BRIGHAM AND WOMEN'S HOSPITAL

The Lung Center

# Sleep Disordered Breathing, Chronic Hypercapnic Respiratory Failure and Non-invasive Ventilation

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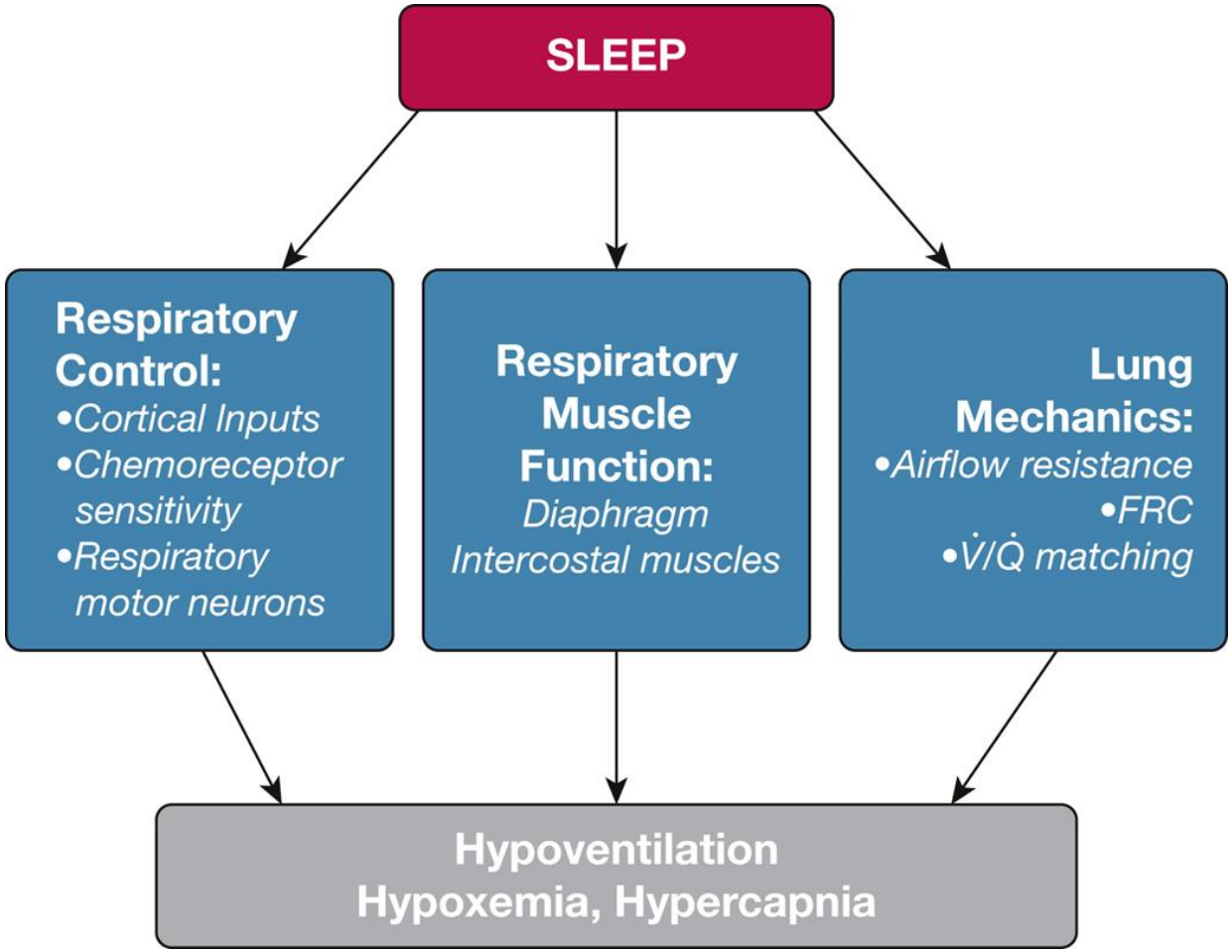
# Disclosures

- I have no relevant financial or nonfinancial conflicts to disclose.

# Outline

- Respiratory physiology during sleep and chronic hypercapnic respiratory failure
- Positive airway pressure therapy and non-invasive ventilation (NIV).
- Sleep Disordered Breathing (SDB) and chronic hypercapnic respiratory failure; use of NIV in special patient populations:
  - Obesity Hypoventilation Syndrome (OHS).
  - Neuromuscular disease (NMD).
  - Stable hypercapnic COPD.




Walter T. McNicholas, MD, FCCP. CHEST 2017; 152(6):1318-1326

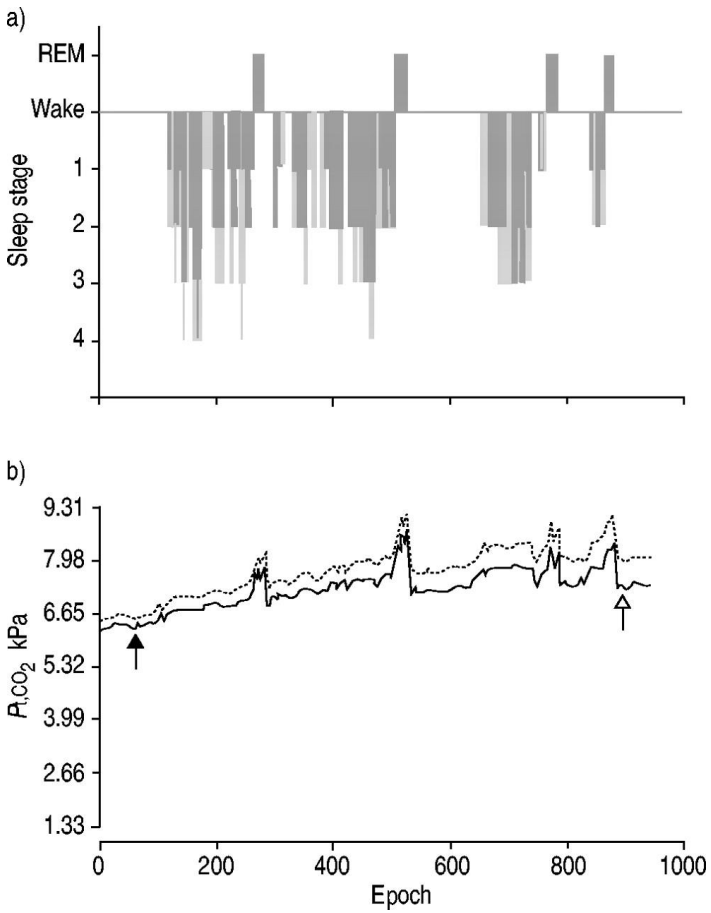
# Respiratory changes during Sleep

- ↓ in minute ventilation 0.5-1.5 L
- ↓ in metabolic rate ($CO_2$) production 10-15%
- ↓ in hypoxic and hypercapnic ventilatory response 20-30%
- ↓ PaO2 3-10 mmHg
- ↓ SaO2 2%

- ↑ in upper airway resistance
- ↑ PaCO2 2-8 mmHg

Mohsenin, Semin Resp Crit Care Med 2005

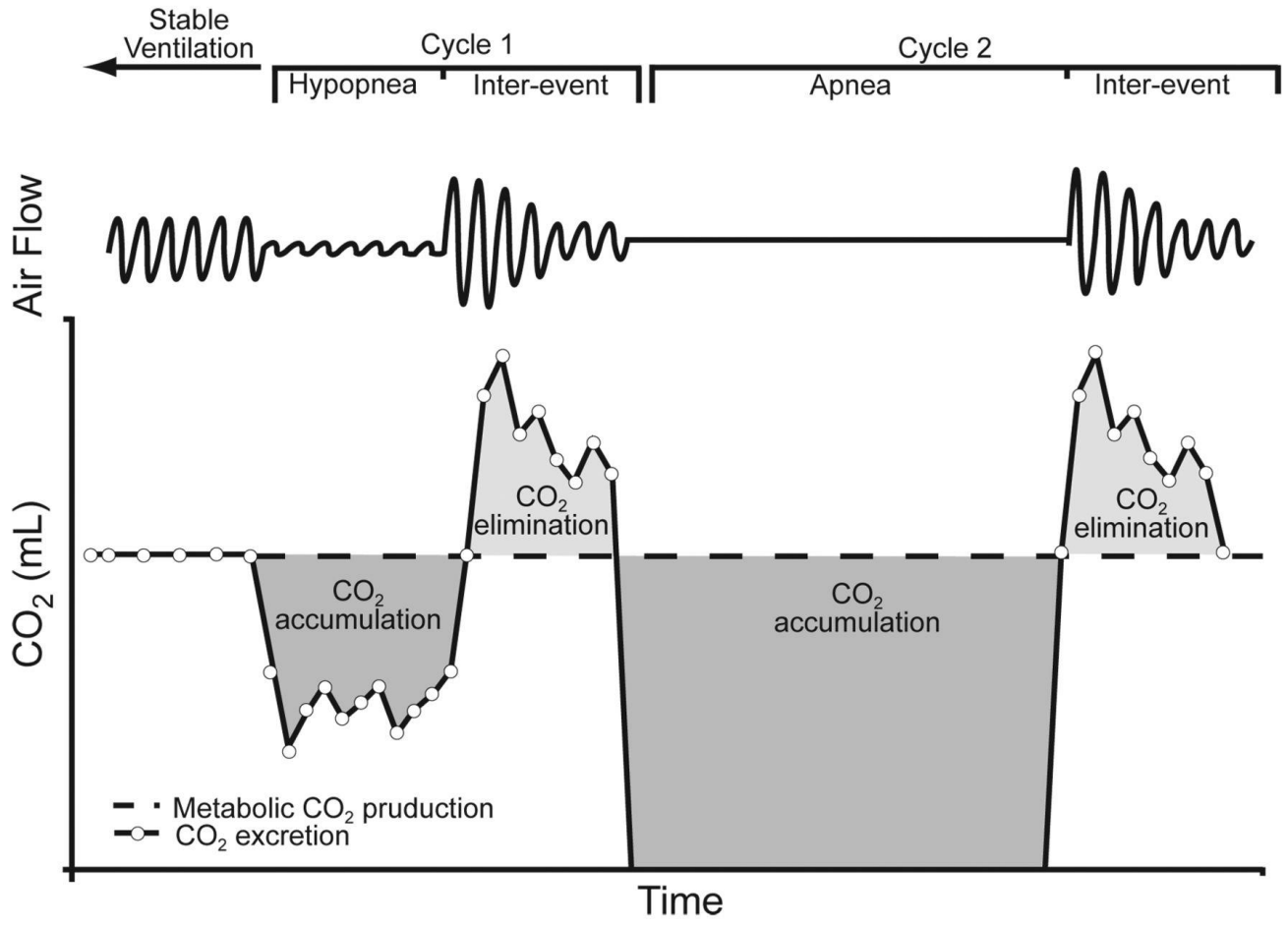
# Consequences of REM-atonia




**a) Sample hypnogram and b) transcutaneous carbon dioxide tension (Pt,CO2) record illustrating Pt,CO2 corrections.**

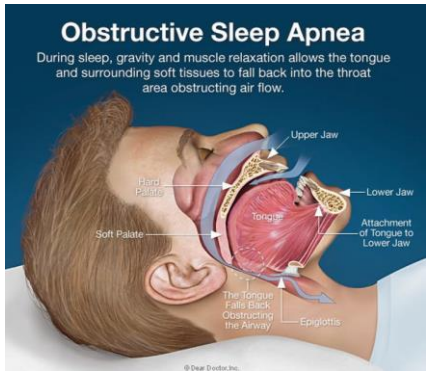
F.J. O'Donoghue et al. Eur Respir J 2003;21:977-984

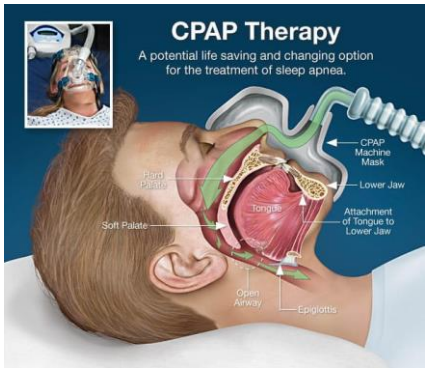
# Obstructive Sleep Apnea and Hypoventilation

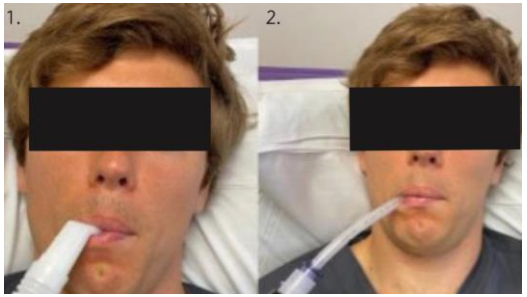



Berger et al. J Appl Physiol 2000;88(1):257-264

# Non-invasive Positive Pressure Ventilation



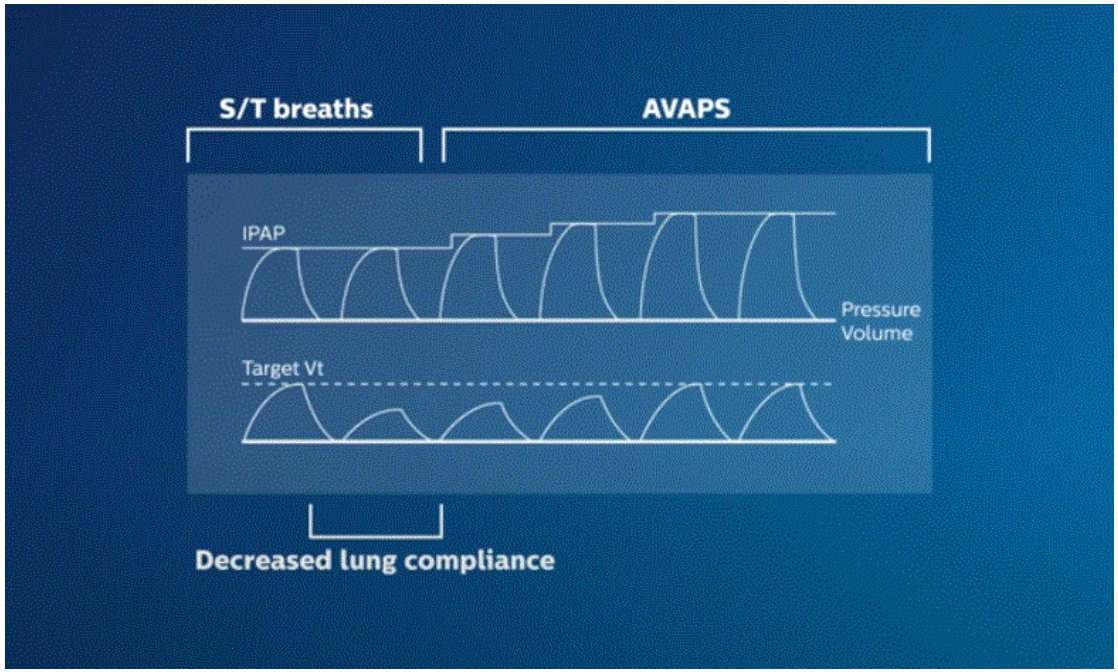




# Respiratory Assist Devices (RADs) (E0470/E0471)

| PAP Mode | Settings/Target |
|---|---|
| BPAP<br>BPAP-ST, with back up rate (BR) | IPAP, EPAP<br>Pressure support = IPAP-EPAP<br>BR = Spontaneous timed (ST) or timed (T) |
| Adaptive Servo Ventilation (ASV) | Pressure support varies to stabilize breathing (PS min, PS max)<br>EPAP varies to eliminate airway obstruction (EPAP min, EPAP max) |
| Volume-assured Pressure Support<br>AVAPS or iVAPS | Pressure support varies to meet a target tidal volume or alveolar ventilation<br>EPAP set to eliminate airway obstruction<br>Set a back up rate 2 breaths < spontaneous RR |

# Benefits of VAPS




- REM/NREM changes in ventilation
- Positional changes in ventilation
- Fluid shifts/changes in lung compliance seen in OHS
- Progression of disease seen in ALS
- Intermittent exacerbations seen in COPD

# Non-Invasive Ventilation

| Respiratory Assist Devices (RAD) (E0470/E0471) | Home mechanical ventilation (HMV) (E0465/E0466) |
|---|---|
| Bi-level devices with or without back up respiratory rate capability | Life supporting/sustaining devices |
| BIPAP-S (E0470)<br>BIPAP-ST/ASV/VAPS (E0471) | Invasive: trach (E0465), Non-invasive: (E0466)<br>Trilogy, Astral |
| Limited settings | At least 6 pressure modes and 3 volume modes |
| External batteries optional | Internal (6-18 hours) and external batteries |
| Only oronasal masks | Can switch between a mouthpiece and oronasal mask |
| Limited alarms | More sophisticated monitoring and alarm system |

# Obesity Hypoventilation Syndrome (OHS)

# Definition

- Obesity (BMI >30 kg/$m^2$)
- Awake arterial PaCO2 > 45 mmHg
- No alternative neuromuscular, mechanical or metabolic explanation for hypoventilation

Mokhlesi et al Proc Am Thorac Soc 2008; 5: 218–225.

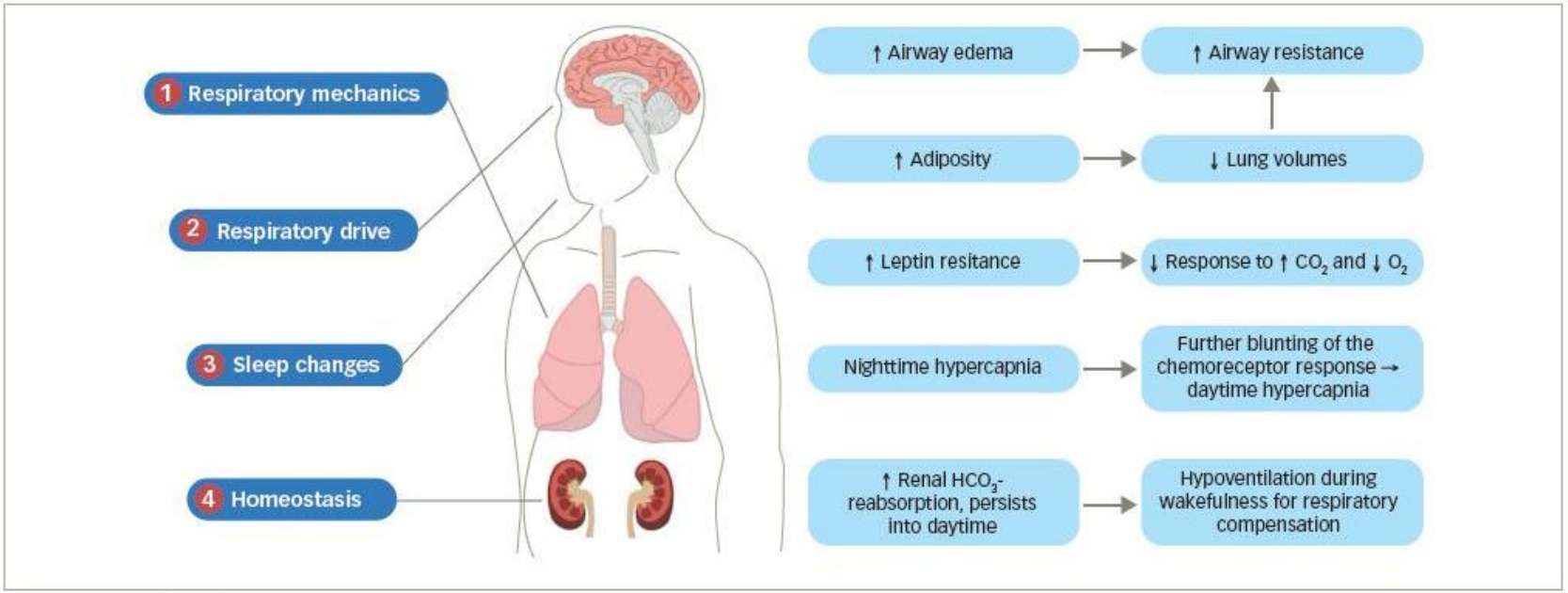
# OHS Phenotypes

- Obstructive:
  - 90% of patients with OHS have OSA (AHI ⩾5/hr).
  - 70% of patients have concomitant severe OSA (AHI ⩾30/hr)

- Non-obstructive:
  - 10% have non-obstructive sleep hypoventilation (etPCO2 or tcPCO2 >55 mmHg for >10 min or an increase >10 mmHg compared to awake PaCO2 to a value >50 mmHg for >10 min)

Masa et al. Am J Respir Crit Care Med 2015. Berry et al. J Clin Sleep Med 2012

# Pathophysiology




Greer et al. US Respiratory and Pulmonary Diseases. 2020

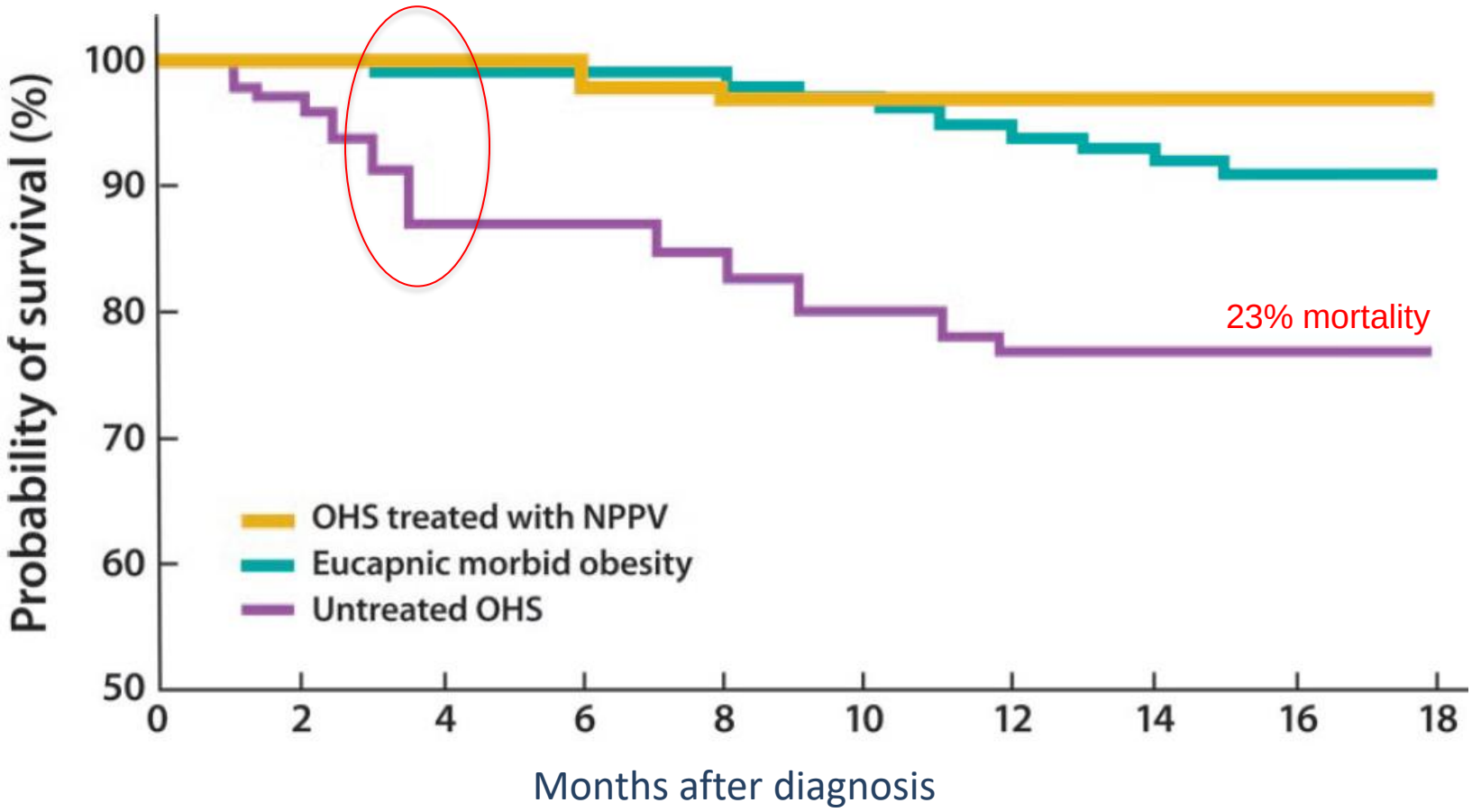
# Epidemiology

- Prevalence between 8% and 20% of obese patients referred to sleep centers for evaluation of sleep disordered breathing
- BMI > 50:  50% prevalence
- Inpatients with BMI > 35:  31 % have OHS
- OHS remains largely underdiagnosed. 75% were misdiagnosed and treated for obstructive lung disease (despite normal FEV1/FVC)

- No gender difference
- More often associated with DM, HF, PH than OSA

Nowbar S, et al., Am J Med 2004. Sugerman HJ, et al., Am J Clin Nutr 1992. Massa JF, et al., CHEST 2001

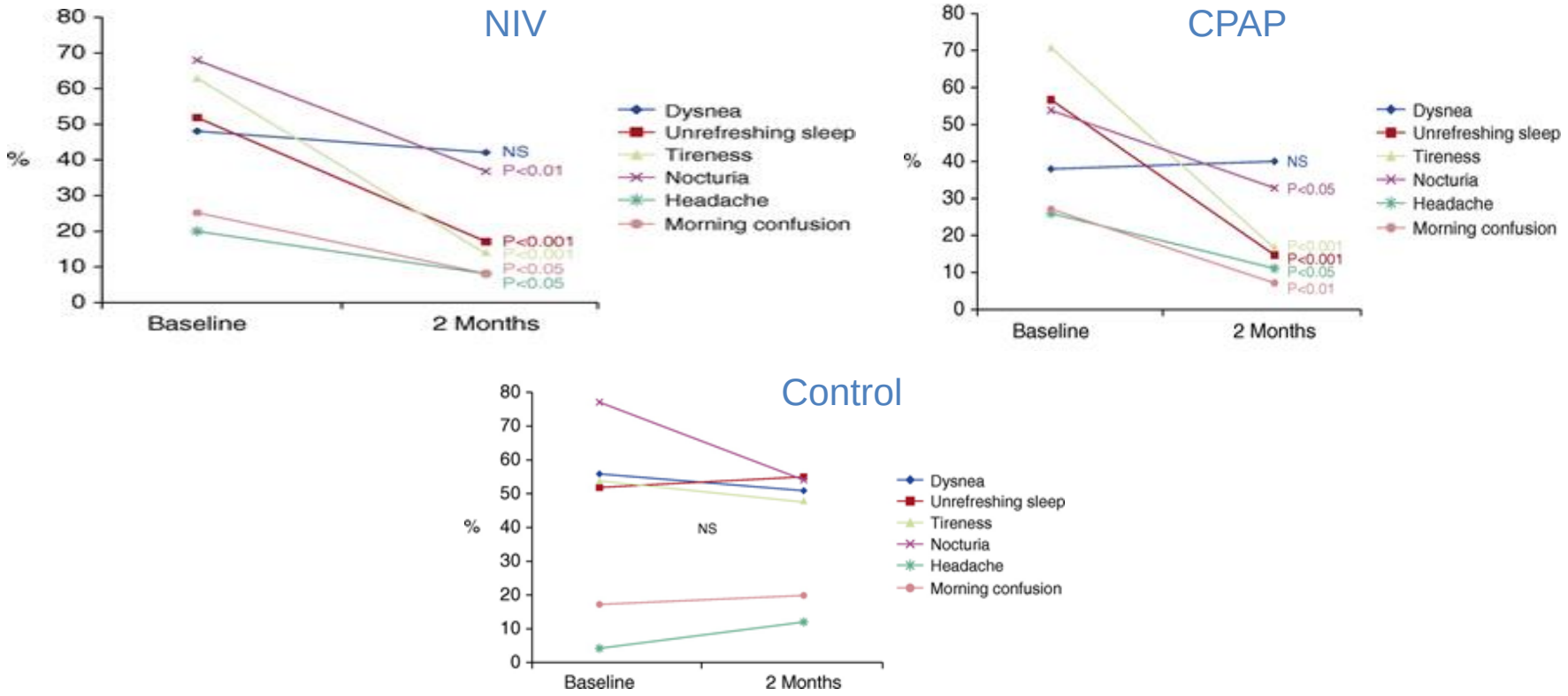
# OHS Mortality / NIV Survival




Nowbar S, et al., Am J Med 2004;116:1–7. Budweiser et al. J Intern Med 2007;261:375–383

# Efficacy of Different Treatment Alternatives for OHS + Severe OSA

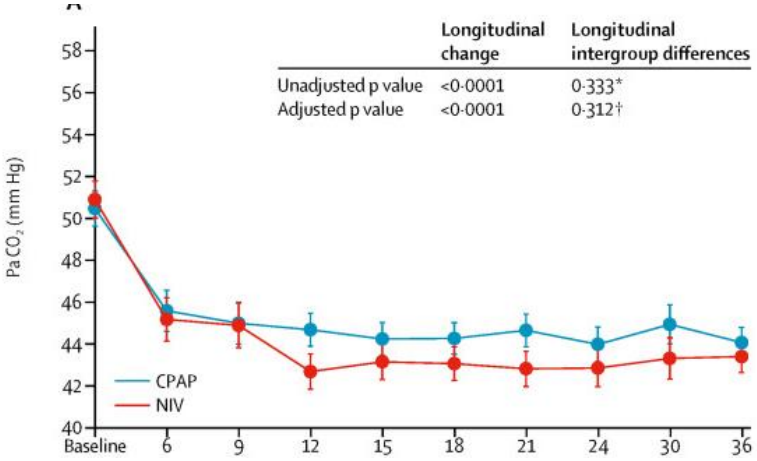
Pickwick Study (N=221)

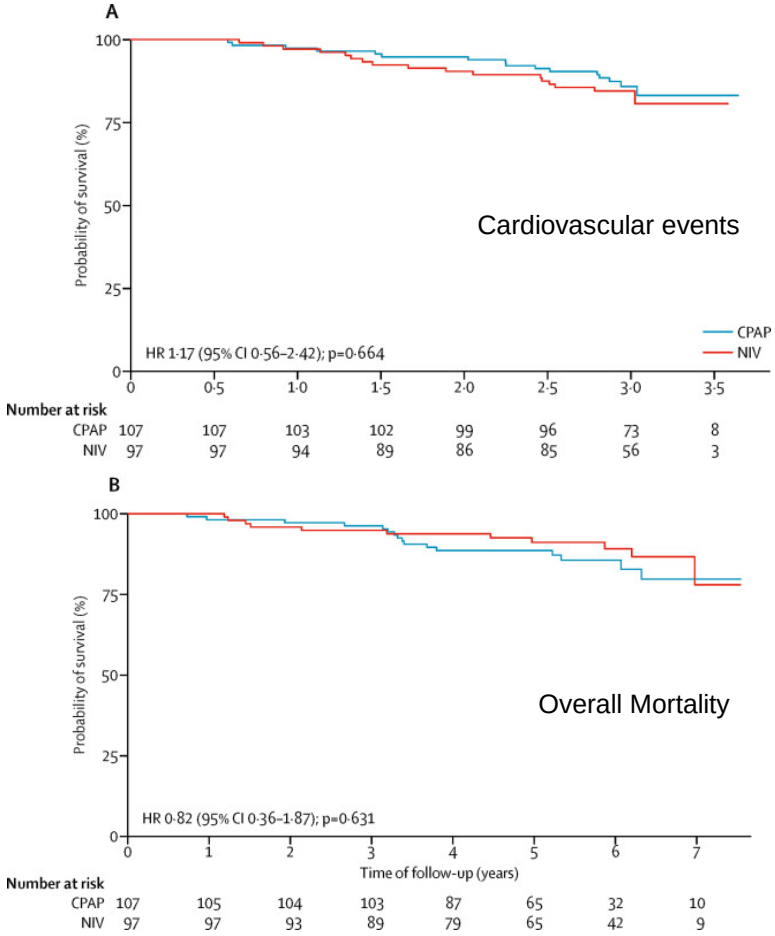



Masa et al. AJRCCM Vol 192;1,July 1 2015

# Long-term Effectiveness of CPAP vs NIV in OHS + Severe OSA

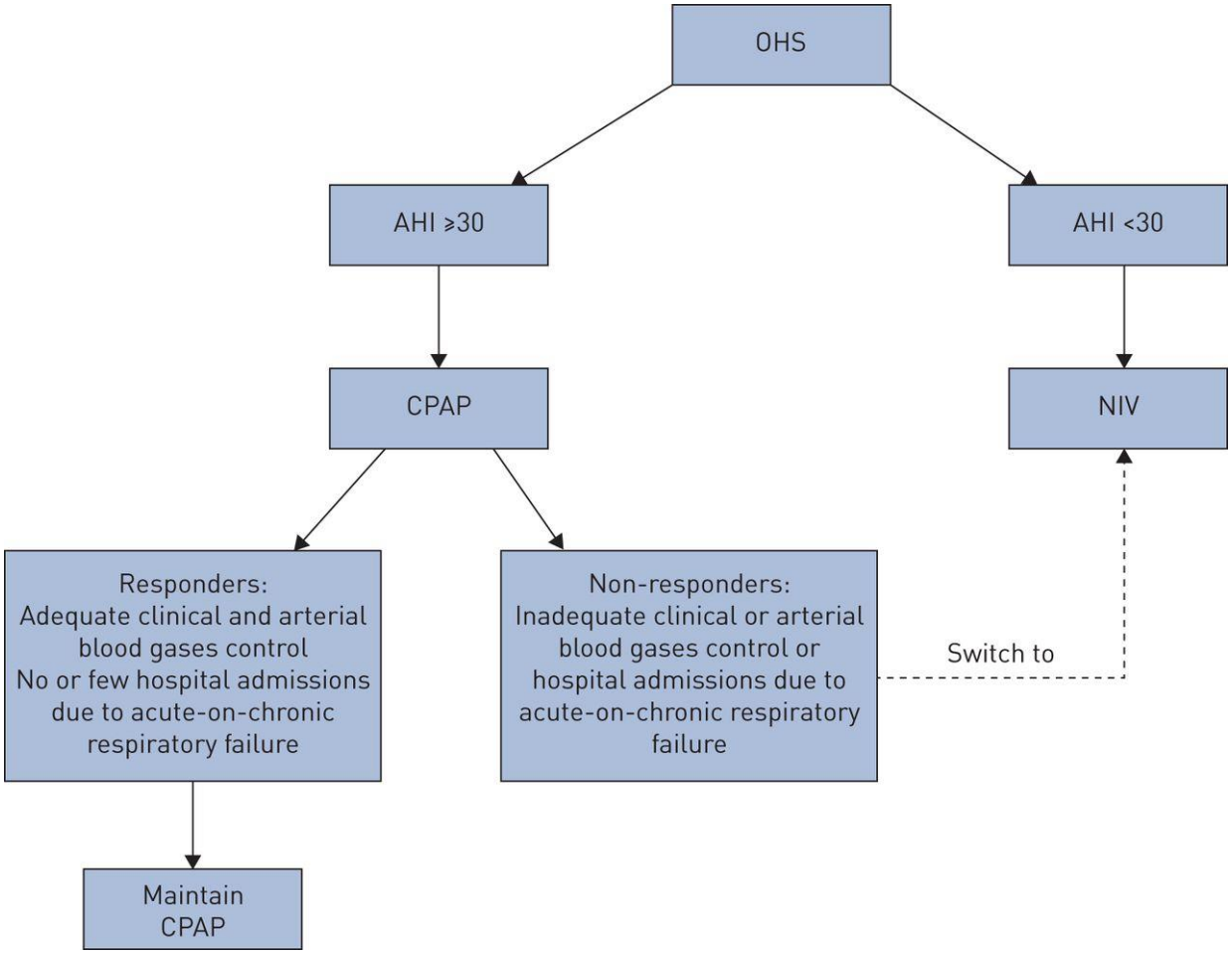
## Long-Term Pickwick Randomized Controlled Clinical Trial (N=221)



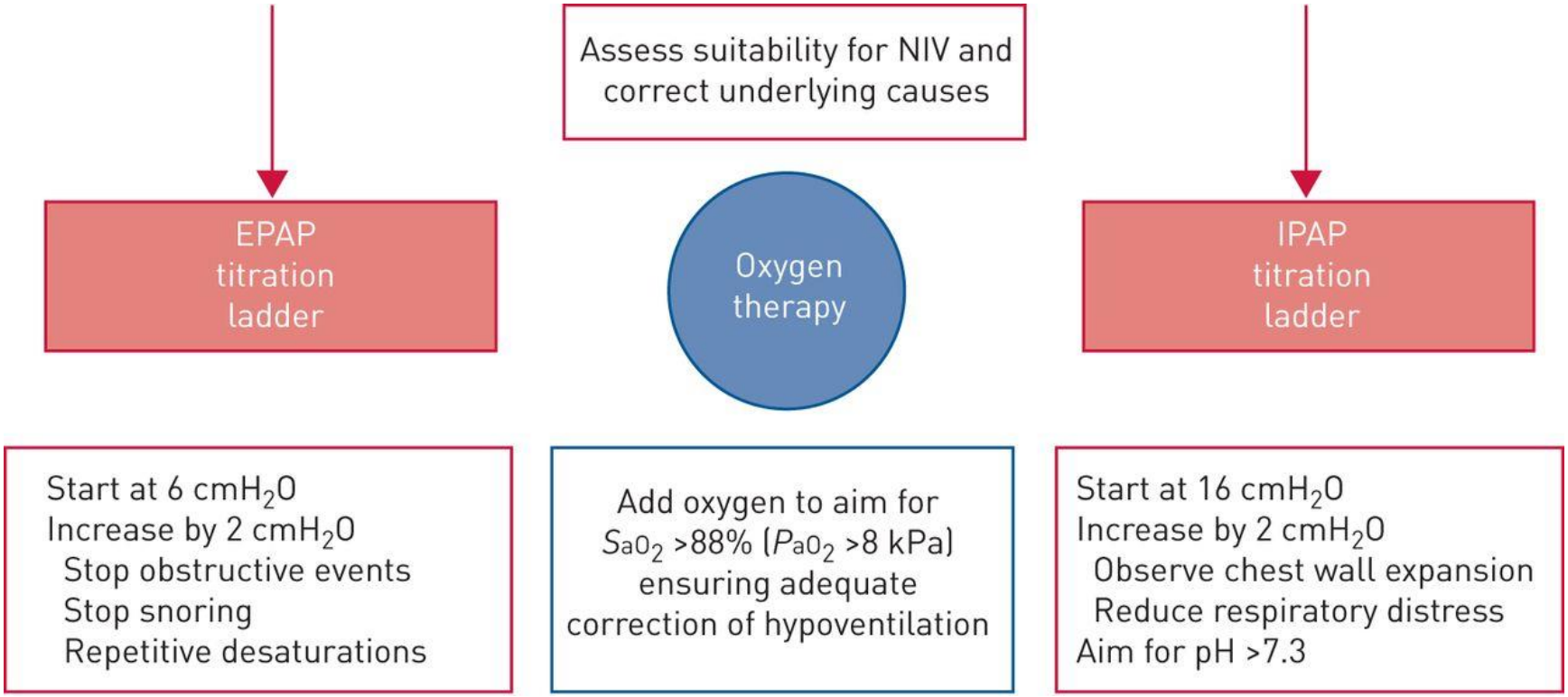

Masa et al. The Lancet, Vol 393, issue 10182, page 17215. Apr 27, 2019

# Choice of Positive Pressure Ventilation




Masa et al. Eur Respir Rev 2019

# Management - NIV



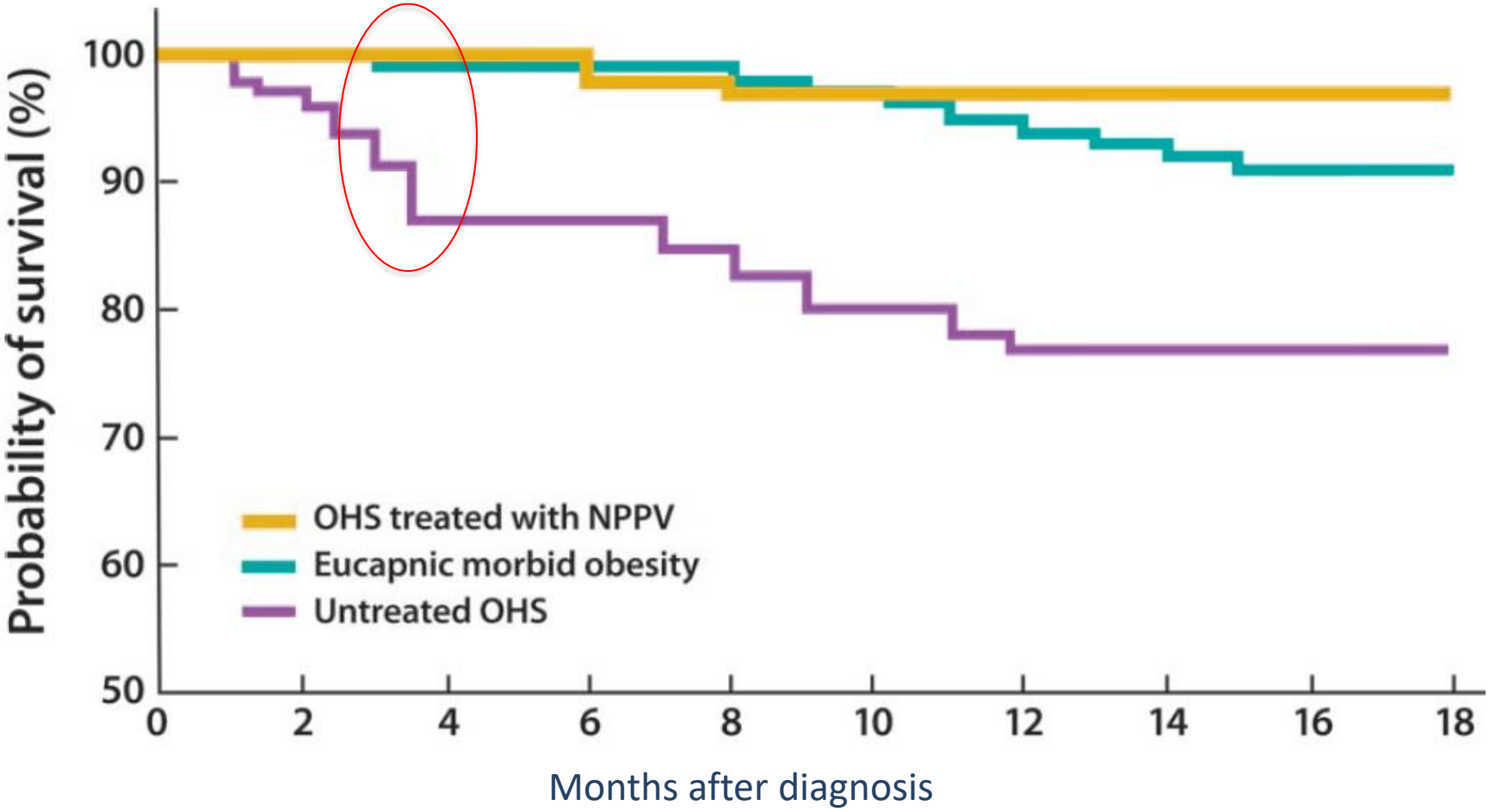

Masa et al. Eur Respir Rev 2019

# Question #1

- A 57 year old man, with a BMI of 45 $kg/m^2$, admitted with pneumonia, and acute on chronic hypercapnia. Admission PaCO2 was 75 mmHg, with a pH 7.25 and HCO3 34.
- Intubated for three days but now extubated and successfully treated with BiPAP 16/8 cmH2O only during sleep
- Morning PaCO2 now 50 mmHg, with a normal pH
- An ABG following a night without NIV showed a PaCO2 60
- The home care company says they need a Polysomnogram (PSG) to get the NIV paid by insurance.
- The patient is all ready for discharge, what should you do?

# Question #1

- A. Use the patient's diagnosis and ABG results to qualify for NIV, and order an outpatient attended PSG in 2-3 months.
- B. Keep the patient one more night and get a portable sleep study off NIV
- C. Discharge the patient without NIV and get the PSG as soon as you can
- D. Patient has to pay out of pocket and buy his own machine.




Nowbar S, et al., Am J Med 2004;116:1–7. Budweiser et al. J Intern Med 2007;261:375–383

Mokhlesi et al. ATS Clinical Practice Guideline. AJRCCM Vol 200, Iss 3, pp e6–e24, Aug 1, 2019

# Qualifying Criteria

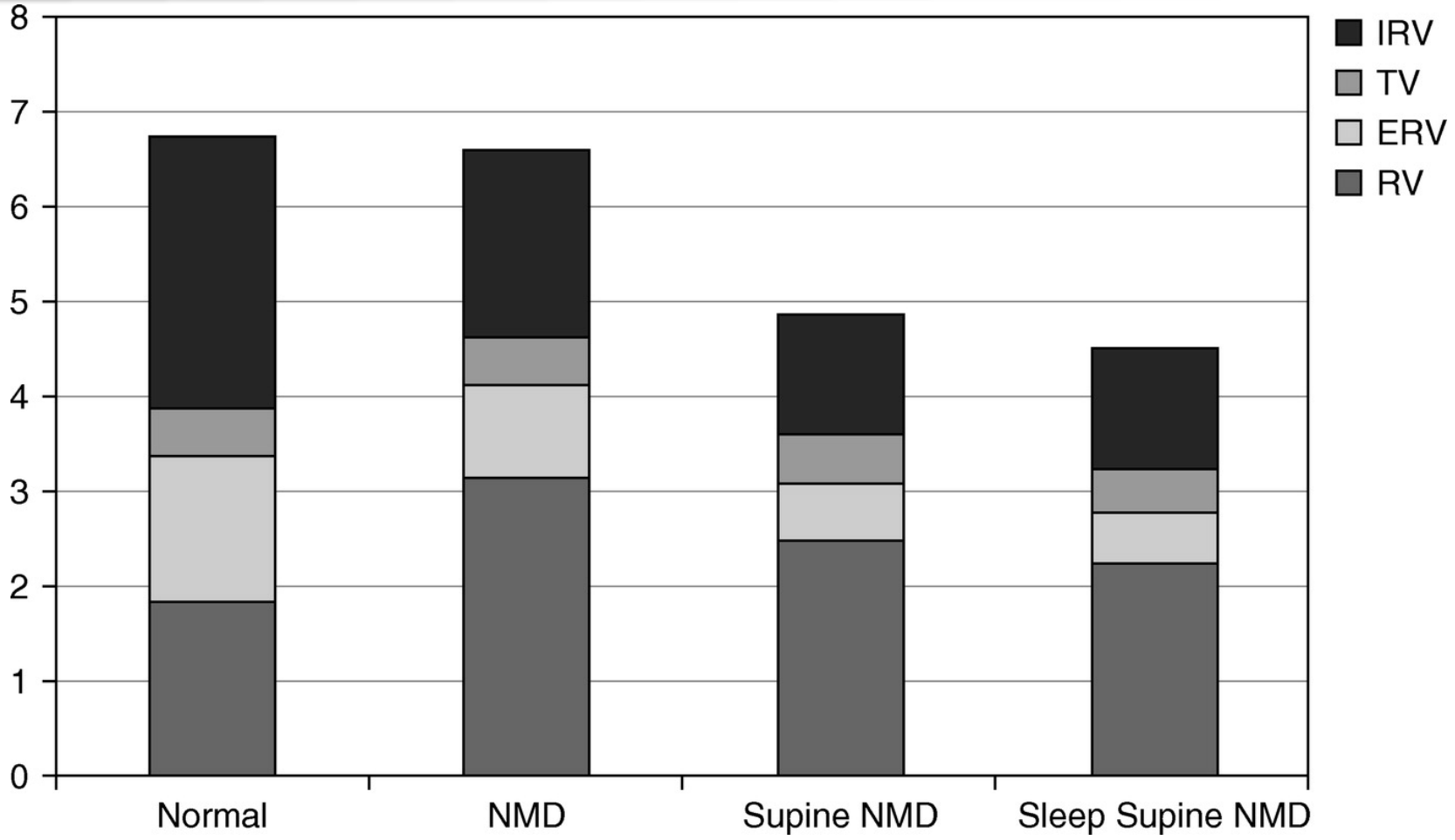
- E0470 (BIPAP-S)
  - Awake ABG $PaCO_2$ ≥45 mm Hg on prescribed $FIO_2$, AND
  - COPD has been considered and ruled out, AND
  - ABG on awakening with $PaCO_2$ ≥7 from baseline, OR
  - PSG or HST demonstrates desaturation ≤ 88% for ≥ 5 minutes of recording not due to obstruction (AHI < 5)
- E0471 (BIPAP-ST/VAPS)
  - Despite BIPAP-S use, AGB on awakening with $PaCO_2$ ≥7 mmHg from qualifying $PaCO_2$, OR
  - PSG or HST on BIPAP-S demonstrates desaturation ≤ 88% without OSA
- E0466 (HMV)
  - Persistent Hypercapnia or need for higher IPAP >25 CMW
  - Significant dyssynchrony (longer insp time, higher EPAP, adjust rise time)
  - Need for daytime support (>10 hrs)

# Neuromuscular Disease (NMD)

# Neuromuscular Disease

- Brain/Spinal Cord
  - Multiple Sclerosis (transient, migratory)
  - Trauma (permanent)
- Motor Neuron
  - Post-polio syndrome (very slowly progressive)
  - Amyotrophic lateral sclerosis (rapidly progressive)
  - Spinal muscular atrophy (progressive)
- Motor Nerves
  - Charcot-Marie-Tooth disease (very slowly progressive)
  - Diaphragm paralysis (slowly reversible)
- Neuromuscular Junction
  - Myasthenia gravis (reversible)
- Muscle
  - Duchenne muscular dystrophy (slowly progressive)
  - Myotonic dystrophy (progressive)
  - Metabolic: acid maltase deficiency (slowly progressive)

# Neuromuscular Disease and respiratory pathophysiology




Aboussouan et al. AJRCCM Vol 191, Iss 9, pp 979–989, May 1, 2015

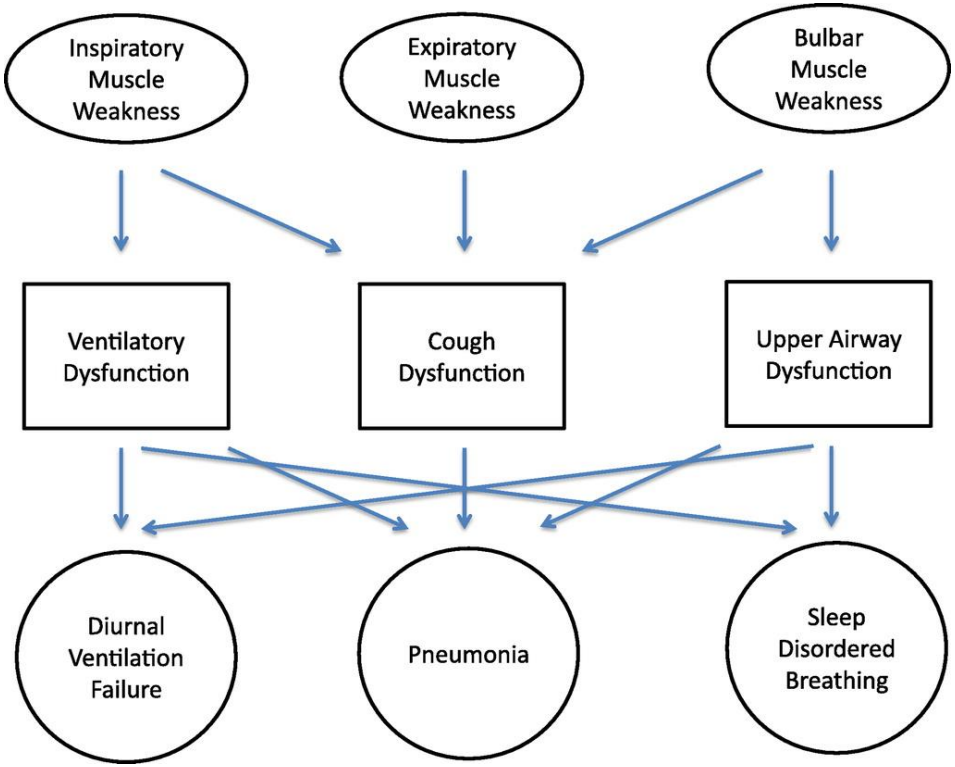
# Question # 2

- Nocturnal desaturation in patients with NMD occurs due to (choose A-D):
    A. Worsening Hypoventilation
    B. Periodic apneas and hypopneas
    C. Ventilation/perfusion mismatch
    D. All the above

# Neuromuscular Disease and respiratory pathophysiology

Loss of muscle tone in REM sleep

Reduced chemosensitivity

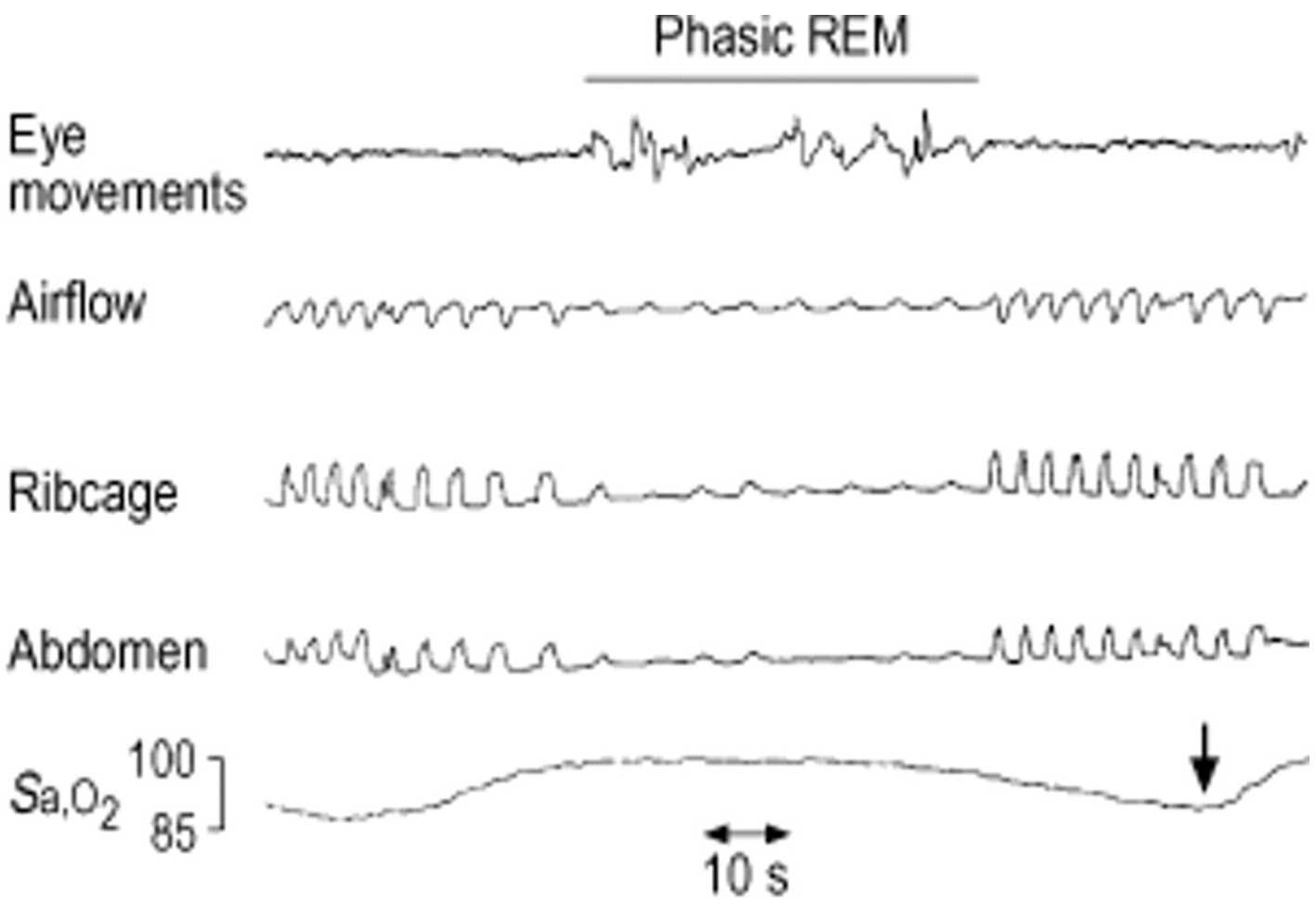



Reduced activity of pharyngeal dilators

Cardiomyopathy

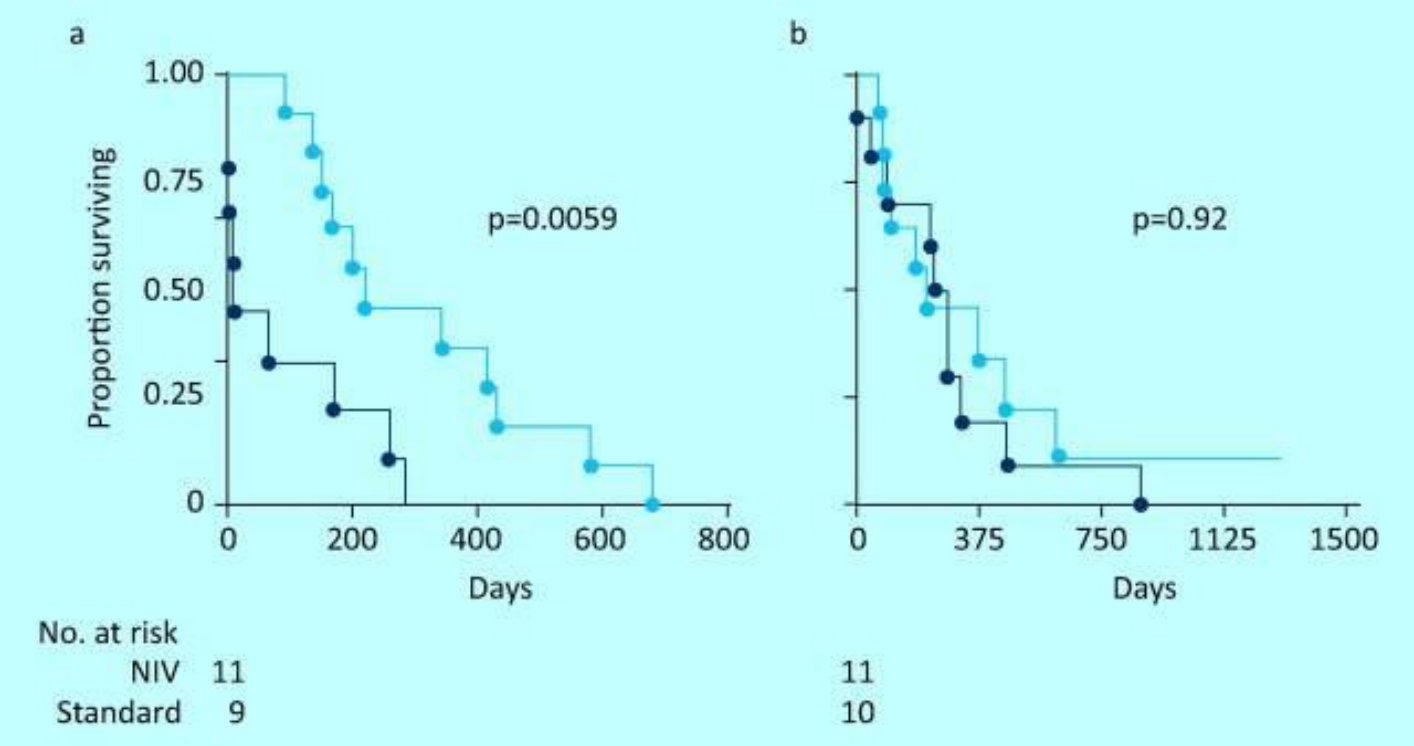
Benditt et al. AJRCCM Vol 187, Iss. 10, pp 1046–1055, May 15, 2013

# Diaphragmatic Events




Bourke et al. Eur Respir J 2002; 19: 1194–1201

# Survival Benefit of NIV in ALS
# RCT (N=41)




Survival non-invasive ventilation (blue) compared with standard care (black) in patients with ALS and (a) normal or only moderately impaired bulbar function and (b) severe bulbar impairment.

Bourke et al. *Lancet Neurol. 2006 Feb; 5(2):140-7*.

# Identifying who will benefit from NIV in ALS/MND in a clinical cohort

- Retrospective study (N=929)
- Patients who refused NIV were taken into the control group
- The NIV group had a 13 months survival benefit (including patients with poor bulbar function)
- NIV delayed deterioration of respiratory function (FEV1, FVC, MIP/MEP, Sniff nasal insp pressure-SNIP)
- Quality of life questionnaires and Sleep quality questionnaires also showed improvement.

Berlowitz DJ, et al. J Neurol Neurosurg Psychiatry 2016;87:280–286

# Question # 3

- A 57 year old man admitted with pneumonia, acute on chronic hypercapnia and ALS.
- Admission PaCO2 was 75 mmHg, pH 7.25 and HCO3 34
- Intubated for 5 days but now extubated and successfully treated with BiPAP 15/5 cmH2O during sleep
- Morning PaCO2 now 50 mmHg with a normal pH
- A bedside spirometry showed an FVC 40% predicted
- You would like to send this patient home on NIV
- The home care company says they need a Polysomnogram (PSG) to get the NIV paid by insurance.
- The patient is all ready for discharge, what should you do?

# Question # 3

- A. Use the patient's current diagnosis and ABG results to qualify for NIV
- B. Keep the patient one more night and get a portable sleep study off NIV
- C. Discharge the patient without NIV and get the PSG as soon as you can
- D. Obtain an outpatient full PFTs with seated/supine spirometry to qualify for NIV.

# Qualifying Criteria

- E0470/E0471 (BIPAP-S, BIPAP-ST/VAPS):
  - Diagnosis of progressive neuromuscular disease, AND
  - Awake $PaCO_2 > 45$ mmHg while on prescribed $FiO_2$, OR
  - Overnight oximetry shows $SaO_2 \leq 88\%$ for > 5 minutes (minimum recording of 2 hours) on prescribed $FIO_2$, OR
  - Max inspiratory pressure < - 60 $cmH_2O$, or FVC < 50% predicted AND COPD is not contributing to symptoms.

# Initiating NIV

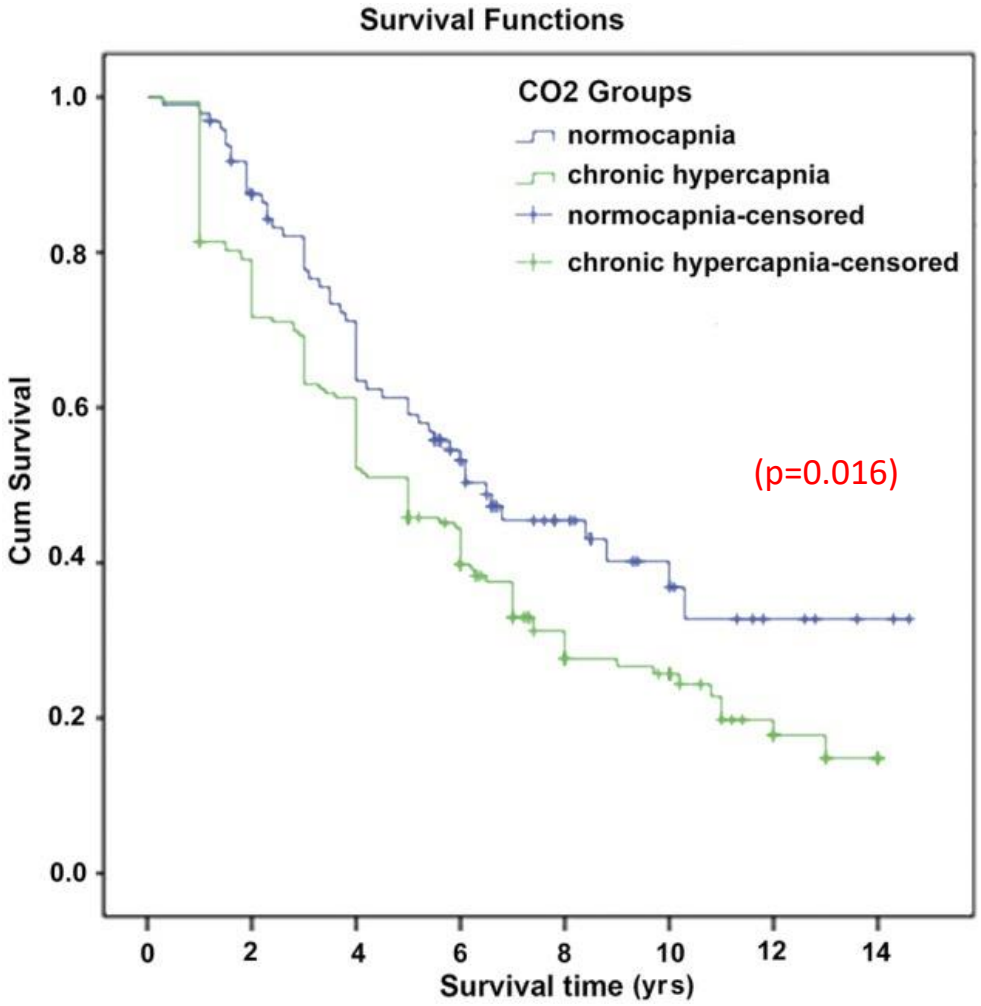
- Where? During in-patient admission, sleep lab or the Outpatient setting.
- Modes of NIV:

| BPAP-ST | VAPS (iVAPs or AVAPS) |
|---|---|
| - IPAP: 8-10 cmH2O<br>- EPAP: 4-5 cmH2O<br>- BR: 2 below spont RR | - EPAP: 4-5 cmH2O<br>- IPAP min: 4-6 cmH2O, gradually increase to reach target tidal volume of 8 ml/kg<br>- IPAP max: IPAP min + 5-6 cmH2O<br>- BR: 2 below spont RR |
| - Adjust IPAP by 1-2 cmH2O to alleviate dyspnea, decrease RR, and increase tidal volume | - Adjust trigger sensitivity, rise time, inspiratory time, to alleviate dyspnea and patient comfort |

- Follow downloaded data, monitor for symptoms, overnight oximetry/TcCO2, VBG or HCO3. PSG only if patient can't adapt or you suspect OSA.
- If daytime ventilation becomes necessary, consider mouthpiece ventilation rather than tracheostomy (Switch to HMV if not already initiated)

# Stable Hypercapnic COPD

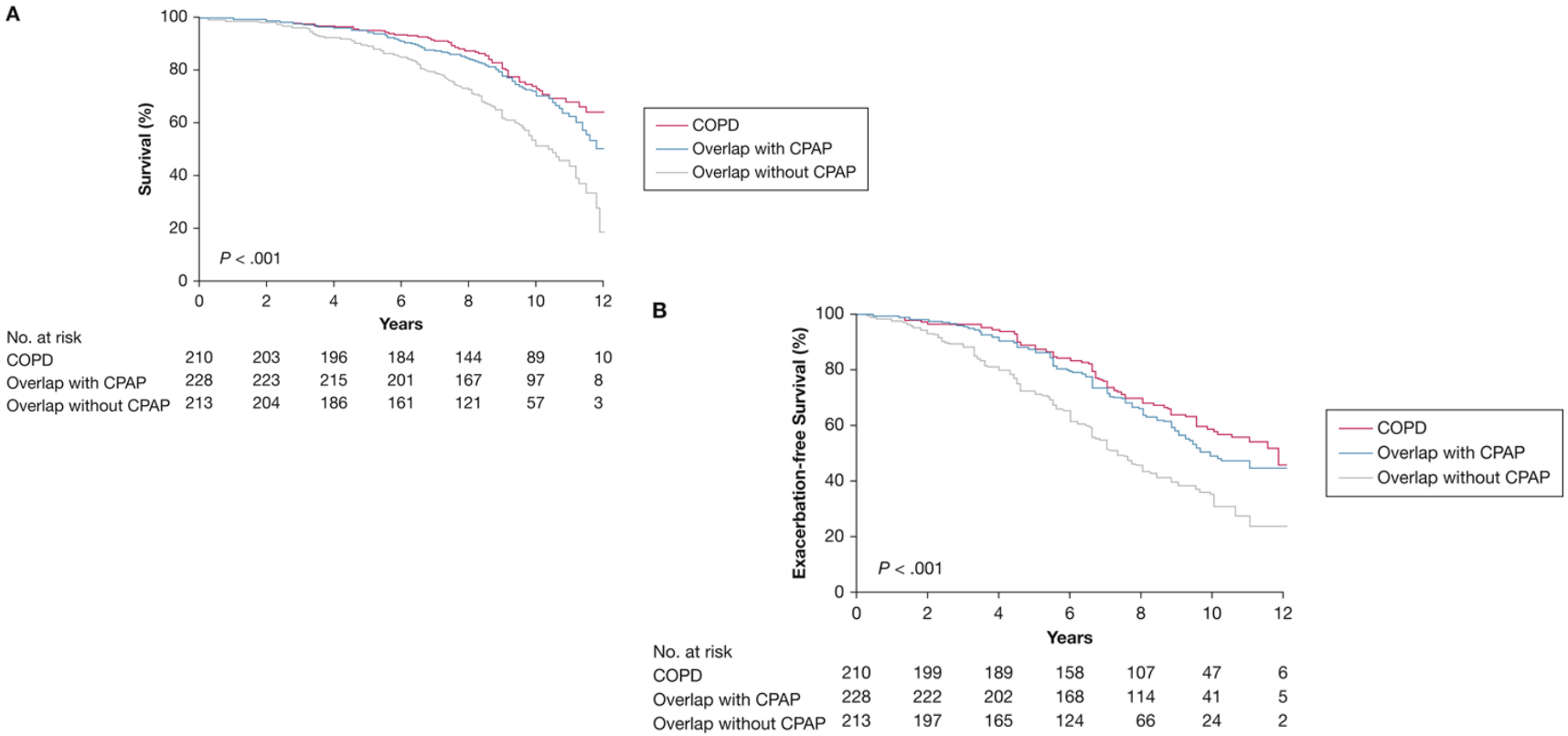
# Hypercapnia in COPD and Survival




- Increased Dyspnea
- Decreased QOL
- More frequent hospitalizations

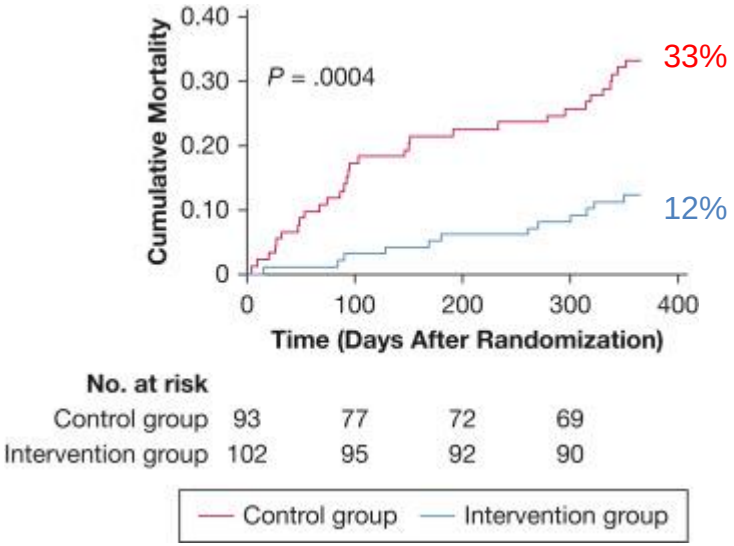
Yang H. et al. BMJ Open 2015;5:e008909

# Overlap Syndrome - ↑ Mortality
## (Prevalence = 29%)




Marin J.M. et al. Am J Respir Crit Care Med. 2010; 182: 325-331

# High Intensity BIPAP for COPD with Chronic Hypercapnia

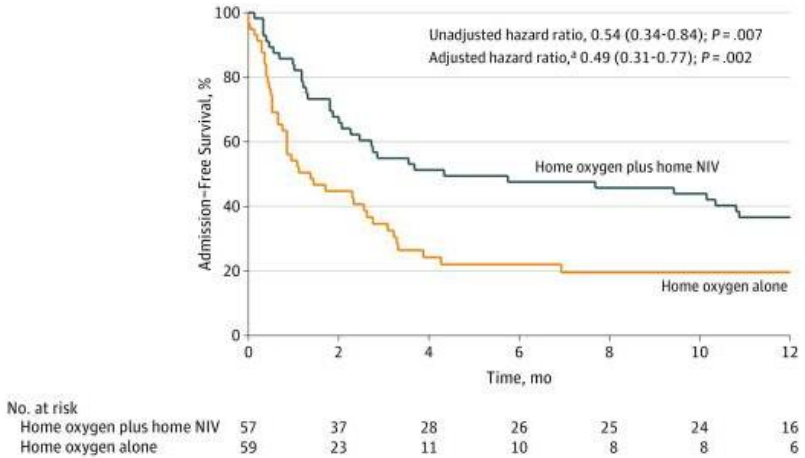



- Long Term RCT (N = 201): COPD Gold IV (PaCO2 > 52 and pH > 7.35)
  - HI NIV (IPAP 24-28 cmH2O with back up rate) aimed to reduce PaCO2 >20% from baseline or below 48, vs standard of care for the control group (home oxygen)
  - Improved 1 year mortality (p=0.0004)
  - Improved PaCO2, pH, SaO2, FEV1 and HRQOL with HI NIV

Kohnlein, T et al Lancet Respir Med 2014

# If Hospitalized - When to Initiate Home NIV?

- The Home Oxygen Therapy-Home Mechanical Ventilation Trial
  HOT-HMV trial (N=116)
  - Patients with persistent hypercapnia (PaCO2 > 53) at 2-4 weeks post discharge were assigned to HOT-HMV or HOT alone.
  - Median HMV settings: IPAP 24 cmH2O, EPAP 4 cmH2O, RR 14/min
  - HOT-HMV showed reduction in readmission or death by 50%




- The Rescue trial (N=201)
  - Patients with persistent hypercapnia at 48 hrs, assigned to NIV vs standard of care
  - At 1 year, NO reduction in mortality or frequency of exacerbations or time to readmission
  - Patients recruited right after exacerbation, many did not have persistent hypercapnia

- In the US, assess 2-4 weeks post discharge for a PaCO2 > 52, and if present, initiate NIV

*Murphy et al. JAMA. 2017 Jun 6; 317(21). Struik et al. Thorax. 2014 Sep; 69(9)*

# Qualifying Criteria

- E0470 (BIPAP-S)
  - ABG with PaCO2 ≥52 AND,
  - Overnight oxygen desaturation ≤88% on 2 lit oxygen or on patient's prescribed supplemental oxygen (whichever is higher), for > 5 minutes, AND
  - OSA is considered and ruled out (Sleep study not required)
- E0471 (BIPAP-ST/VAPS)
  - PaCO2 ≥7 mmHg from baseline, AND persistent overnight desaturation despite use of BIPAP-S, for at least 2 months, average 4 hours per night.
- E0466 (HMV)
  - Persistent Hypercapnia despite highest BIPAP-ST support (IPAP >25 CMW)
  - Significant dyssynchrony (shorter insp time, adjust rise time)
  - Increased oxygen requirement (more than 40% FiO2)
  - Need for daytime support (>10 hrs) or the need of a mouthpiece.

# Take Home Points

- In ambulatory patients with stable OHS and OSA, CPAP is preferred.
- Use NIV if non obstructive OHS or persistent hypoventilation despite CPAP
- Both CPAP and NIV improve survival, in addition to sleep quality, and daytime symptoms.
- If hospitalized, initiate NIV upon discharge (consider PSG in 3 months)

- In ambulatory patients with neuromuscular disease, use of home NIV is associated with improved survival and quality of life metrics.
- If hospitalized, initiate NIV upon discharge (PSG only if needed)

- In ambulatory patients with stable hypercapnic COPD, high intensity BIPAP is associated with lower mortality, hospital admissions, and improves measures of quality of life.
- IF hospitalized, reassess 2-4 weeks post discharge, and initiate NIV if persistent hypercapnia despite medical optimization.