BRIGHAM AND WOMEN'S HOSPITAL

The Lung Center

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

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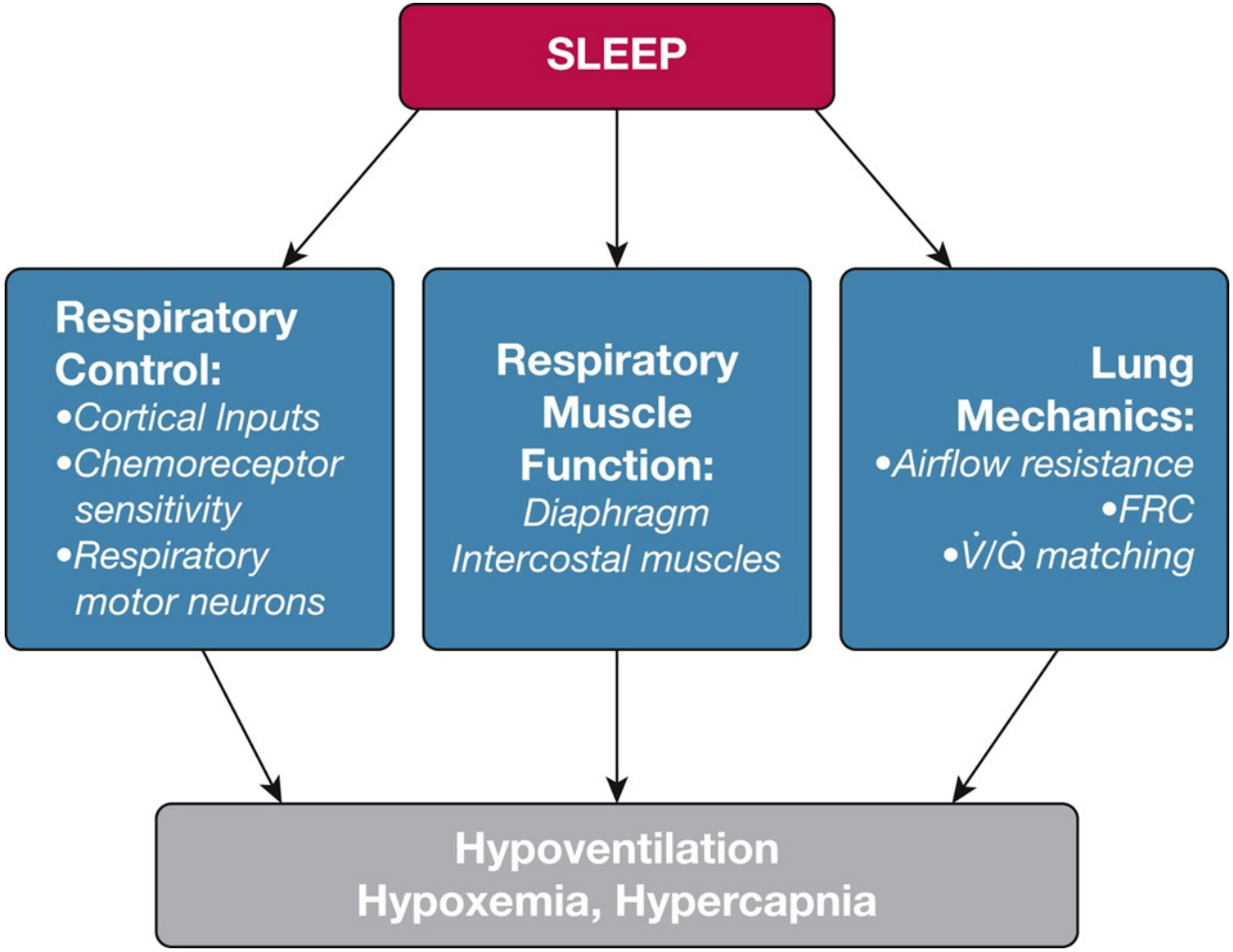
Disclosures

- 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

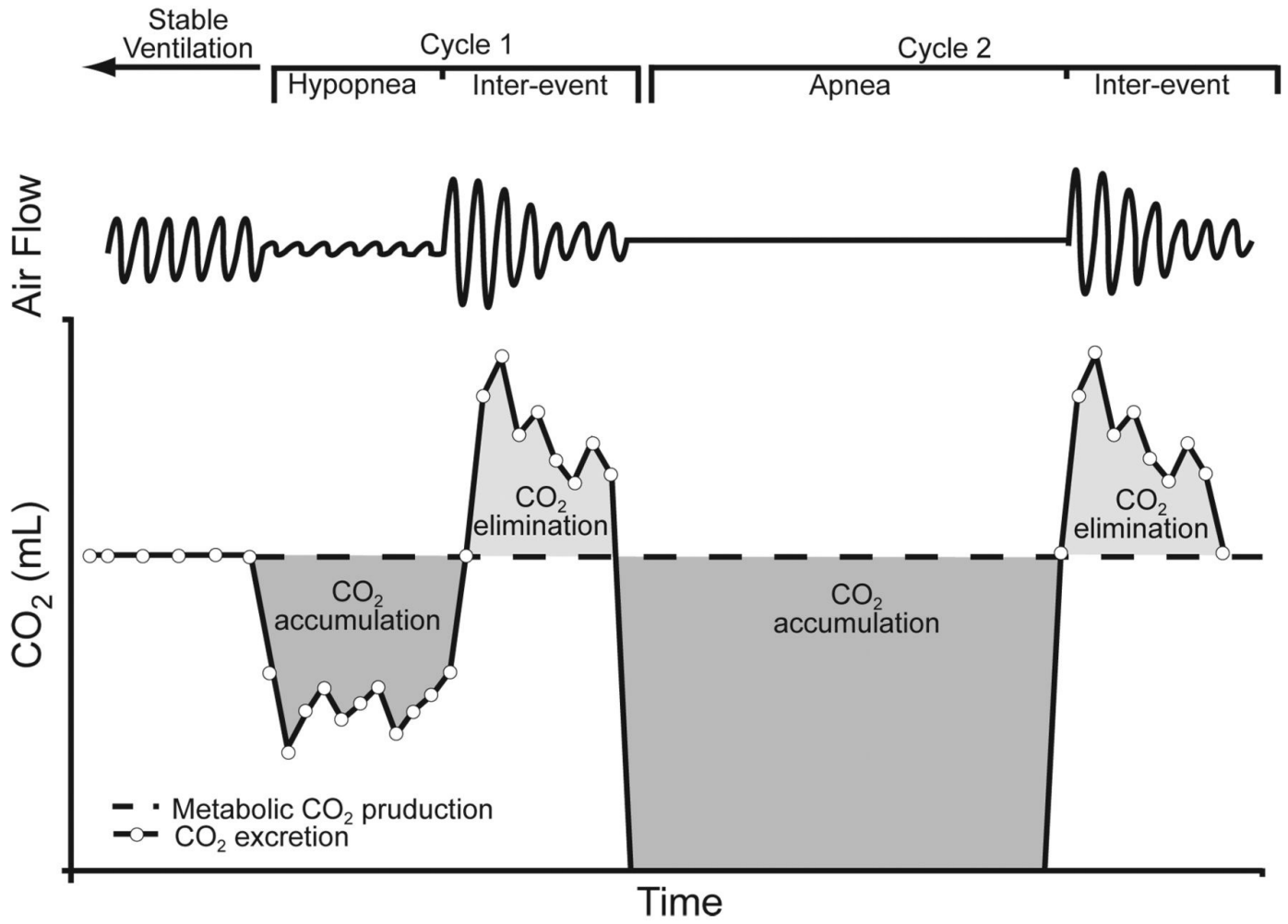
Respiratory changes during Sleep

- ↓ 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

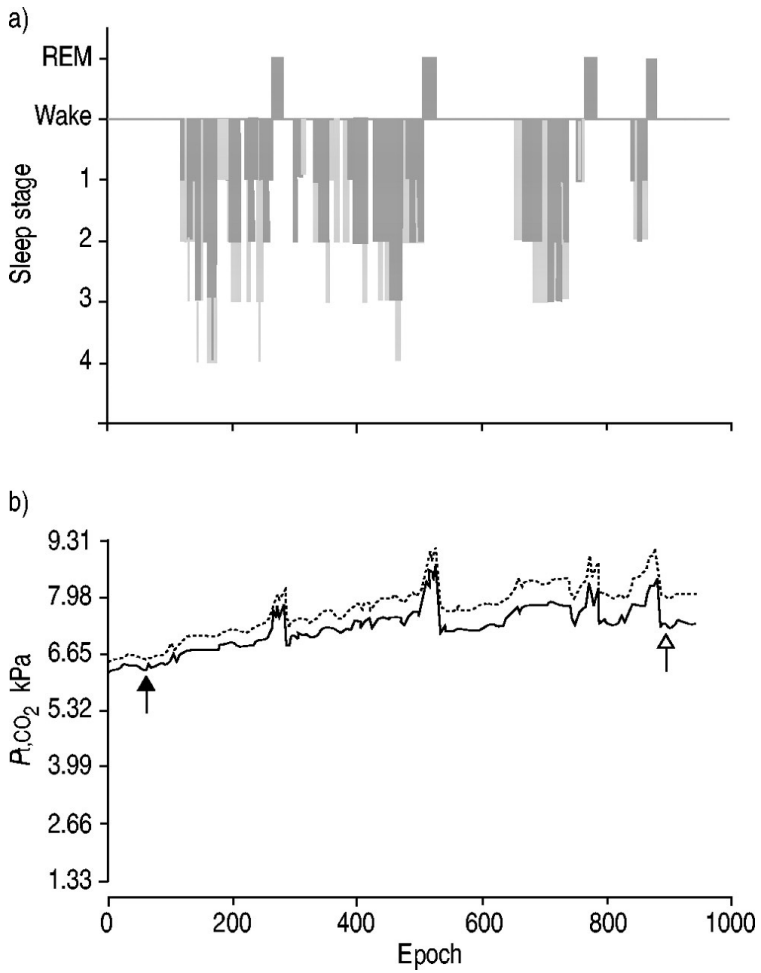
Mohsenin, Semin Resp Crit Care Med 2005

Obstructive Sleep Apnea and Hypoventilation



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

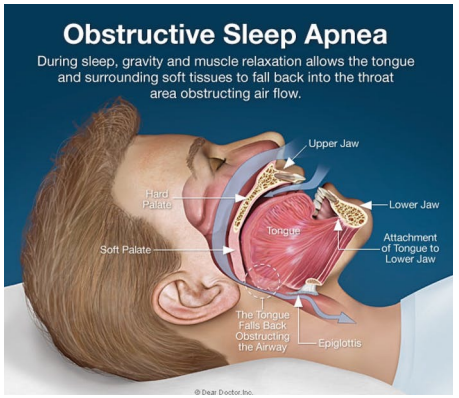
Consequences of REM-atonia

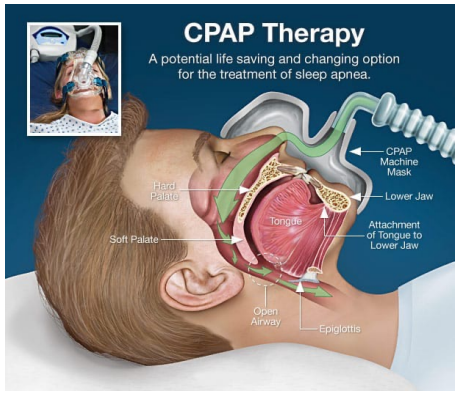


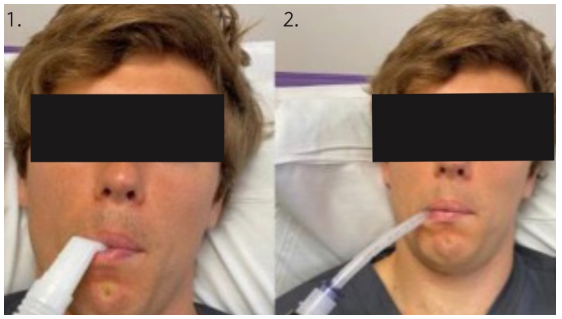
a) Sample hypnogram and b) transcutaneous carbon dioxide tension (Pt,CO2) record illustrating Pt,CO2 corrections.

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

Non-invasive Positive Pressure Ventilation



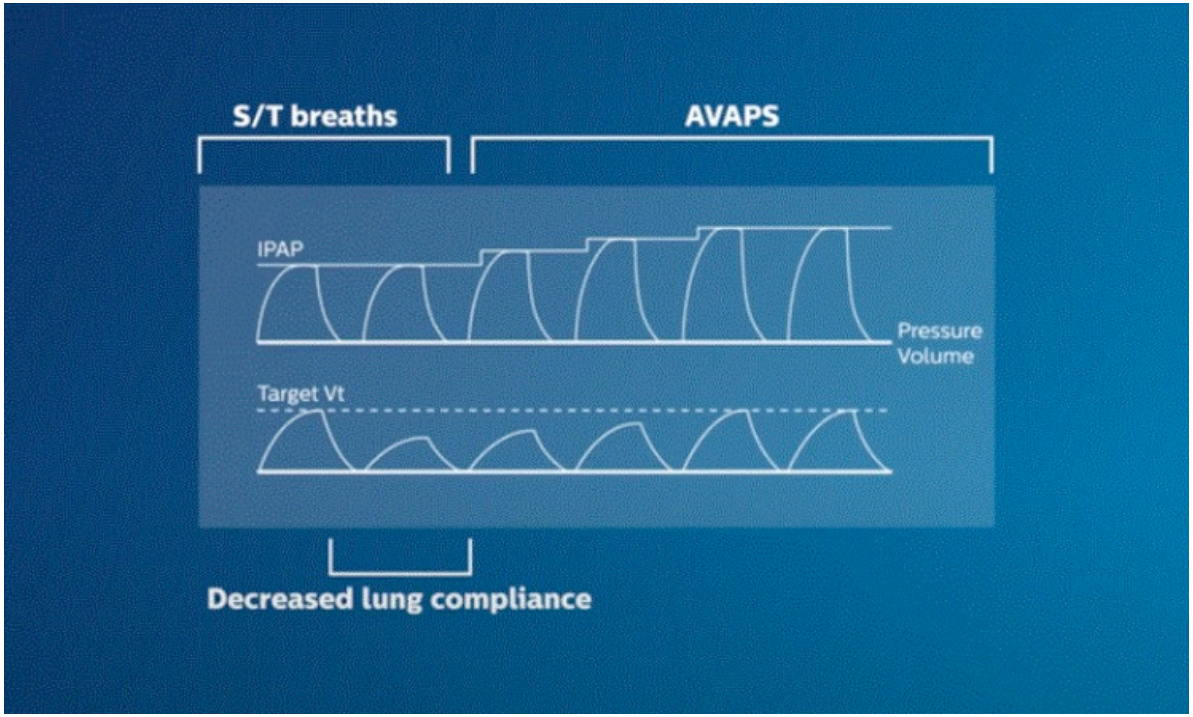




Respiratory Assist Devices (RADs) (E0470/E0471)

PAP Mode	Settings/Target
BPAP BPAP-ST, with back up rate (BR)	IPAP, EPAP Pressure support = IPAP-EPAP BR = Spontaneous timed (ST) or timed (T)
Adaptive Servo Ventilation (ASV)	Pressure support varies to stabilize breathing (PS min, PS max) EPAP varies to eliminate airway obstruction (EPAP min, EPAP max)
Volume-assured Pressure Support AVAPS or iVAPS	Pressure support varies to meet a target tidal volume or alveolar ventilation EPAP set to eliminate airway obstruction 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) BIPAP-ST/ASV/VAPS (E0471)	Invasive: trach (E0465), Non-invasive: (E0466) 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
"Capped rental" payment continues 13 mos (mandated by Deficit Reduction Act).	"Frequent and substantial" payment, continues for the time the beneficiary requires the device

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.

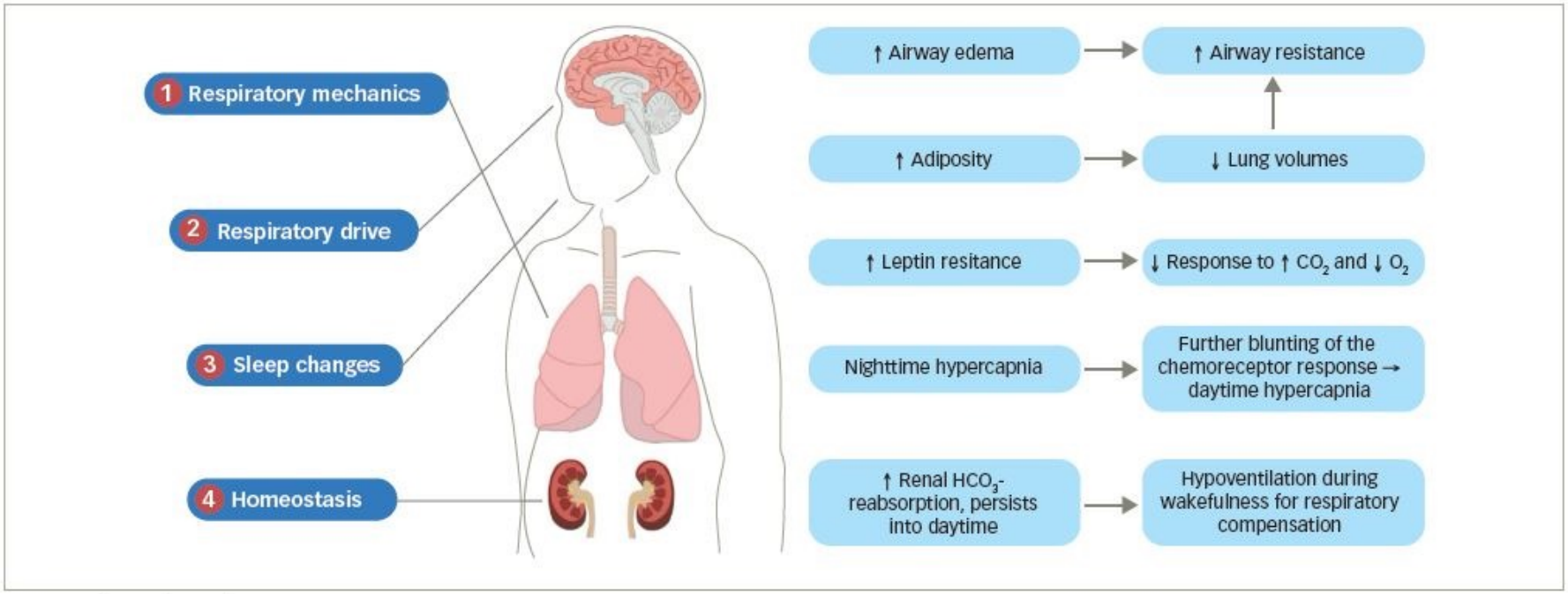
OHS Phenotypes

- 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

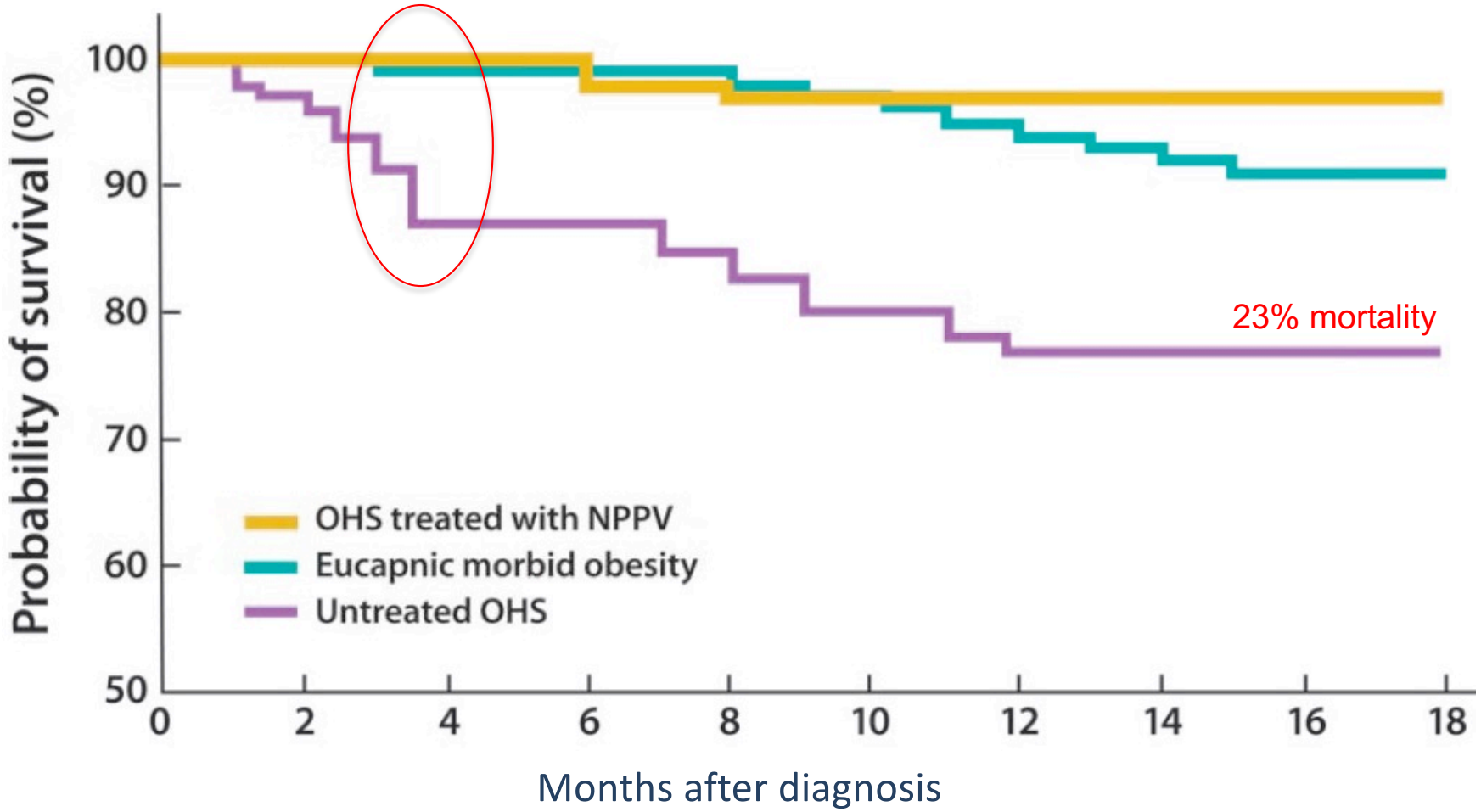
Epidemiology

- 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

- No gender difference
- More often associated with DM, HF, PH than OSA
- OHS remains largely underdiagnosed. 75% were misdiagnosed and treated for obstructive lung disease (despite normal FEV1/FVC)

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

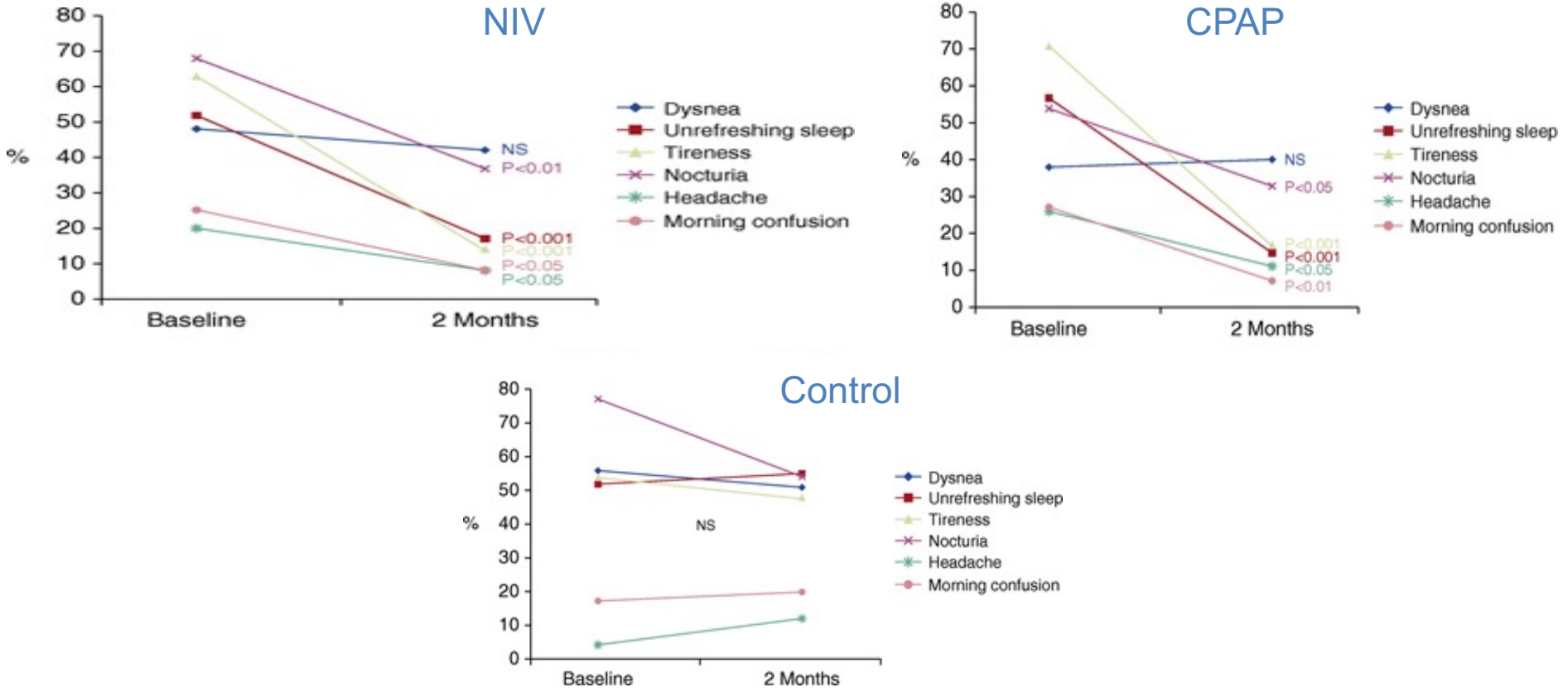
OHS Mortality / NIV Survival



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 Obesity Hypoventilation Syndrome

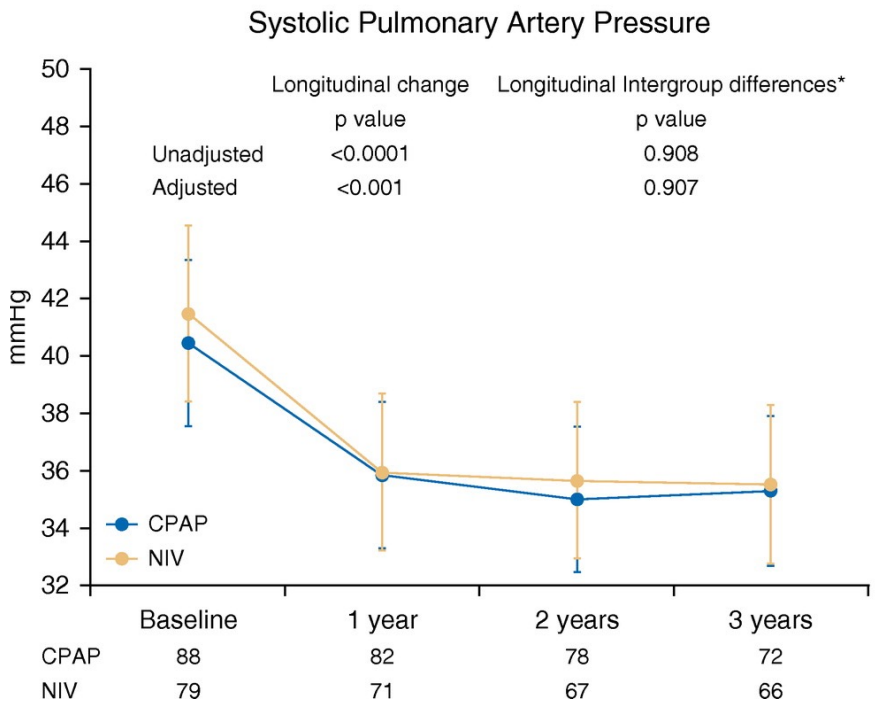
Pickwick Study (N=221)

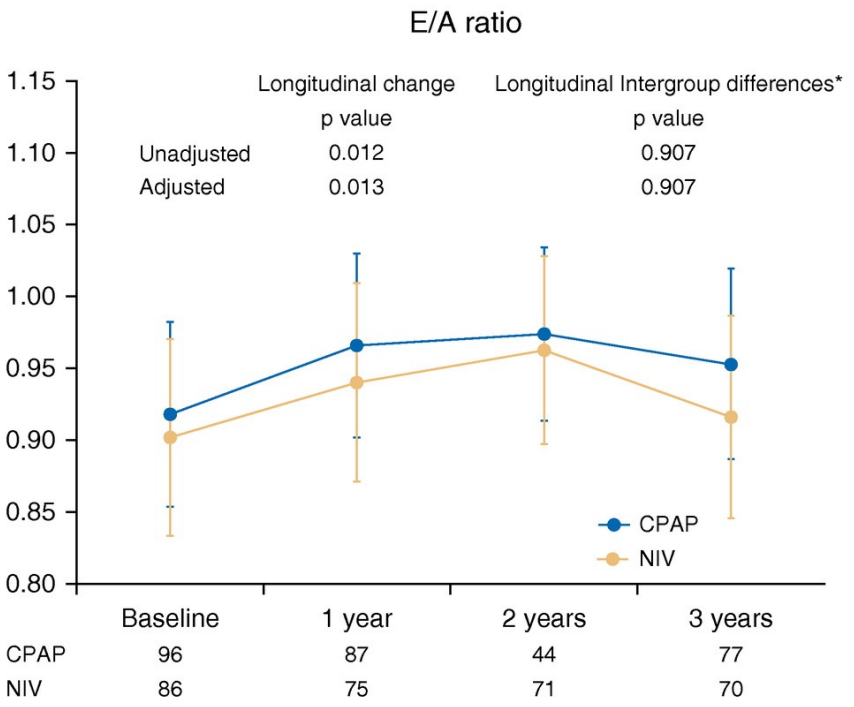


Masa et al. AJRCCM Vol 192;1,July 1 2015

Echocardiographic Changes with Positive Airway Pressure Therapy in Obesity Hypoventilation Syndrome

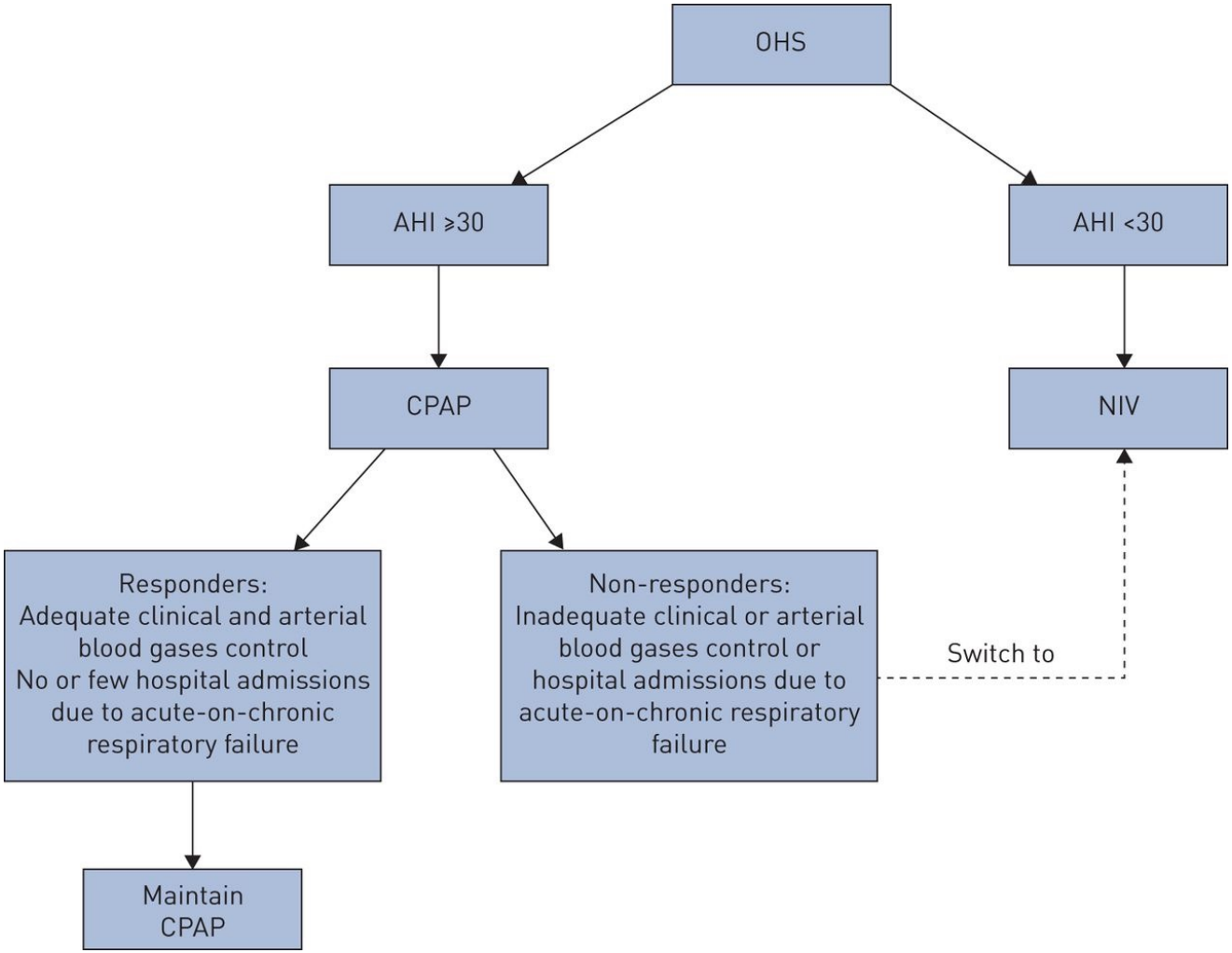
Long-Term Pickwick Randomized Controlled Clinical Trial (N=221)





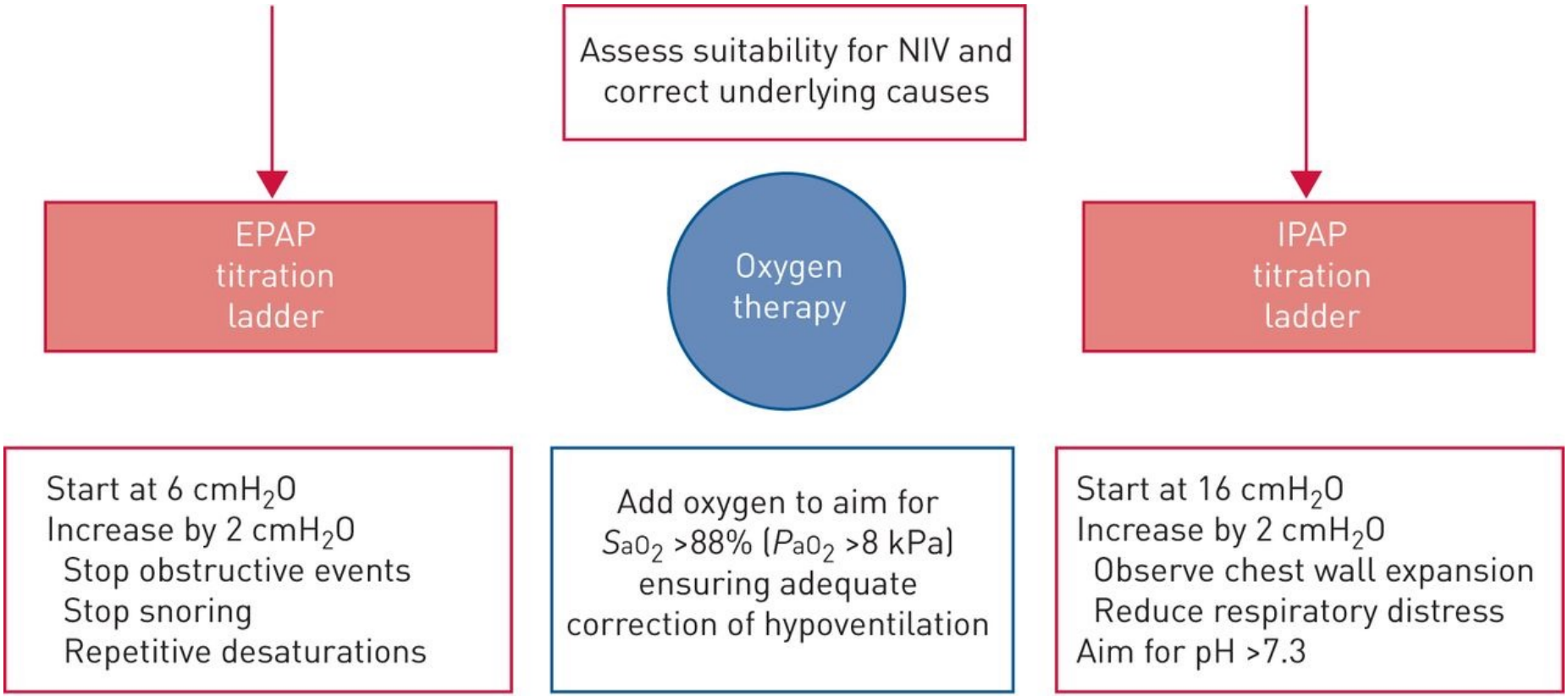
Masa et al. AJRCCM Vol 201;5,Mar 1 2020

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, admitted with pneumonia, acute on chronic hypercapnia, a BMI of 45 kg/m^2. Admission PaCO2 was 75 mmHg, with a pH 7.25 and HCO3 34.
- Intubated for three days but now extubated and successfully treated with Non-Invasive Ventilation 16/8 cmH2O 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.

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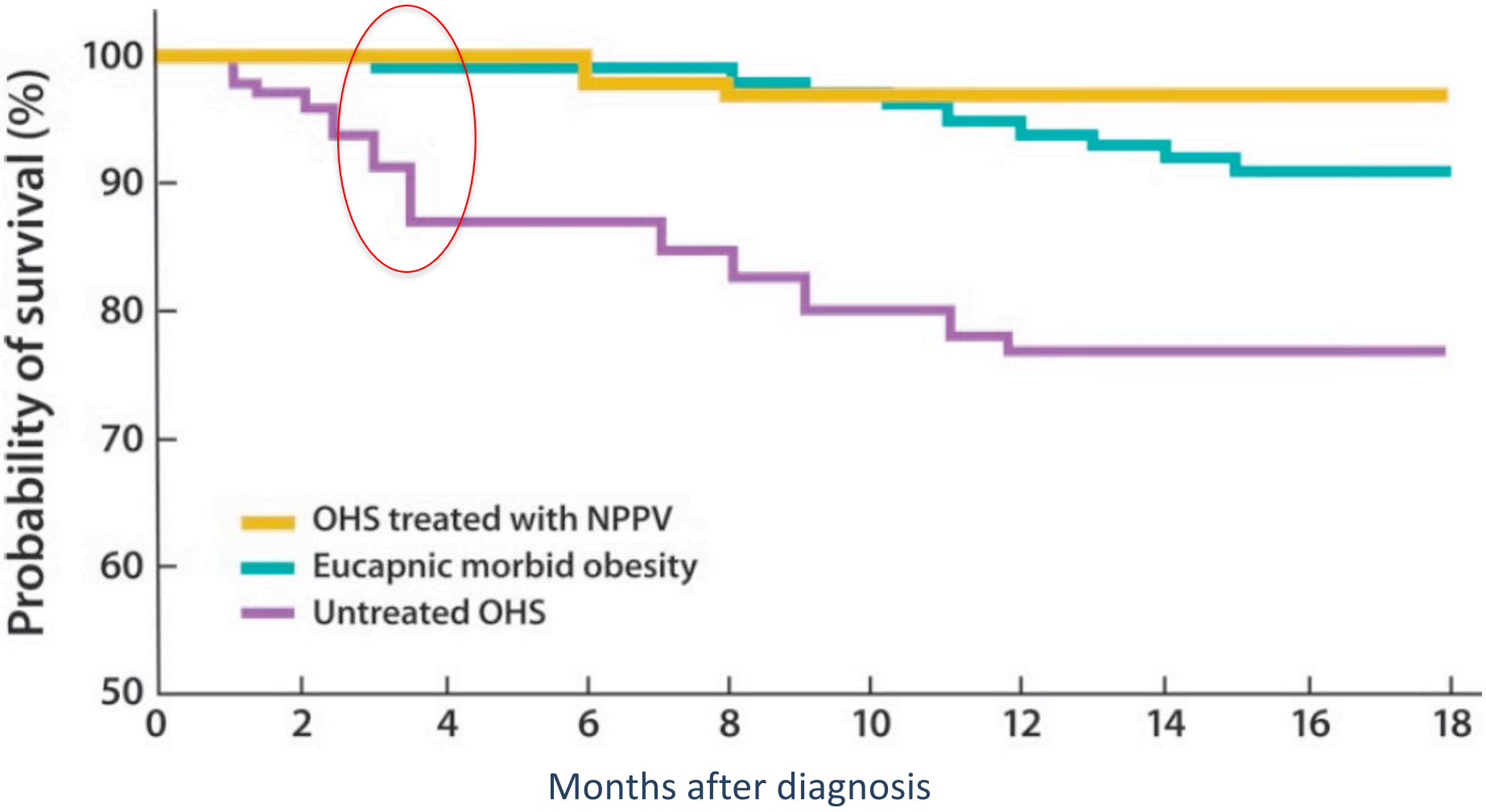


Nowbar S, et al., Am J Med 2004;116:1–7. Budweiser et al. J Intern Med 2007;261:375–383

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

Qualifying Criteria

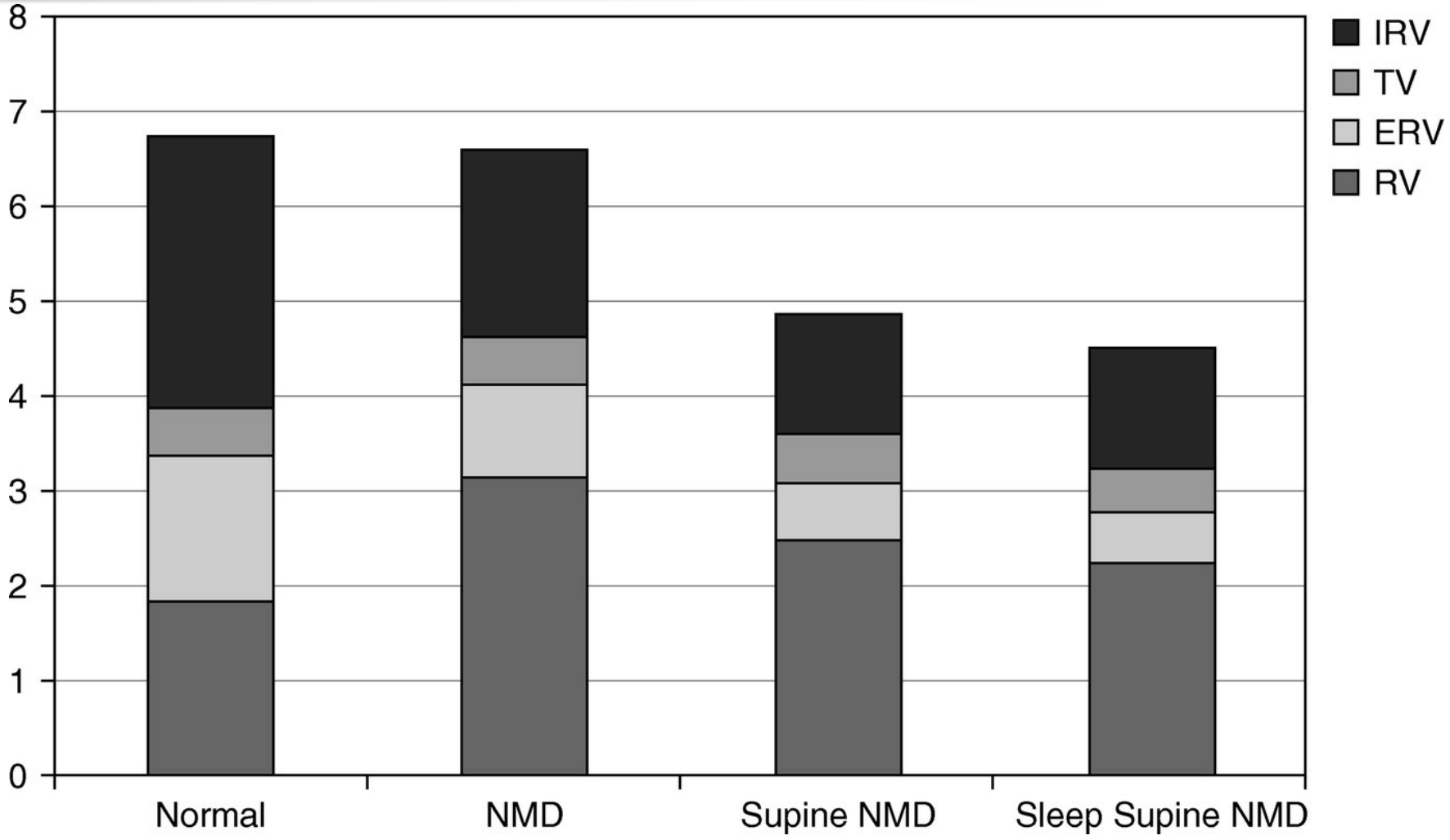
- E0470 (BIPAP-S)
  - Awake ABG PaCO2 ≥45 mm Hg on prescribed FIO2, AND
  - COPD has been considered and ruled out, AND
  - ABG on awakening with PaCO2 ≥7 from baseline, OR
  - PSG or HST demonstrates desaturation ≤ 88% for ≥ 5 minutes of recording not due to obstruction (AHI < 5)
- E0471 (BIPAP-ST/VAPS)
  - Despite BIPAP-S use, AGB on awakening with PaCO2 ≥7 mmHg from qualifying PaCO2, 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

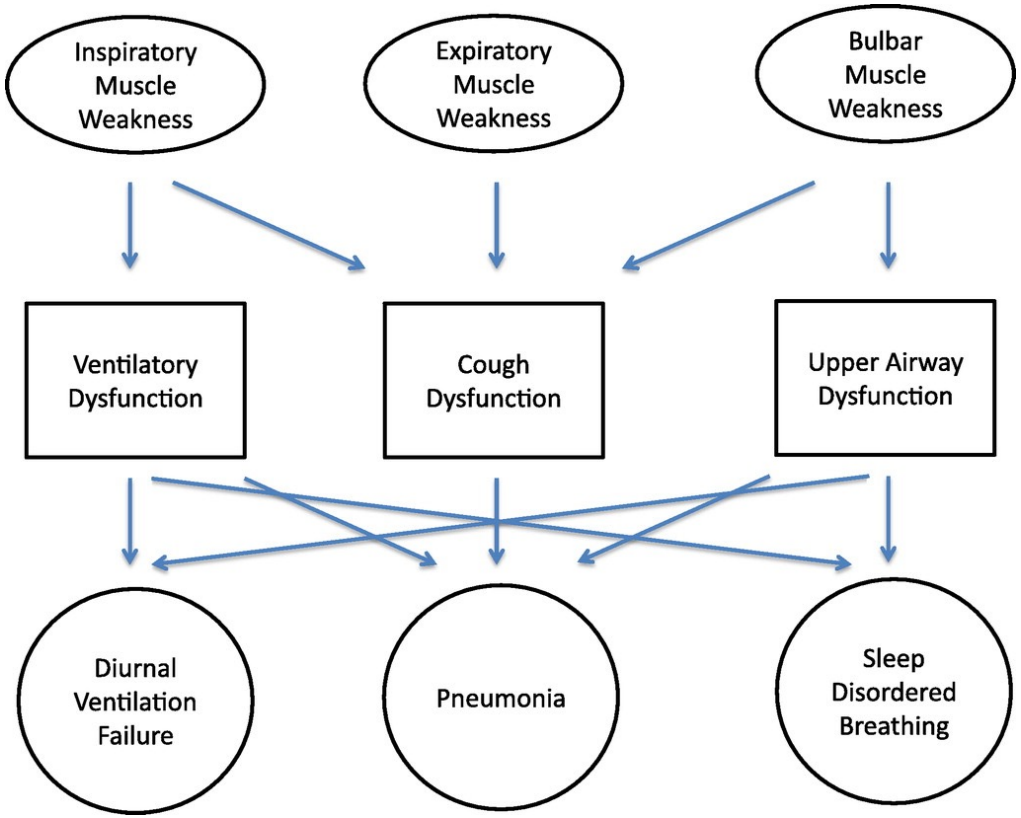
Answer # 2

- 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

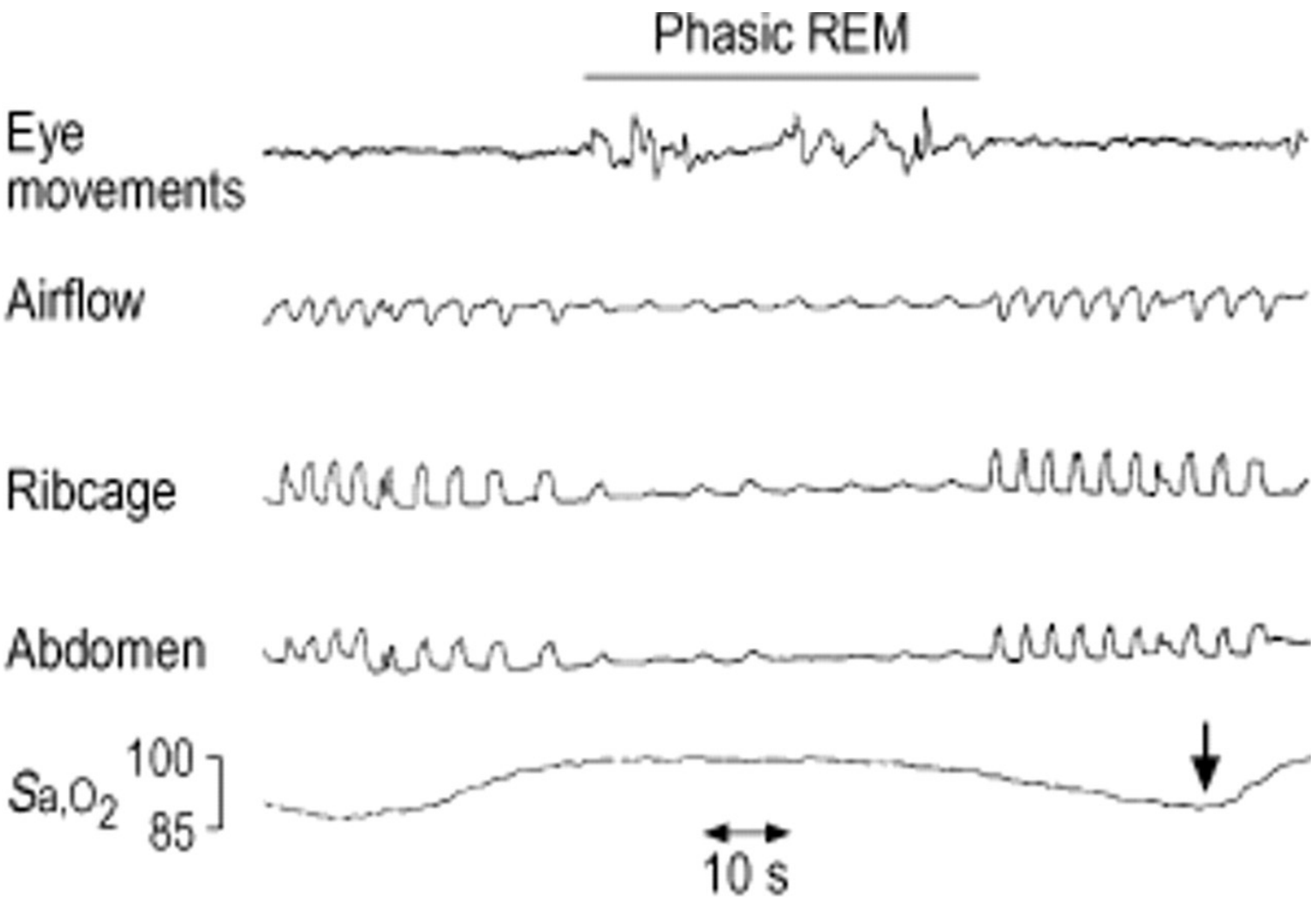


Reduced activity of pharyngeal dilators

Cardiomyopathy

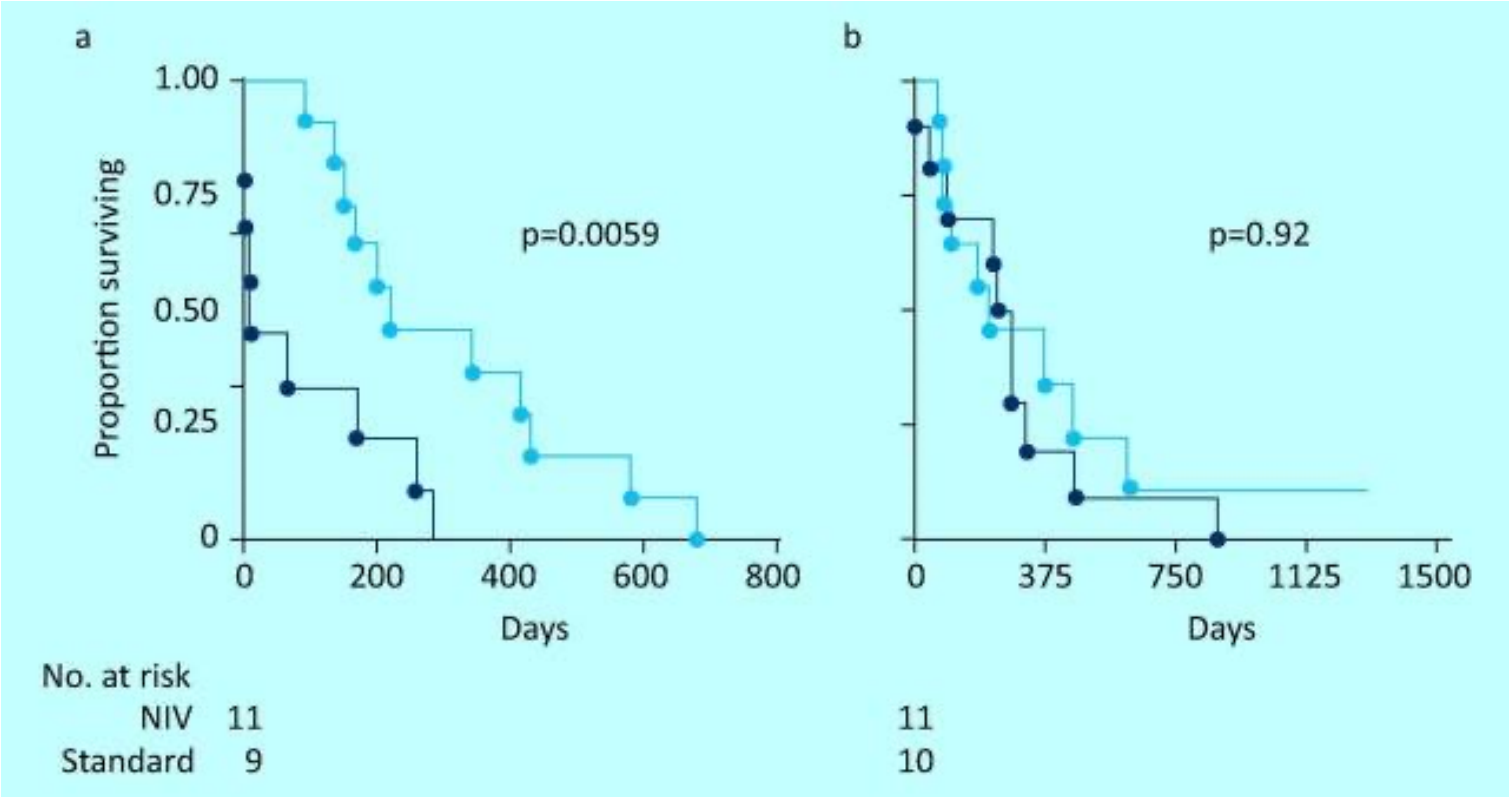
Benditt et al. AJRCCM Vol 187, Iss. 10, pp 1046–1055, May 15, 2013

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
- NIV delays deterioration of respiratory function (FEV1, FVC, MIP/MEP, Sniff nasal insp pressure-SNIP)
- Quality of life questionnaires and Sleep quality questionnaires also show 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 Amyotrophic Lateral Sclerosis. Admission $PaCO_2$ was 75 mmHg, pH 7.25 and HCO_3 34
- Intubated for 5 days but now extubated and successfully treated with Non-Invasive Ventilation 15/5 cmH_2O during sleep (morning $PaCO_2$ now 50 mmHg with a normal pH)
- A bedside spirometry showed an FVC 40% predicted
- 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.

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.

- Daytime measurements may be poor predictor of nocturnal breathing (hypoxia/hypercapnia initially manifest overnight)
- FVC sitting to supine (≥25% fall in VC is 90% sensitive and 79% specific for diaphragm weakness, whereas 40-50% drop suggests bilateral diaphragm paralysis)

Initiating NIV

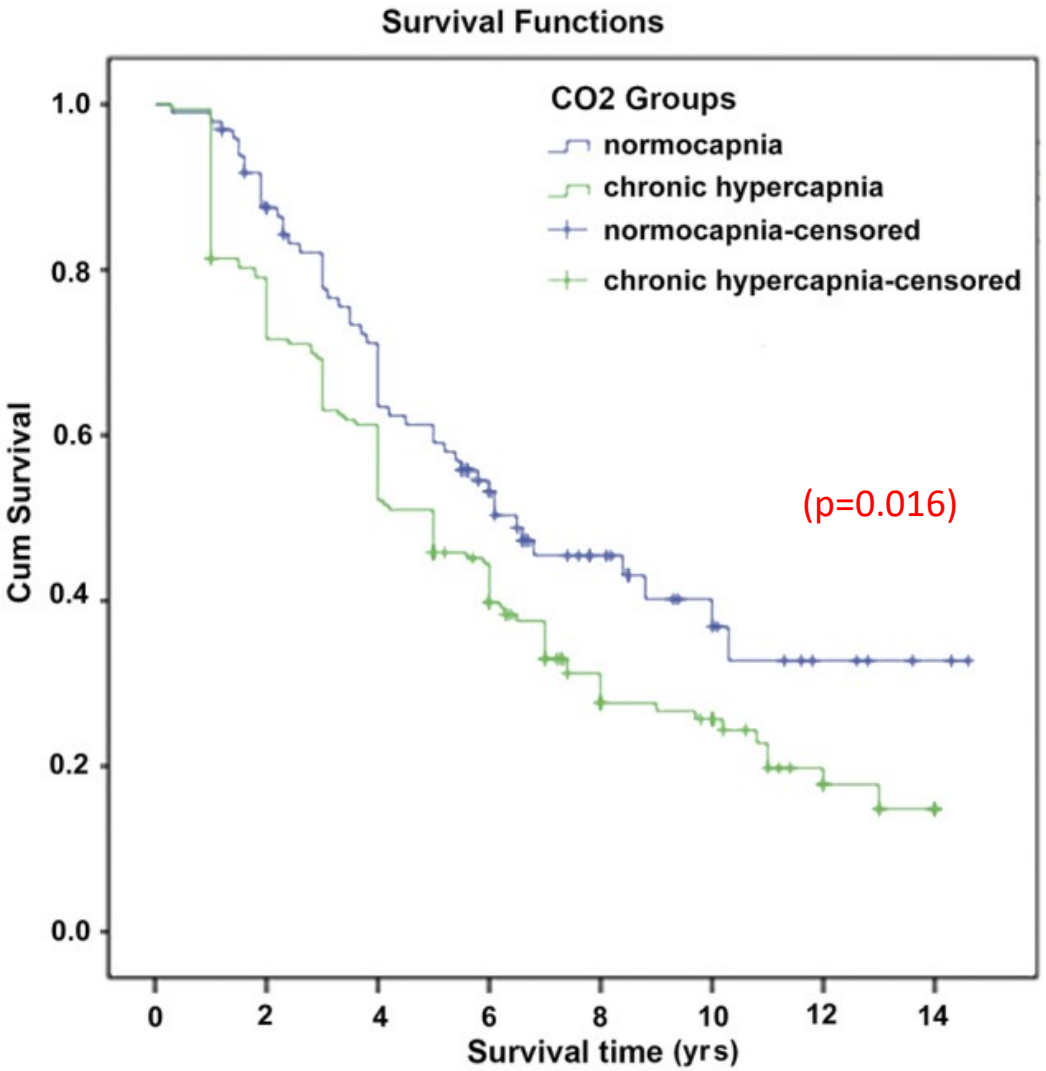
- Where? During in-patient admission, sleep lab or the Outpatient setting.
- Modes of NIV:

BPAP-ST	VAPS (iVAPs or AVAPS)
- IPAP: 8-10 cmH2O - EPAP: 4-5 cmH2O - BR: 2 below spont RR	- EPAP: 4-5 cmH2O - IPAP min: 4-6 cmH2O, gradually increase to reach target tidal volume of 8 ml/kg - IPAP max: IPAP min + 5-6 cmH2O - 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 morning headache, daytime sleepiness overnight oximetry/TcCO2, VBG or HCO3. PSG if patient can't adapt or OSA.
- If daytime ventilation becomes necessary, consider mouthpiece ventilation rather than tracheostomy (Switch to HMV if not already initiated)

SDB and COPD

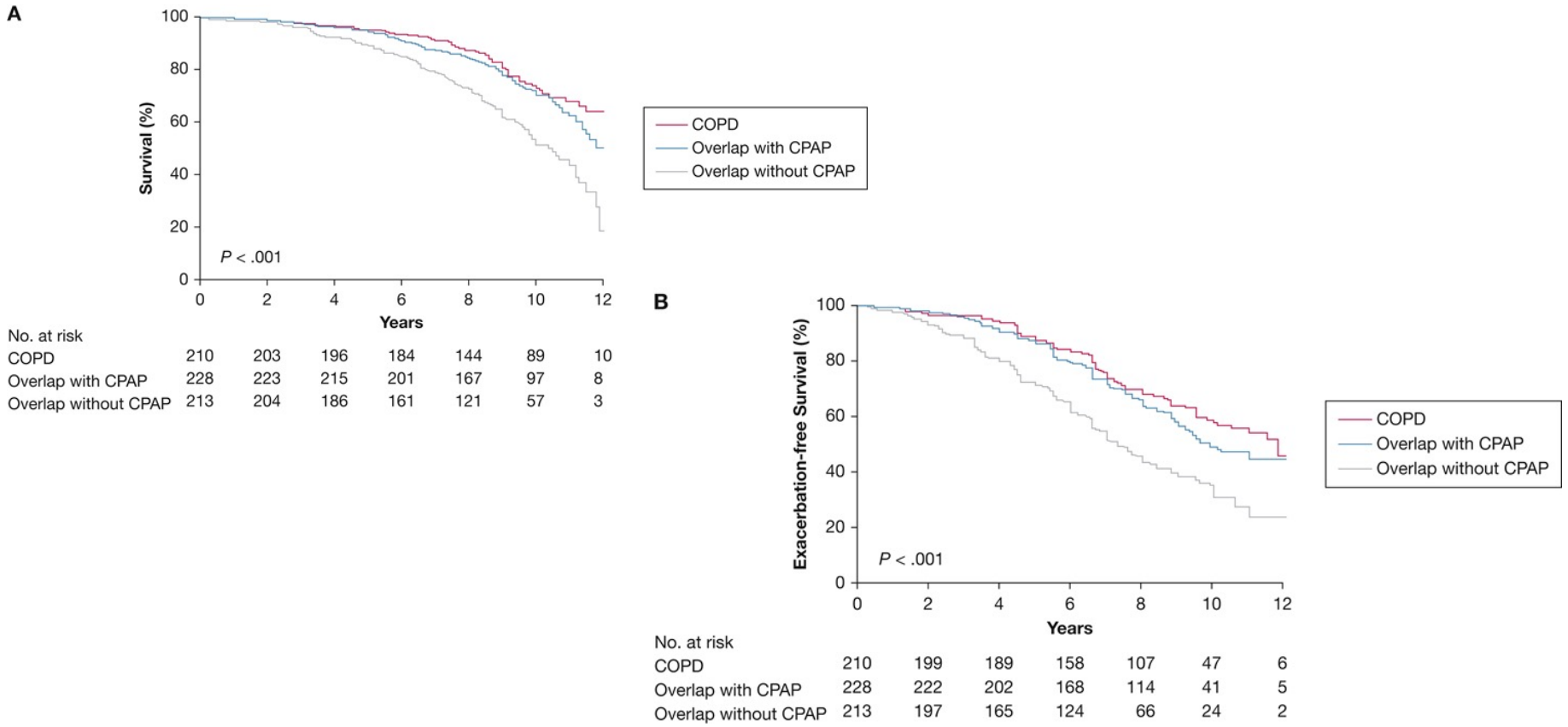
Hypercapnia in COPD and Survival



- Increased Dyspnea
- Decreased QOL
- More frequent hospitalizations

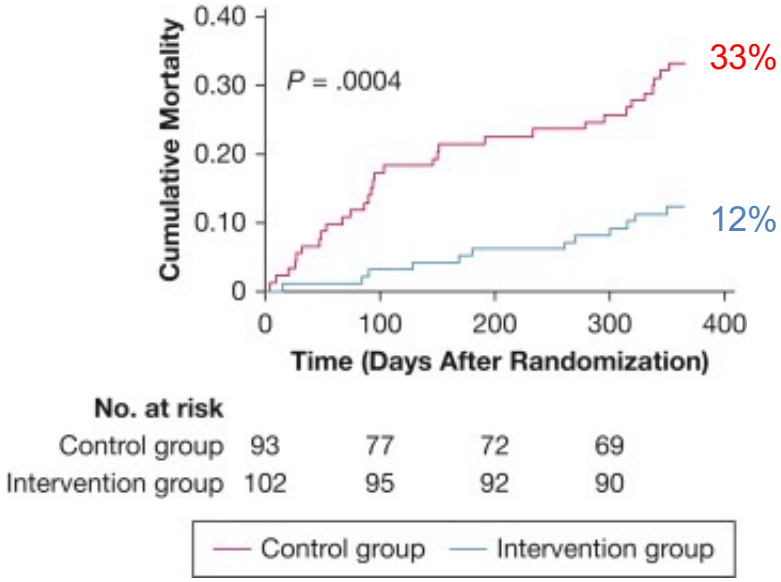
Yang H. et al. BMJ Open 2015;5:e008909

Overlap Syndrome - ↑ Mortality



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 ($PaCO_2$ > 52 and pH > 7.35)
  - HI NIV (IPAP 24-28 cmH_2O with back up rate) aimed to reduce $PaCO_2$ >20% from baseline or below 48, vs standard of care for the control group (home oxygen)
  - Improved 1 year mortality (p=0.0004)
  - Improved $PaCO_2$, ph, SaO_2, FEV1 and HRQOL with HI NIV

Kohnlein, T et al Lancet Respir Med 2014

Question # 4

- A 65 year old cachectic woman with severe COPD (FEV1 25% predicted) comes in with acute on chronic hypoxic respiratory failure.
- ABG: pH 7.15, $PaCO_2$ 82, PaO_2 55, HCO_3 35.
- She was admitted to the ICU and started on BIPAP.
- Her condition has stabilized, and she left the ICU.
- Her ABG now: 7.35, $PaCO_2$ 50, PaO_2 62, HCO_3 32, on 2 lit O_2.
- She is ready to be discharged, you are contemplating home NIV
- The home care company says they need a Polysomnogram (PSG) to get the NIV paid by insurance?

Question # 4

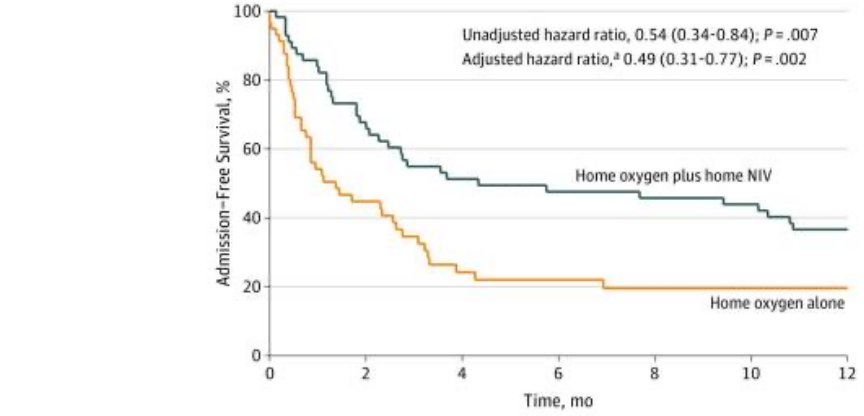
- A. Keep her in the hospital a few more days, continue steroids, antibiotics and inhalers until ABG further improves.
- B. Discharge her home on NIV during sleep and have close (1-2 week) follow up in the office.
- C Discharge to rehab facility in the hopes of her not needing NIV after pulmonary rehab.
- D. Discharge home without NIV and reassess in 2-4 weeks for persistent hypercapnia.

Answer # 4

- A. Keep her in the hospital a few more days, continue steroids, antibiotics and inhalers until ABG further improves.
- B. Discharge her home on NIV during sleep and have close (1-2 week) follow up in the office
- C Discharge to rehab facility in the hopes of her not needing NIV after pulmonary rehab
- D. Discharge home without NIV and reassess in 2-4 weeks for persistent hypercapnia.

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

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 patients with OHS and OSA, CPAP is the initial treatment of choice.
- If persistent hypoventilation despite CPAP, then BIPAP-ST or HMV lower mortality and improve sleep quality.
- Initiate NIV upon discharge after first hospitalization (consider PSG later on)

- In patients with neuromuscular diseases, use of home BIPAP/VAPS is associated with lower mortality and better quality of life.
- Initiate NIV upon discharge after first hospitalization (PSG only if needed)

- In patients with stable hypercapnic COPD, high intensity BIPAP was associated with lower mortality, intubations, hospital admissions, and improved measures of quality of life.
- Initiate NIV if persistent hypercapnia despite medical optimization.

- Head to head comparison in outcomes between BPAP and HMV is lacking.