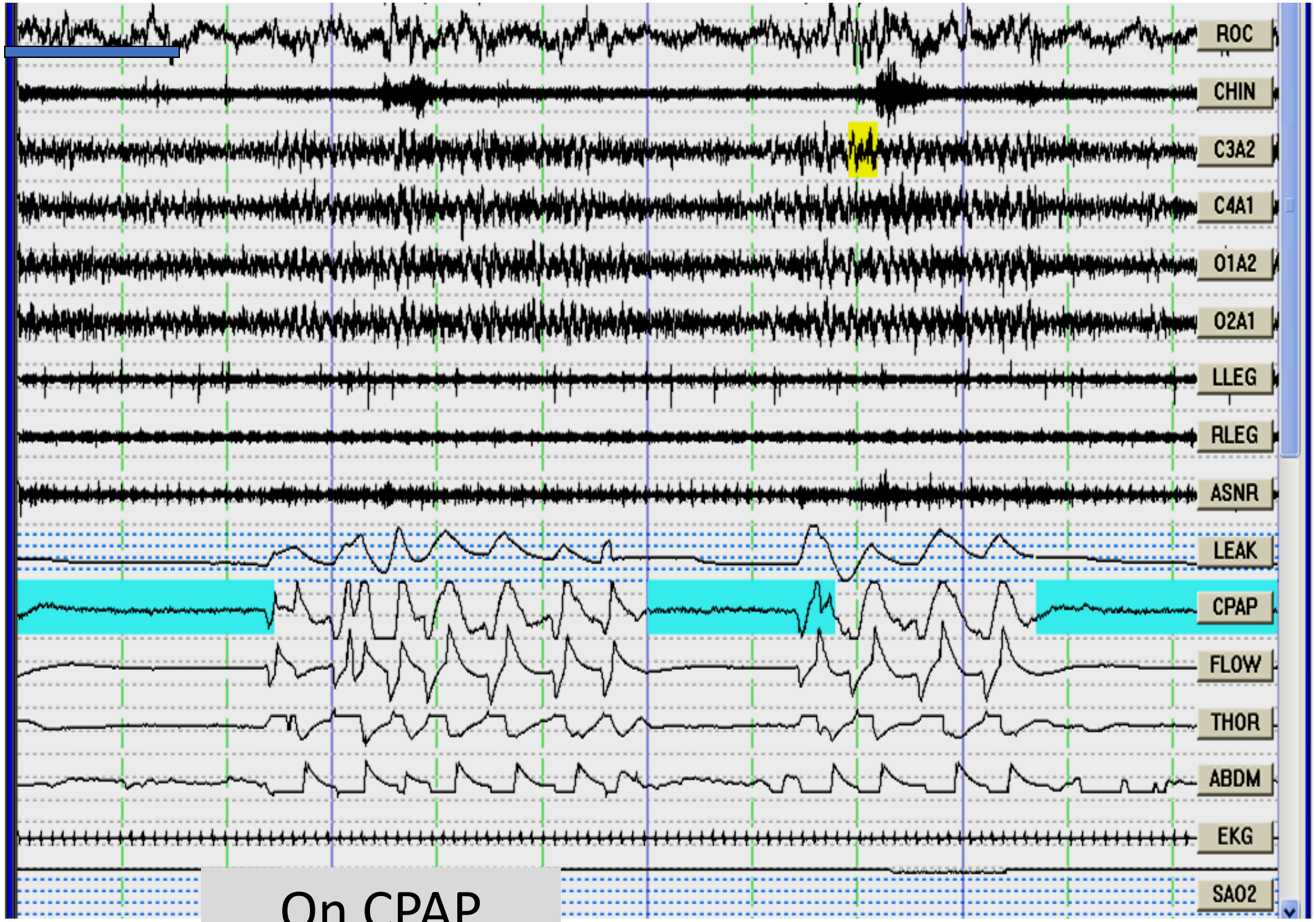


Javaheri S et al. Circulation. 1998;97:2154-2159

American Heart Association.



Baseline: Pre-CPAP


ROC
CHIN
C3A2
C4A1
O1A2
O2A1
LLEG
RLEG
ASNR
LEAK
CPAP
FLOW
THOR
ABDM
EKG
SAO2

On CPAP

Question #5

Which of the following statements regarding treatment-emergent central sleep apnea (TECSA) is correct

A. TECSA develops in the majority of patients undergoing split-night titration
B. Indicates the need for BPAP therapy.
C. Only patients with central apnea in the baseline study develop TECSA
D. The majority will experience complete resolution over a few weeks to months.

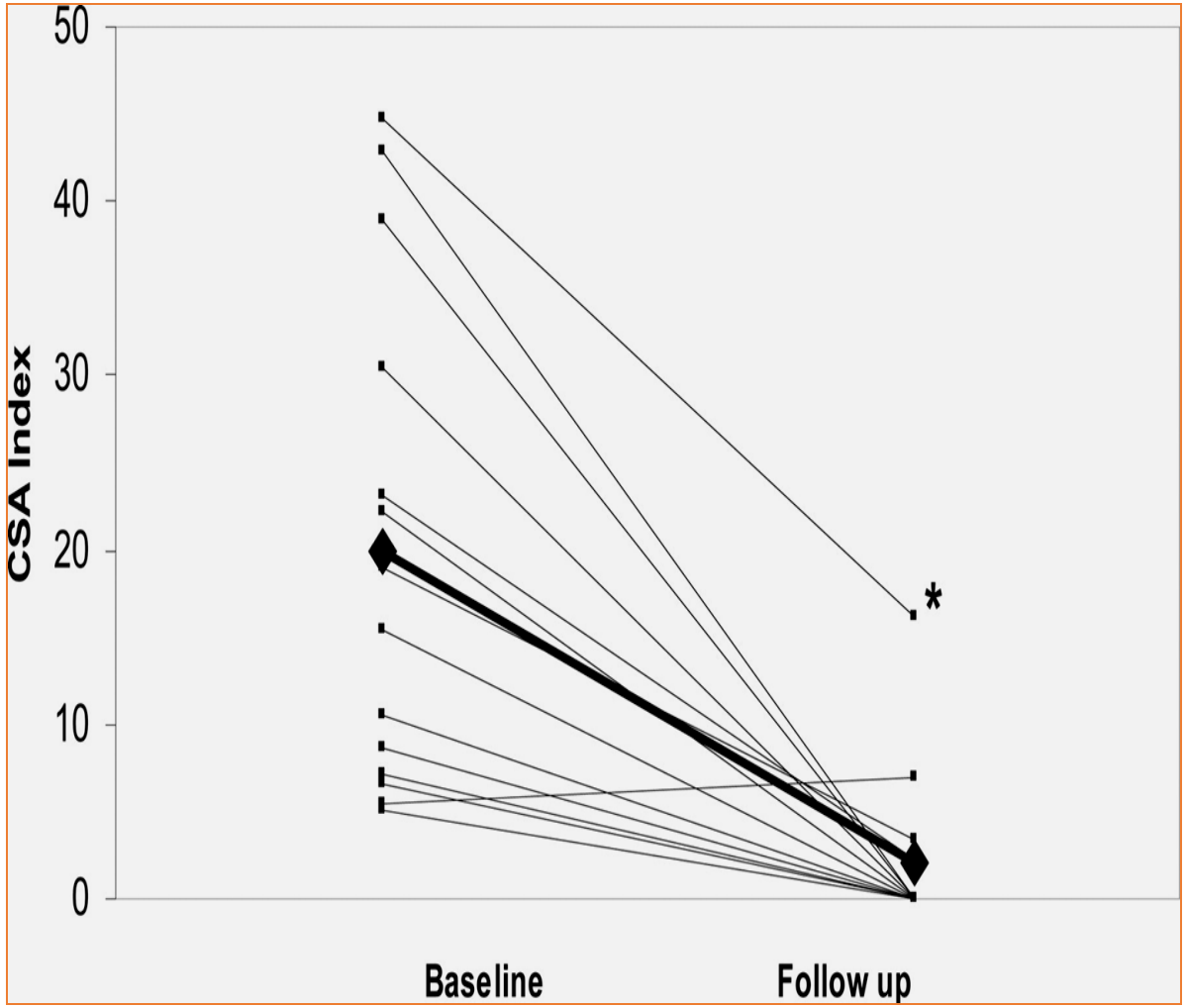
Question #5

Which of the following statements regarding treatment-emergent central sleep apnea (TECSA) is correct

A. TECSA develops in the majority of patients undergoing split-night titration
B. Indicates the need for BPAP therapy.
C. Only patients with central apnea in the baseline study develop TECSA
D. The majority will experience complete resolution over a few weeks to months.

Change in CSAI in ith CPAP-related CSA

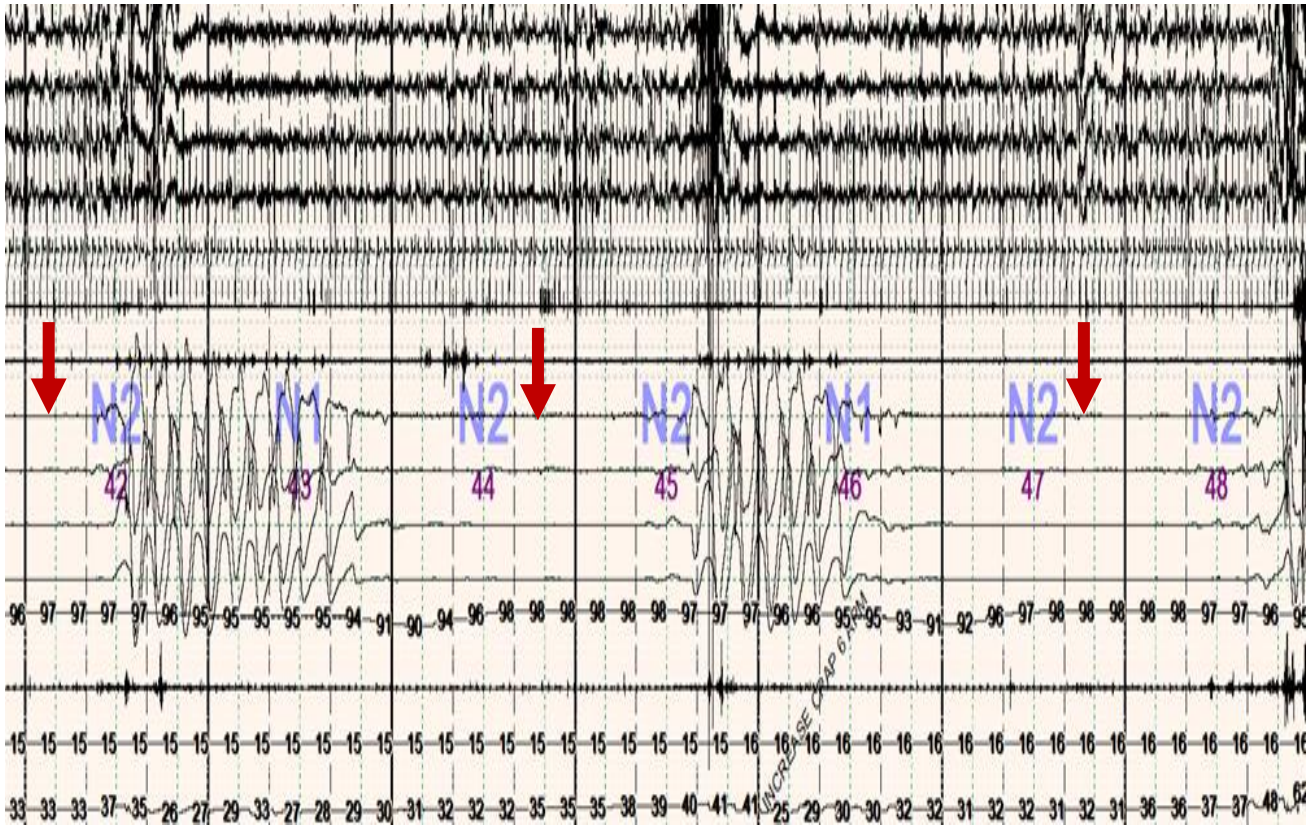
- CSA
- CPAP-Emergent
- N=14



Dernaika, T. et al. Chest 2007;132:81-87

- 86 year old male
- Evaluation of snoring, fragmented sleep and dyspnea on exertion.
- Previous smoking history
- PFTs: Poor effort and mild airflow obstruction
- Echocardiography: EF= 40%

- AHI=60/hour of sleep
- CAI= 20/hour of sleep
- ABGs: P_aO_2= 82 torr, P_aCO_2= 34 torr
- What is your treatment recommendations



Which of the following is considered as STANDARD treatment for central sleep apnea related to heart failure

A. BPAP
B. CPAP
C. ASV
D. Oral acetazolamide

Which of the following is considered as STANDARD treatment for central sleep apnea related to heart failure

A. BPAP
B. CPAP
C. ASV
D. Oral acetazolamide

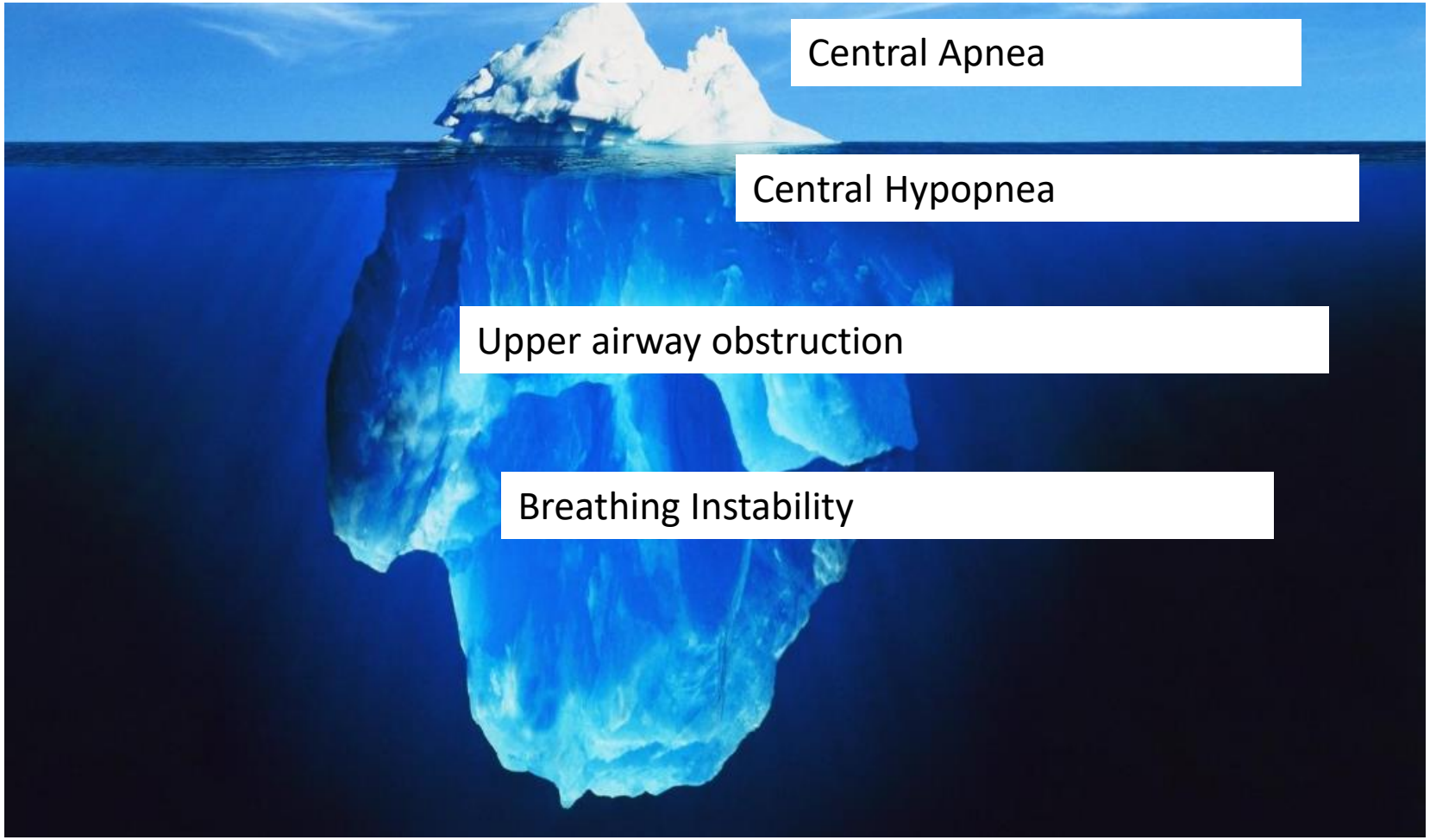
Treatment of Central Apnea

- There is no specific treatment for central apnea
- Most modalities dampen post apneic overshoot.
- Positive Pressure
  - CPAP, BPAP, ASV
- Altering chemical stimuli
  - Supplemental O2 or CO2
- Sleep State: hypnotics
- Ventilatory Drive: Acetzolamide
- Phrenic nerve Stimulation

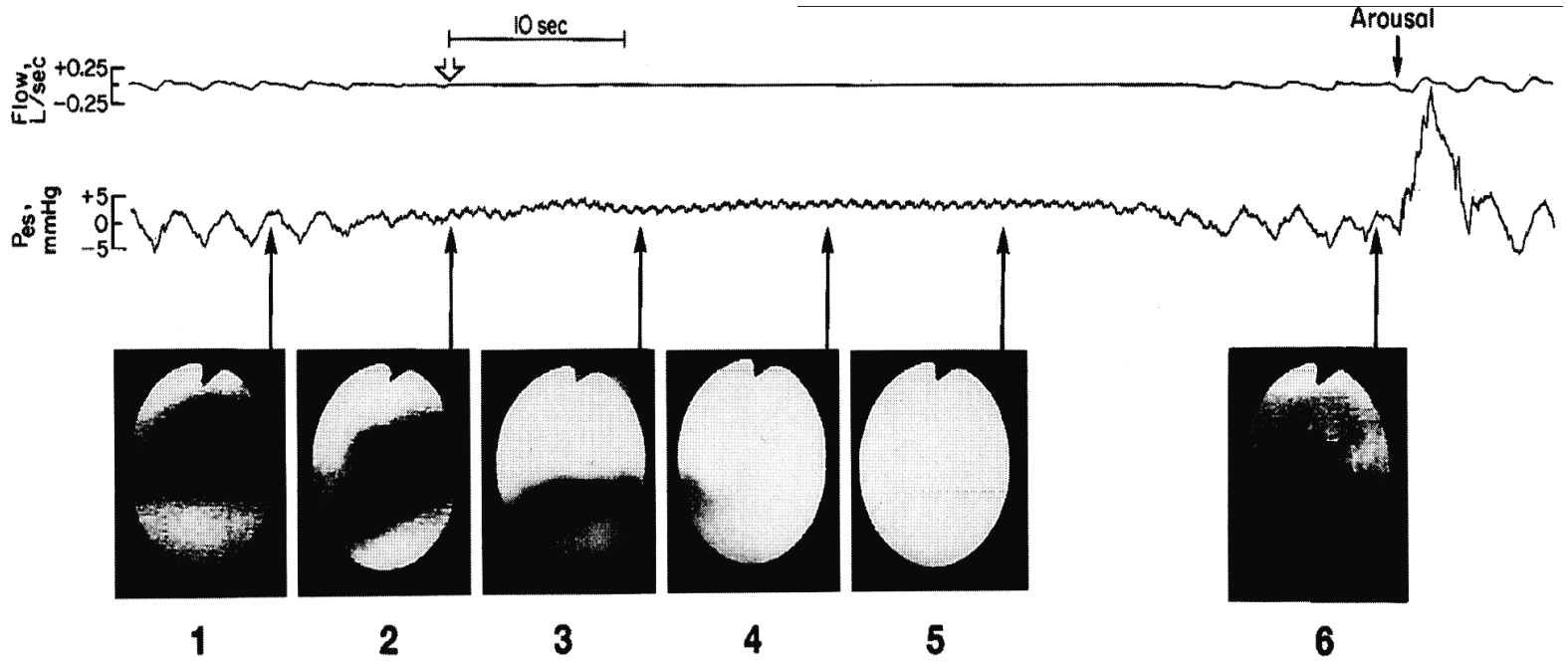
Does nasal CPAP ameliorate central apnea?

- Association with OSA
- Decreasing overshoot: Plant Gain
  - Opening the upper airway
  - Increasing O_2 stores
- CPAP has been used for CSR in CHF
- Improvement in intermediate outcome
-

Treatment of Central Apnea

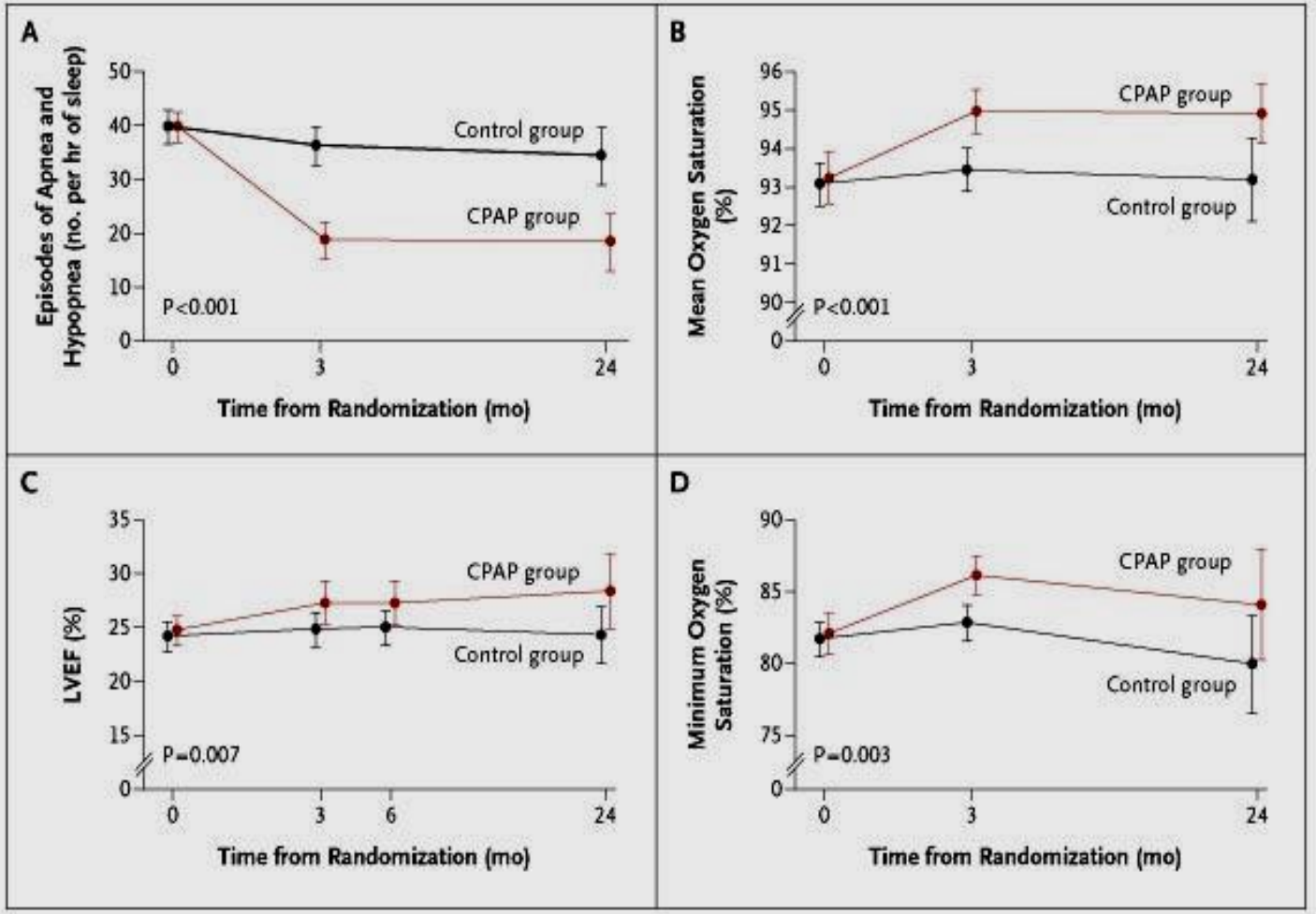


Oropharyngeal airway occlusion during spontaneous CSA

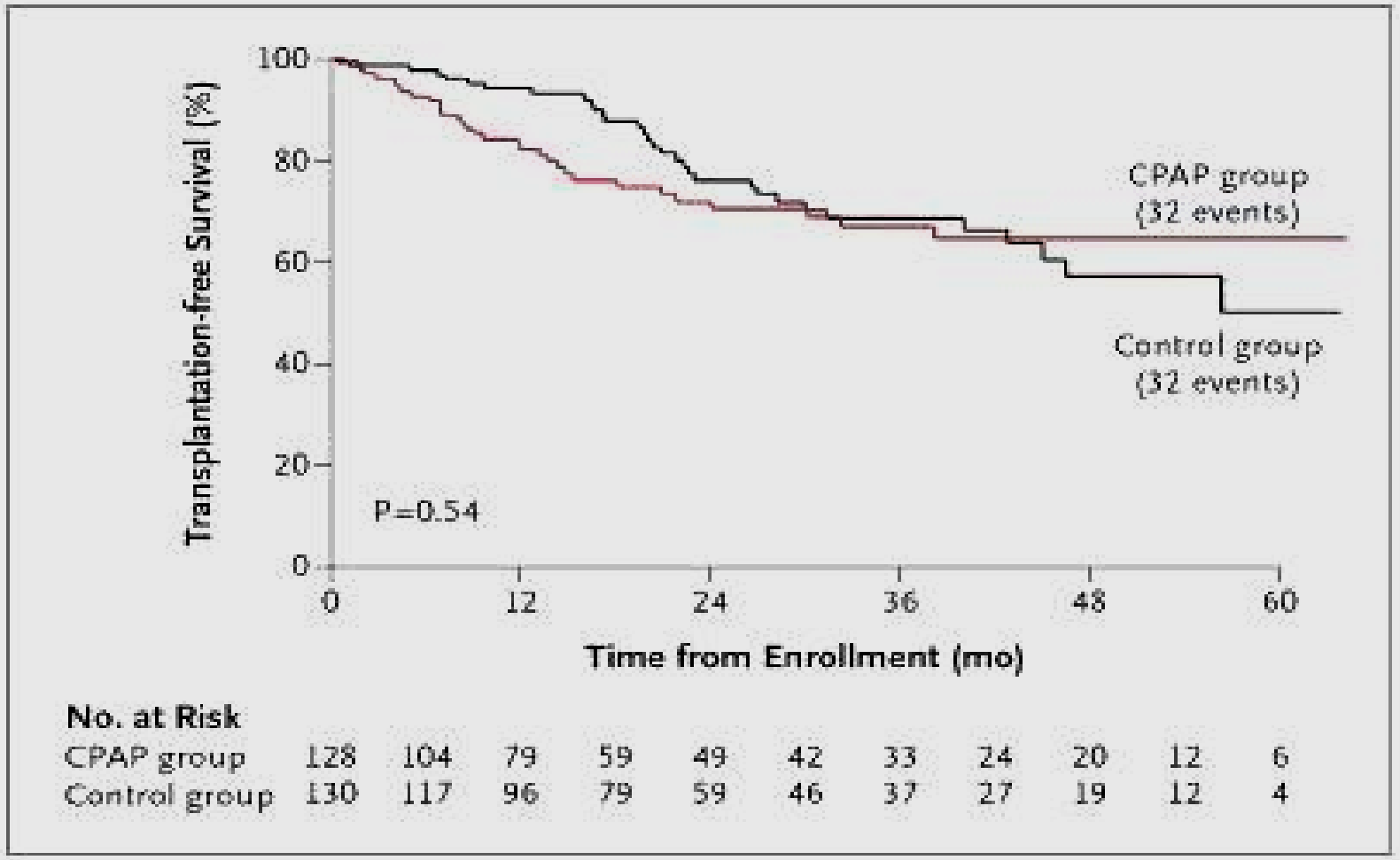


The Canadian Continuous Positive Airway Pressure trial (Can PAP)

N= 258
NCPAP: 128 No-CPAP: 130
2-year Follow up



Heart-Transplantation-free Survival

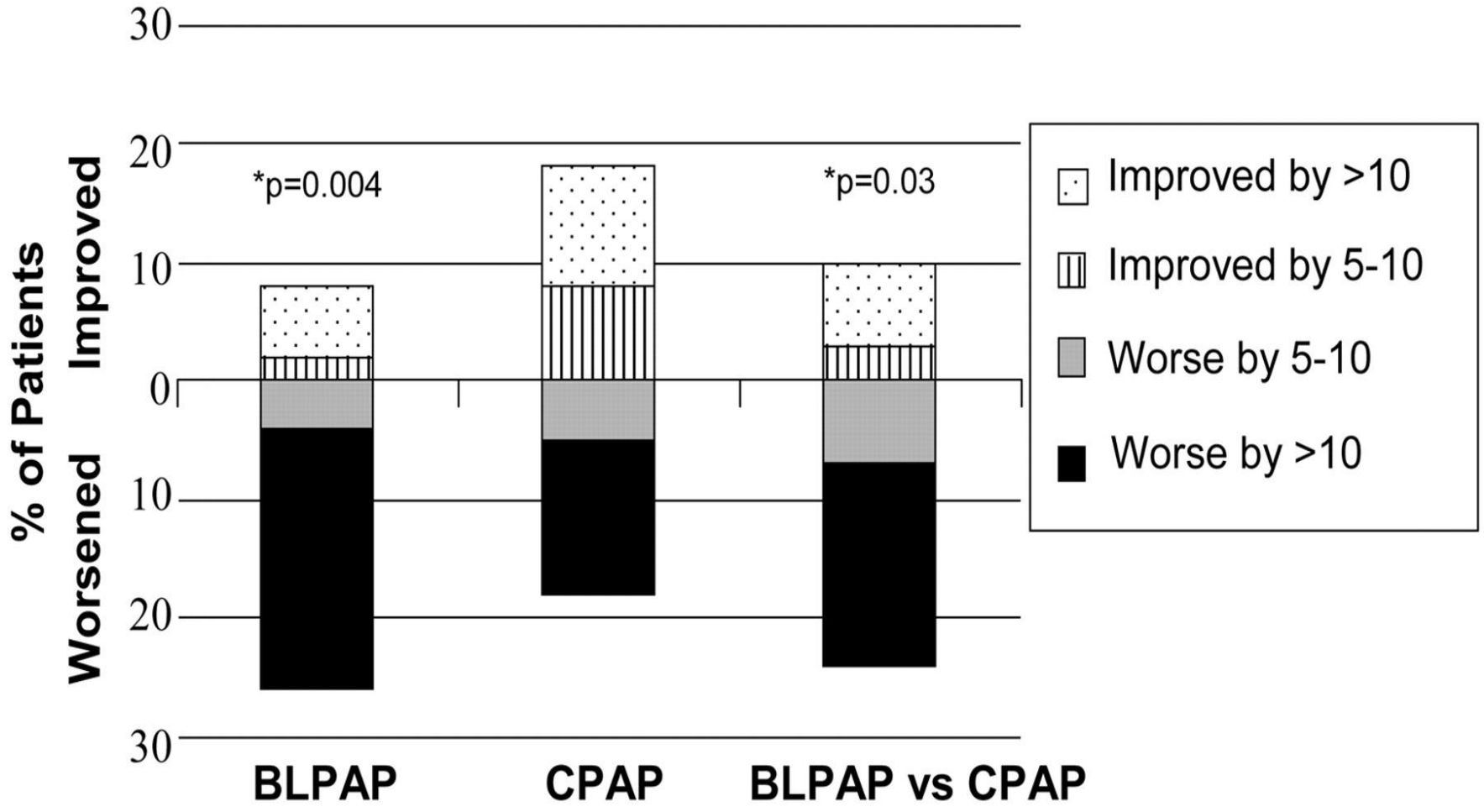


Bradley T et al. N Engl J Med 2005;353:2025-2033

The Canadian Continuous Positive Airway Pressure trial (CanPAP)

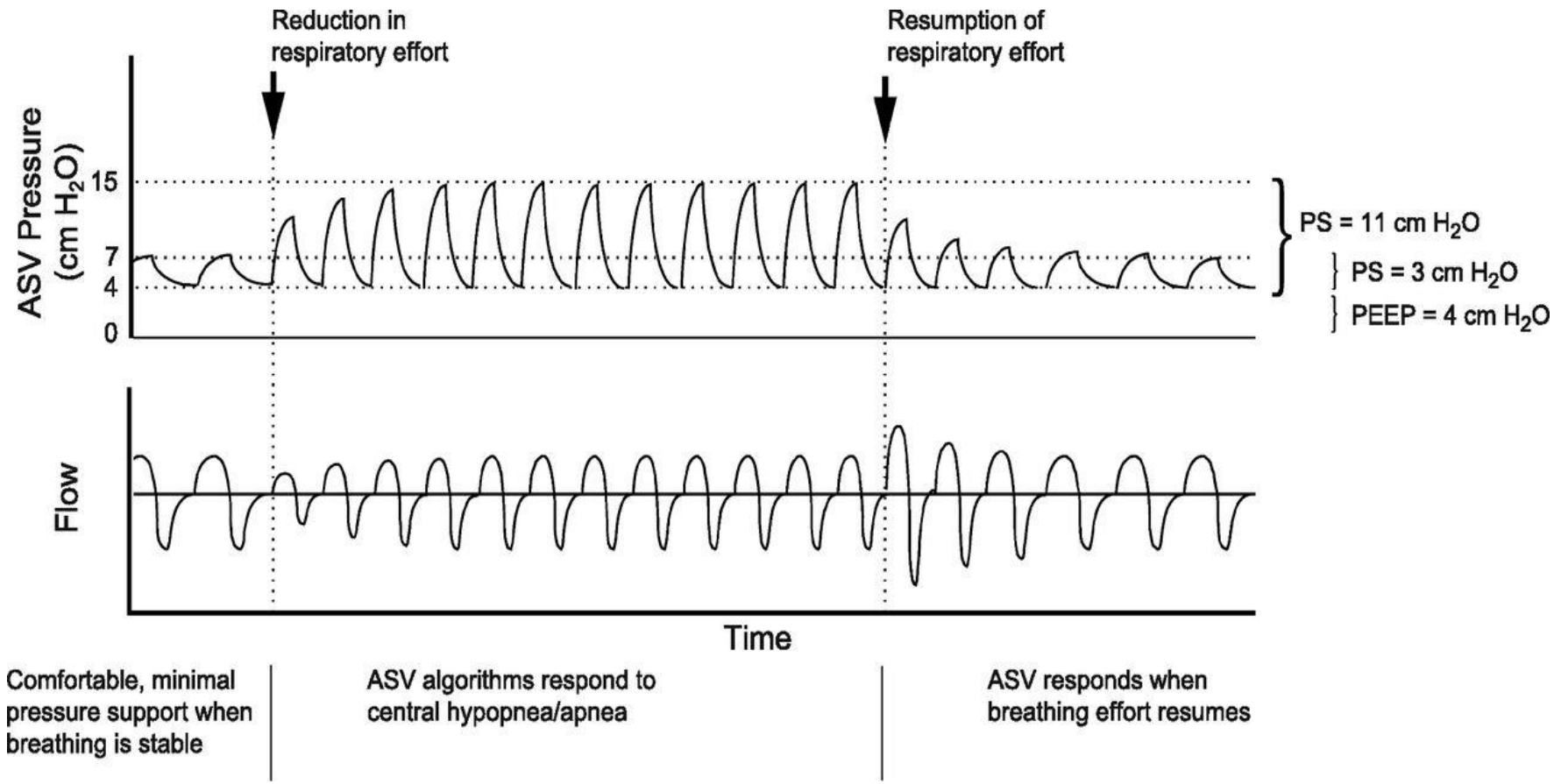
- CPAP vs. placebo at 3 months
  - AHI
  - EF
  - Mean nocturnal oxyhemoglobin saturation
  - Plasma nor-epinephrine levels
  - Six-minute walk,
- N-CPAP had no effect on survival

Effect of Bi-level PAP on central apnea index



Johnson, K. G. et al. Chest 2005;128:2141-2150

CHEST
The Cardiopulmonary and Critical Care Journal

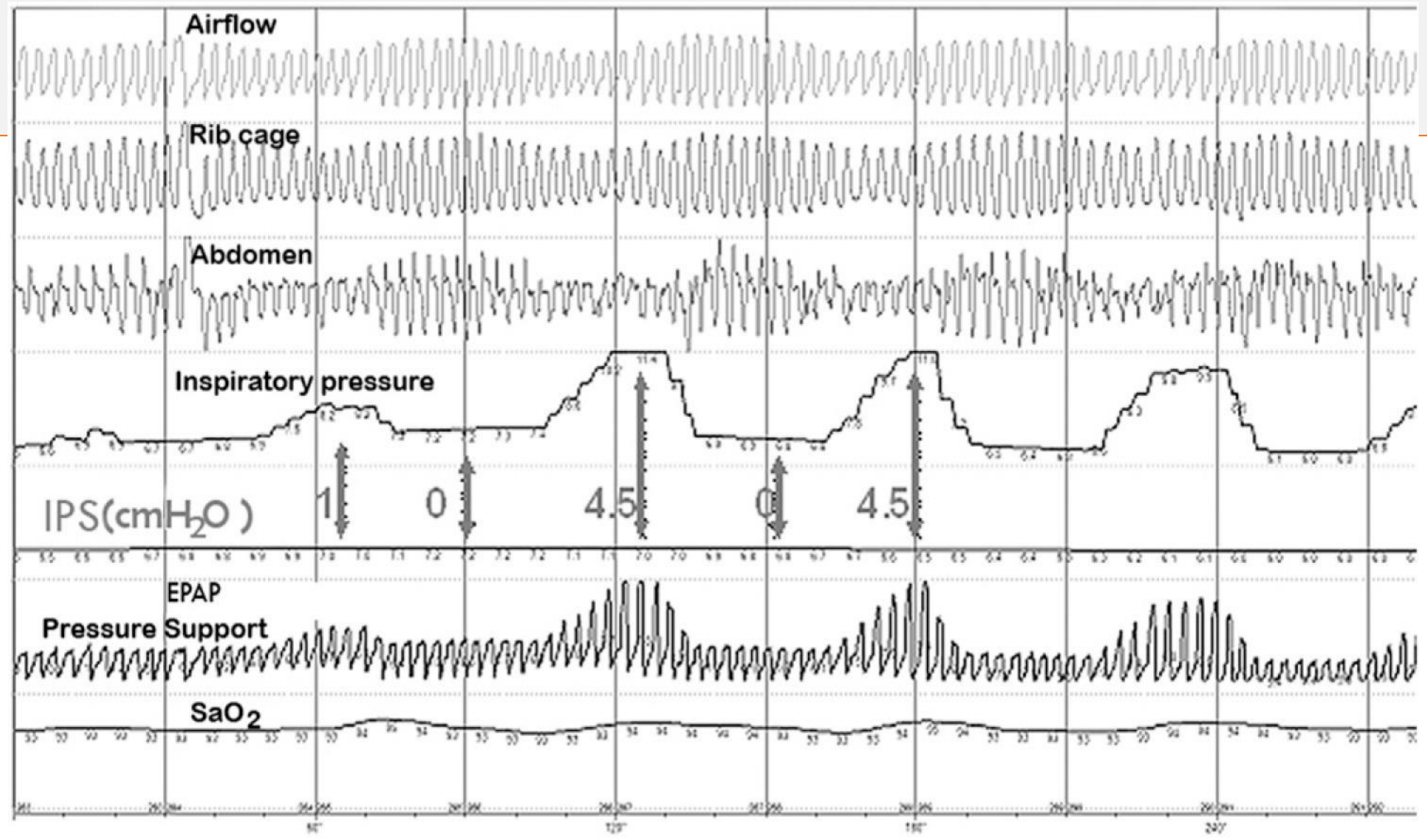

Reduction in respiratory effort
Resumption of respiratory effort
ASV Pressure (cm H_2O)
15
7
4
0
PS = 11 cm H_2O
PS = 3 cm H_2O
PEEP = 4 cm H_2O
Flow
Time
Comfortable, minimal pressure support when breathing is stable
ASV algorithms respond to central hypopnea/apnea
ASV responds when breathing effort resumes

Adaptive Pressure Support Servo-Ventilation

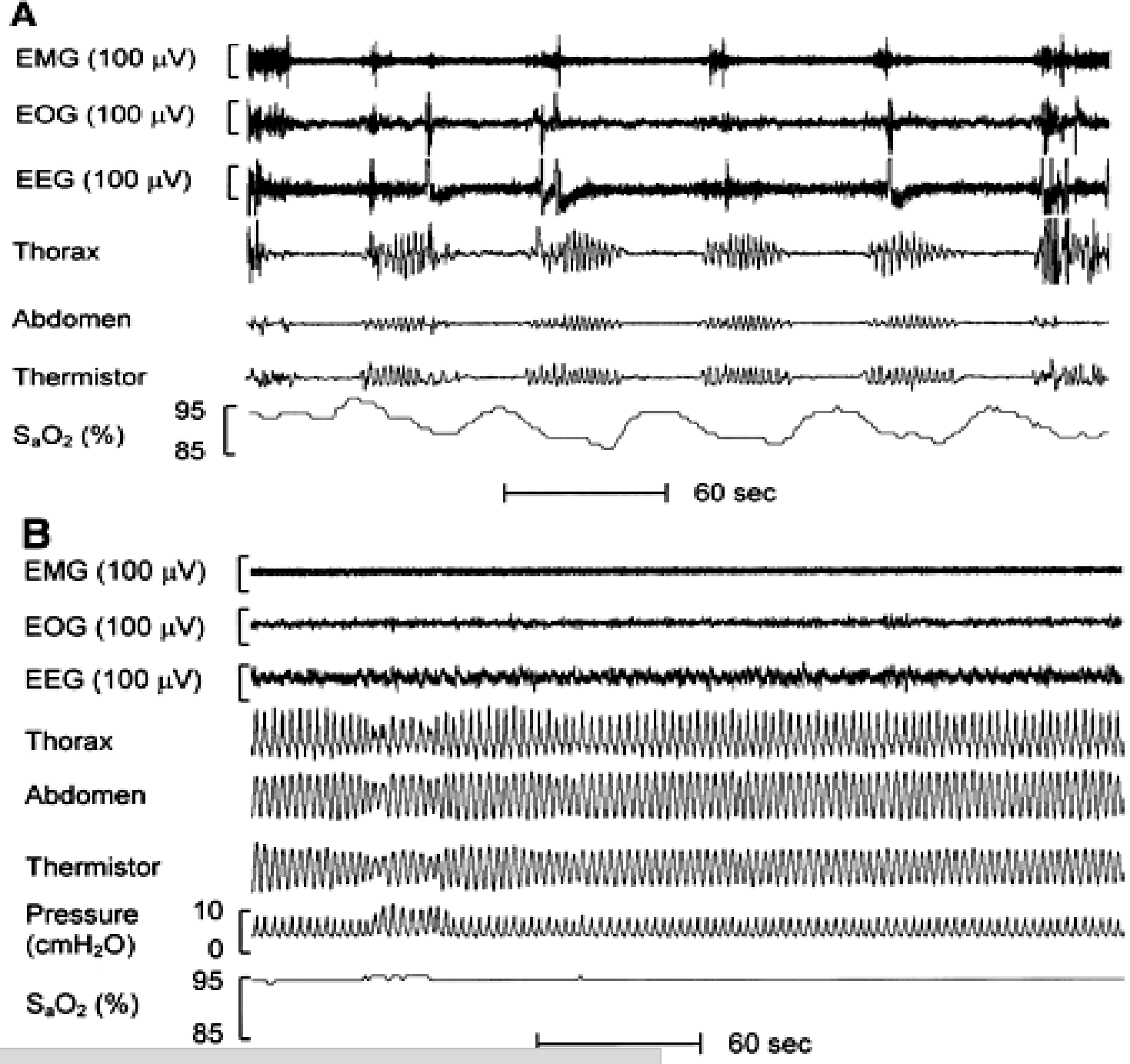
- Small and variable ventilatory support
- The hydrostatic benefits of low levels of nasal CPAP (5 cm H20)
- Baseline pressure swing is 4 cm H2O
- Increases to provide 90% of the long-term average VE.
- No hyperventilation

Teschler et al. AJRCCM, 164, 4, 614-619,2001

Adaptive Pressure Support Servo-Ventilation



Javaheri et al. 146#2 CHEST AUGUST 2014



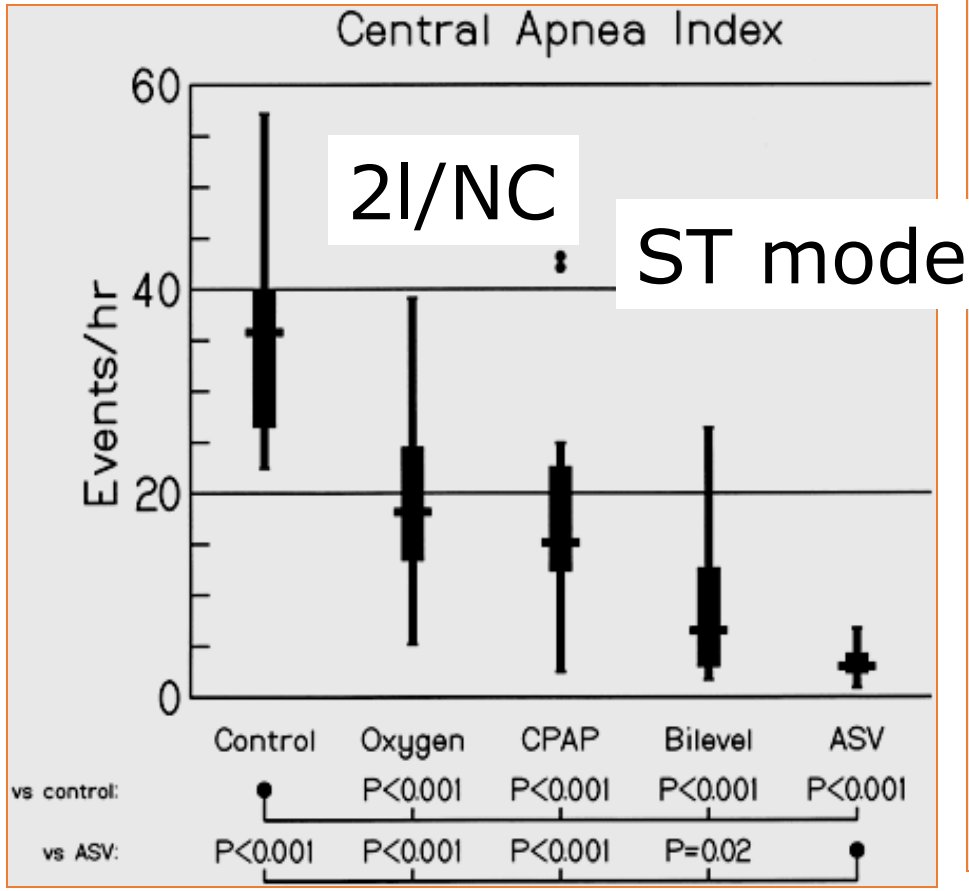
Teschler et al. AJRCCM, 164, 4, 614-619,2001

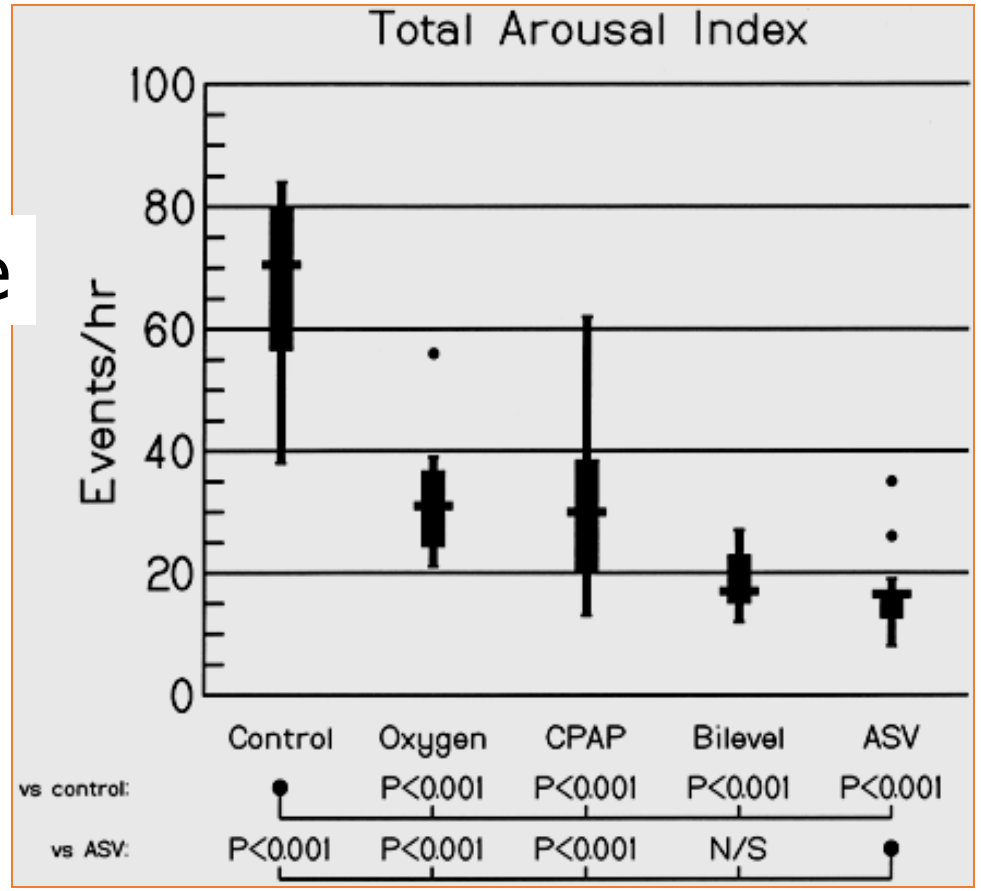
Adaptive Pressure Support Servo-Ventilation

- Prospective, randomized, cross-over design
- N=16; gender?
- Desaturation index (3%) > 15/h
- Five consecutive nights
  - CPAP
  - Supplemental O2 @ 2L/NC
  - Bi-level –ST mode
  - ASV

Teschler et al. *AJRCCM*, 164, 4, 614-619,2001

Adaptive Pressure Support Servo-Ventilation





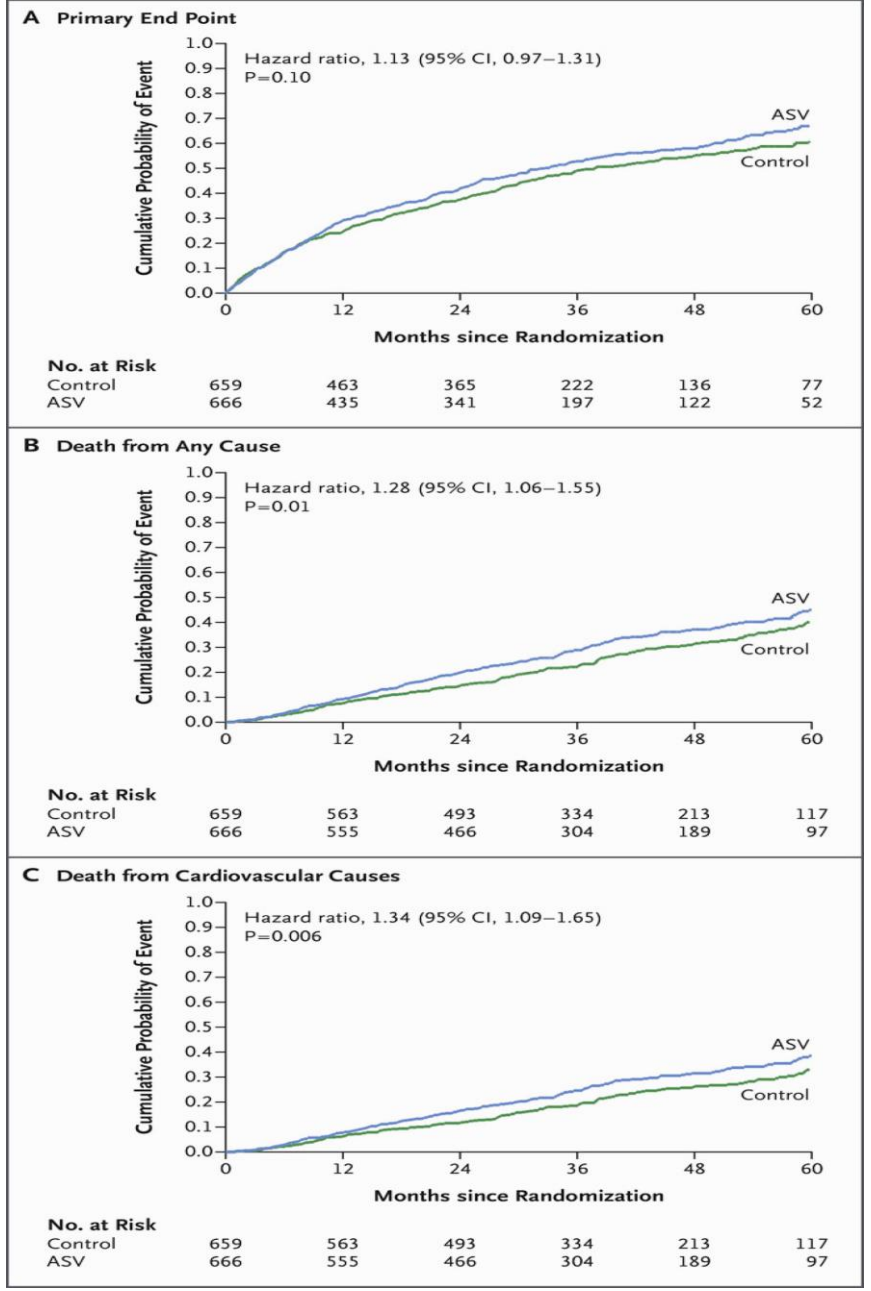
Teschler et al. AJRCCM, 164, 4, 614-619,2001

Which of the following treatments is associated with increased mortality risk in patients with predominantly central apnea

A. CPAP in patients with Heart failure and preserved EF
B. BPAP in patients with opioid-associated central sleep apnea
C. Adaptive-Servo ventilation in patients with heart failure and reduced ejection fraction
D. CPAP in patients with heart failure and reduced ejection fraction

Cumulative Incidence Curves for the Primary End Point, Death from Any Cause, and Cardiovascular Death.

- N=1325 patients
- HF-rEF
- AHI≥15/hour of sleep
- Predominance of central apnea



Which of the following treatments is associated with increased mortality risk in patients with predominantly central apnea

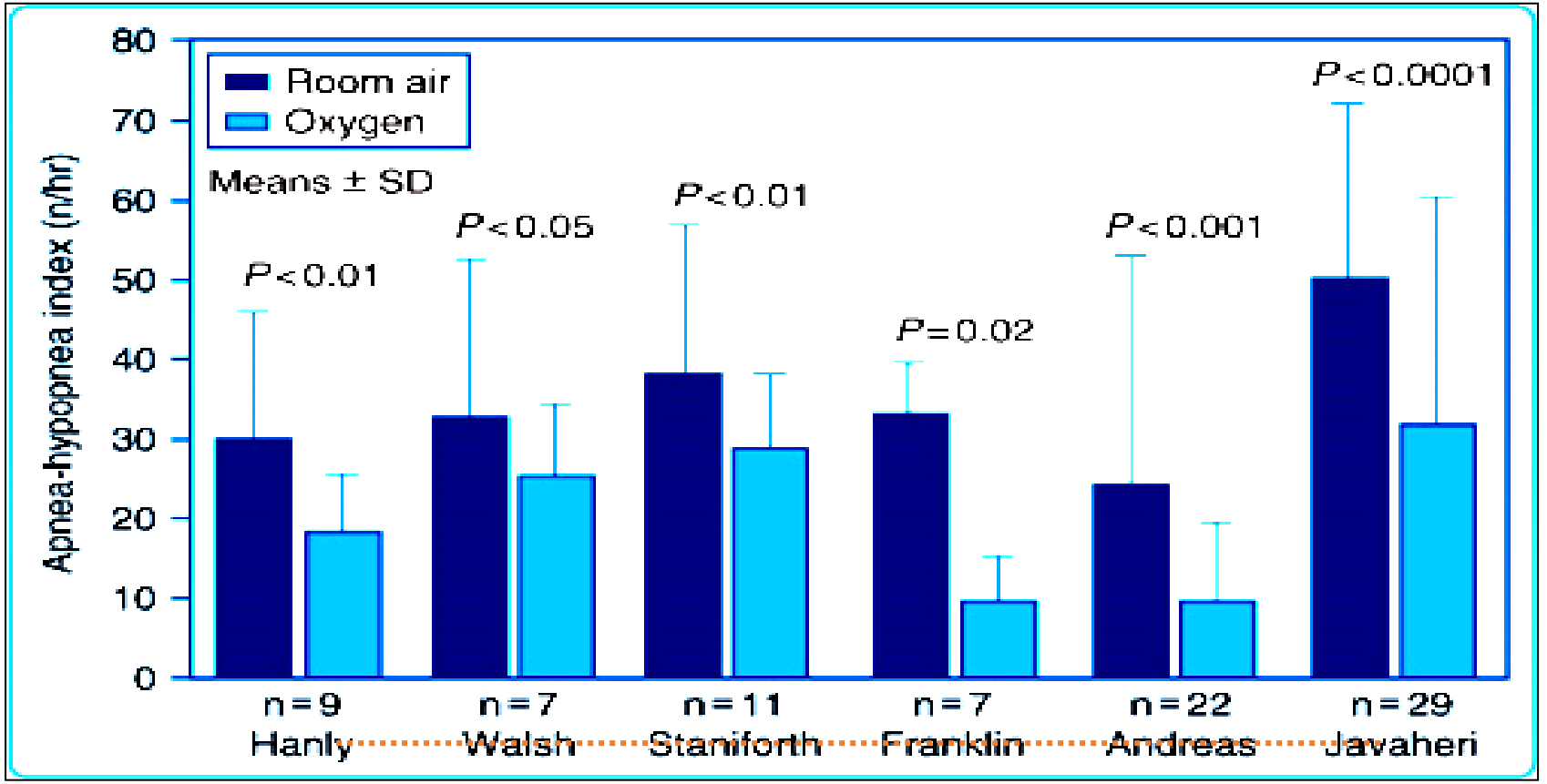
A. CPAP in patients with Heart failure and preserved EF
B. BPAP in patients with opioid-associated central sleep apnea
C. Adaptive-Servo ventilation in patients with heart failure and reduced ejection fraction
D. CPAP in patients with heart failure and reduced ejection fraction

Improvement of Idiopathic Central Sleep Apnea with Zolpidem

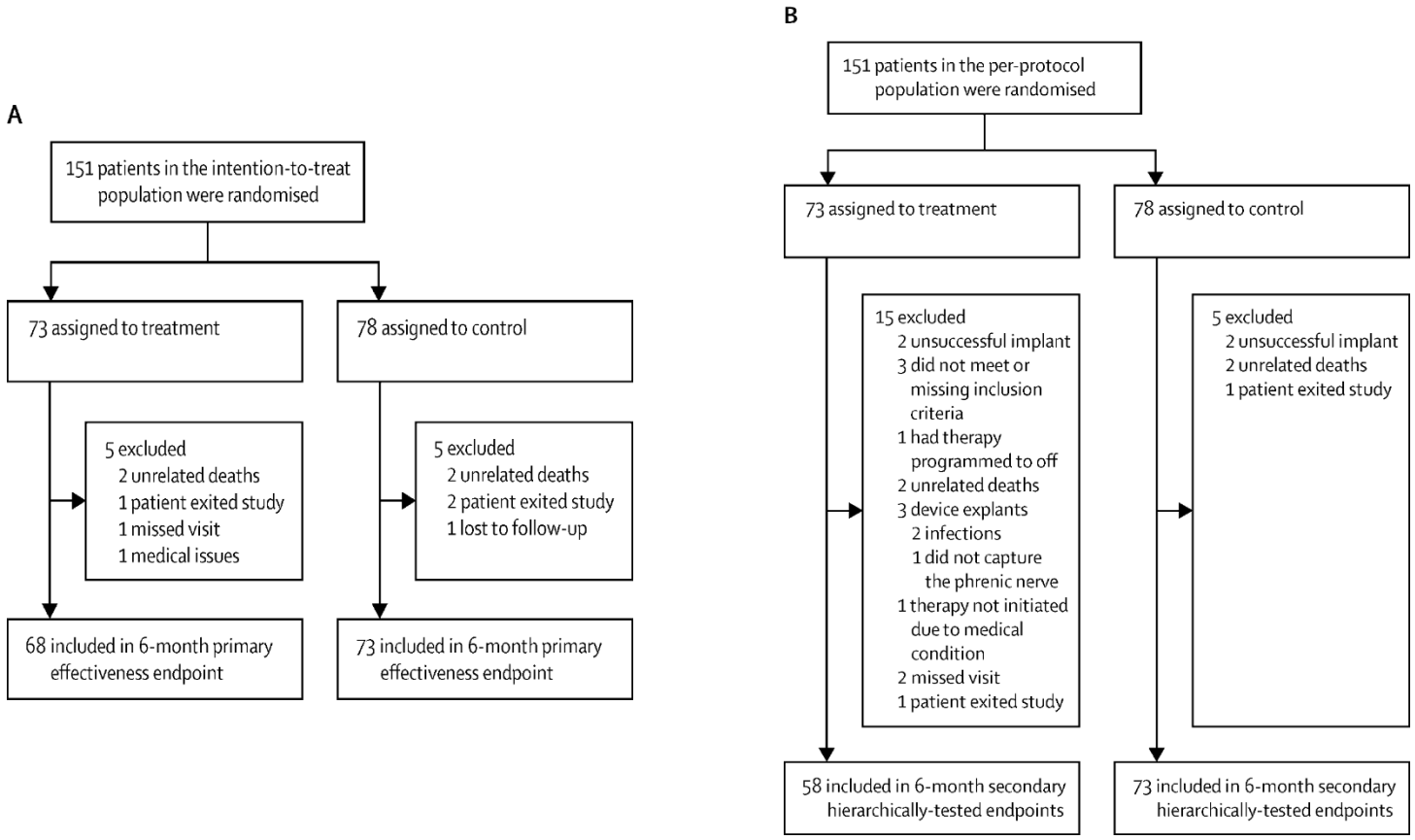
- N=20, 9 weeks
- AHI 30.0 ± 18.1 to 13.5 ± 13.3 ($p = 0.001$),
- CAHI 26.0 ± 17.2 to 7.1 ± 11.8 ($p < 0.001$)
- Arousals 24.0 ± 11.6 to 15.1 ± 7.7 ($p < 0.001$)
- ESS 13 ± 5 to 8 ± 5 ($p < 0.001$).
- OSA increased in 3 patients
- In the absence of a randomized, controlled trial, zolpidem cannot be recommended for treatment of ICSA at this time.

Quadri et al. *J Clin Sleep Med.* 2009 April 15; 5(2): 122–129.

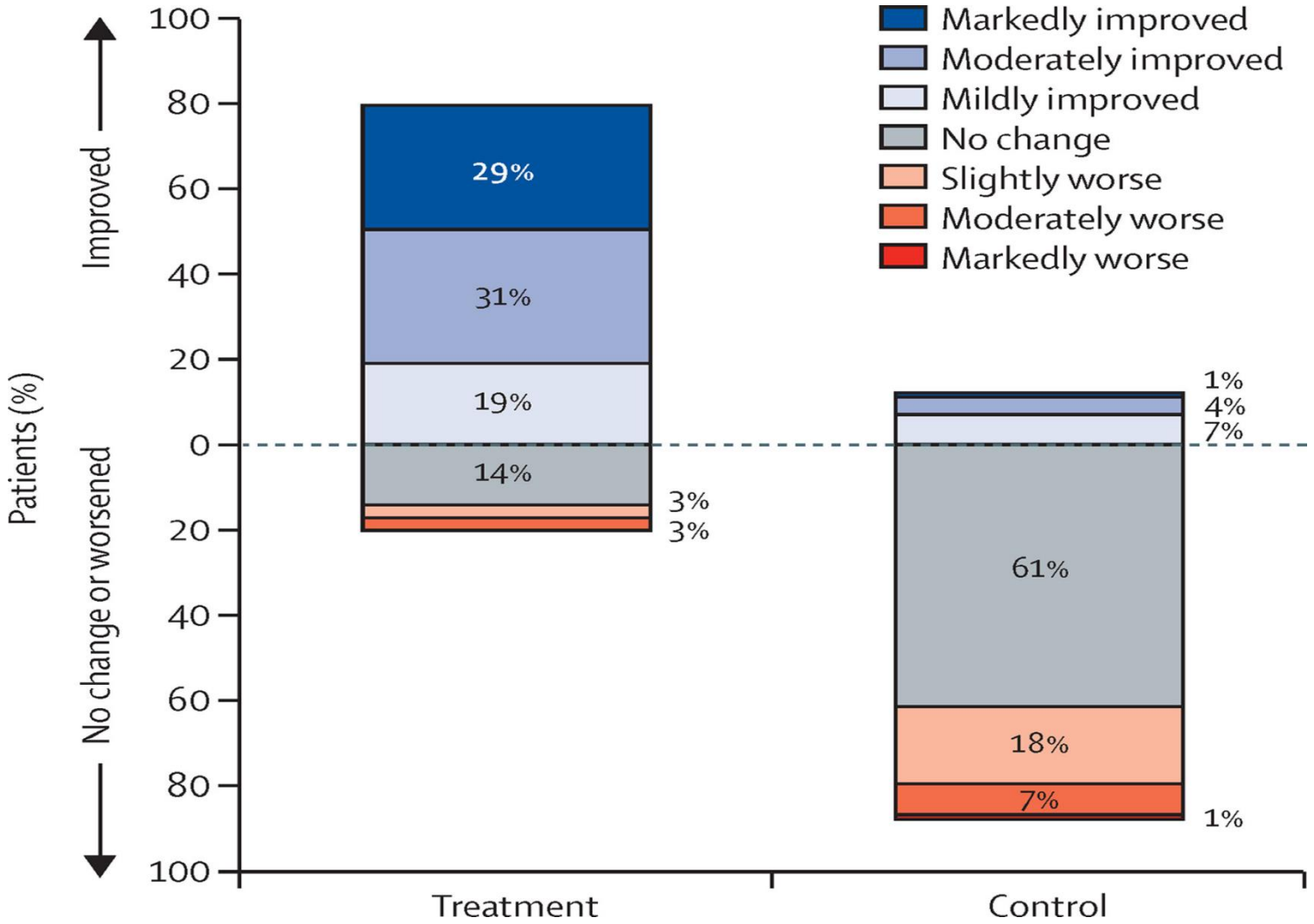
Effect of Supplemental Oxygen on AHI in Patients with CHF



Transvenous neurostimulation for central apnea



Costanzo MR et al. Transvenous neurostimulation for central sleep apnoea: a randomised controlled trial.2016 Sep 3;388(10048):974-82



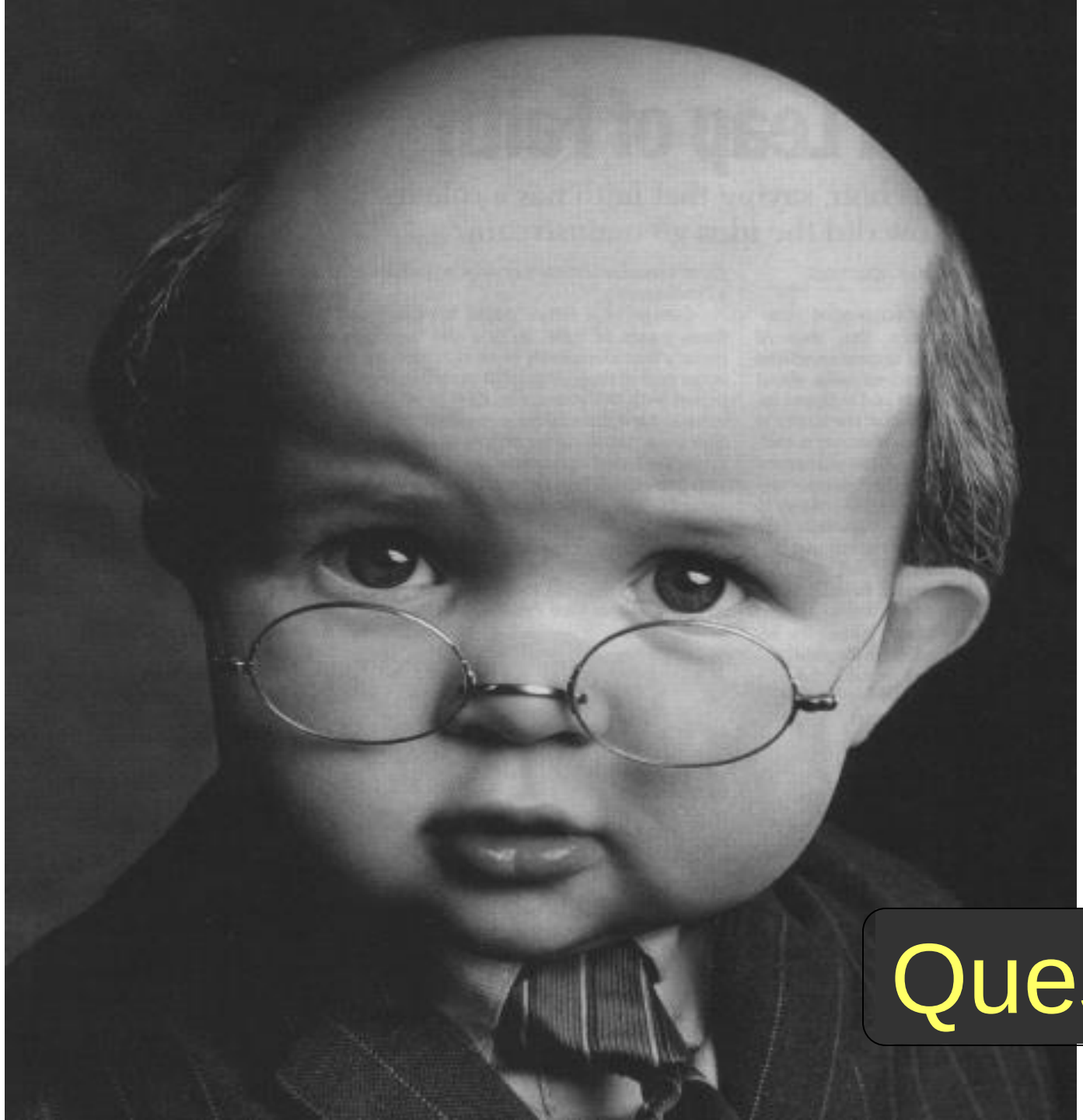
Costanzo MR et al. Transvenous neurostimulation for central sleep apnoea: a randomised controlled trial.2016 Sep 3;388(10048):974-82

Our Approach
When Data are few; experts are many !

- Similar principles in CSA and PAP-emergent CSA
- Treat the underlying condition
- Initiate CPAP is the initial treatment
- No ASV or BPAP for CSA with HFrEF (EF<45%)
- CPAP failure/intolerance in HFrEF patients with CSA
  - Nocturnal oxygen
  - Medical management of heart failure.

Our Approach
When Data are few; experts are many !

- Patients with HFpEF or primary CSA
  - A trial of CPAP
  - A trial of ASV
  - A trial of BPAP with a back-up respiratory rate
  - Intolerant of PAP: A trial of acetazolamide



Questions?