Brigham and Women's Hospital
Founding Member, Mass General Brigham

Sleep Disordered Breathing, Chronic Hypoventilation and Non-Invasive Ventilation

Khalid Ismail, MD
Ambulatory Medical Director
Division of Pulmonary and Critical Care Medicine
Brigham and Women's Hospital
Instructor of Medicine
Harvard Medical School

CONTINUING MEDICAL EDUCATION
DEPARTMENT OF MEDICINE

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Khalid Ismail, MD

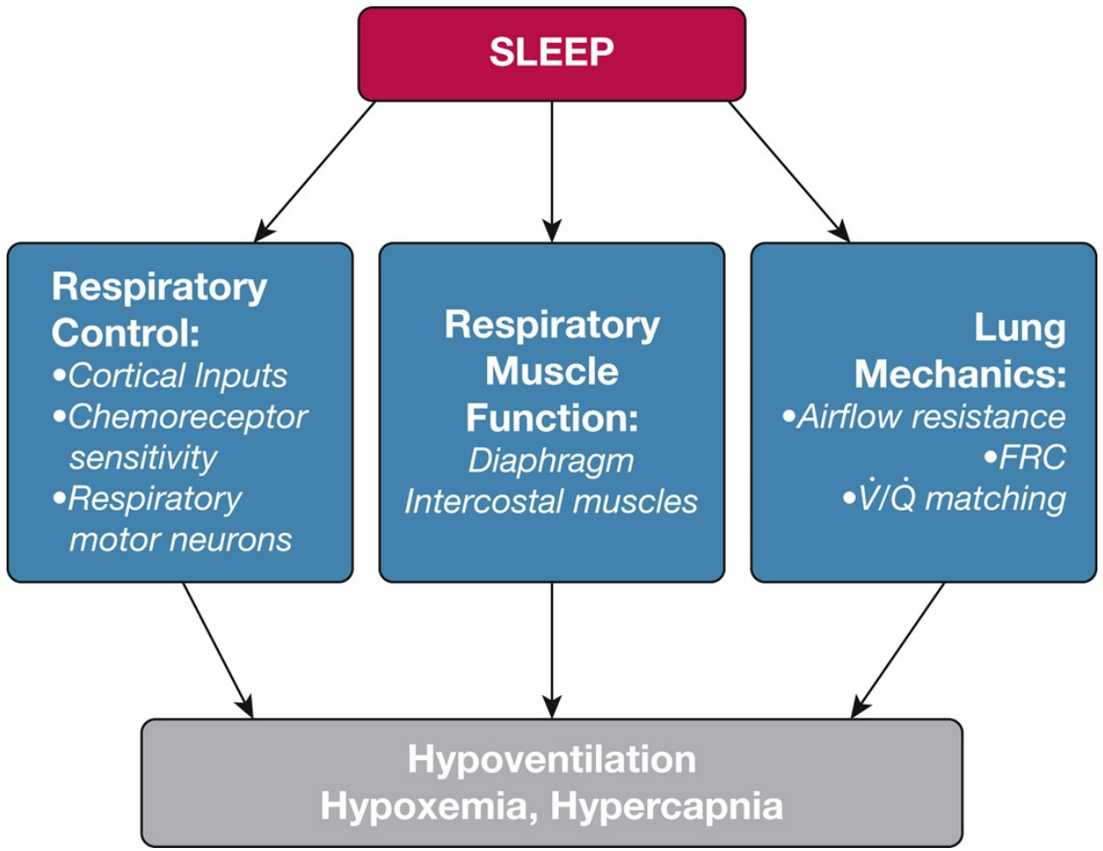
University of Alexandria School of Medicine
Medicine Residency @ St. Joseph Hospital/Northwestern University
Pulmonary and Critical Care Fellowship @ NYU
Sleep Medicine Fellowship @ Lahey Clinic/Tufts Medical School
Instructor of Medicine @ HMS
Joint appointment in Pulmonary/Critical Care, and Division of Sleep Medicine @ BWH

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

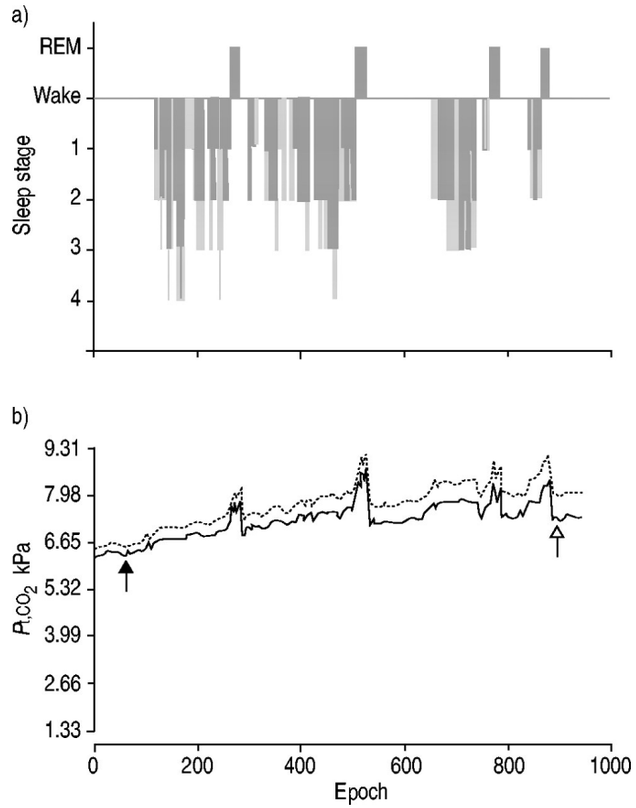
Respiratory changes during Sleep

↓ 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

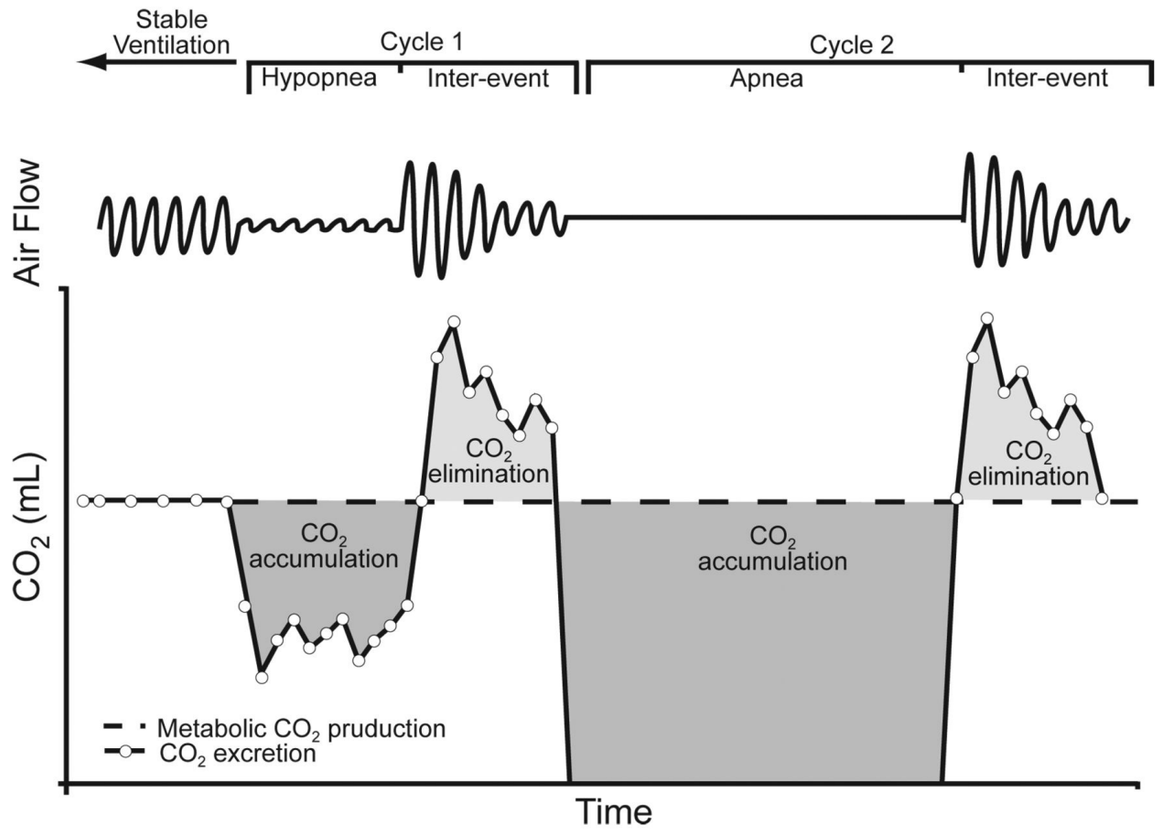
Consequences of REM-atonia



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

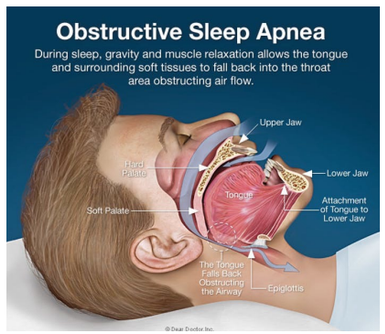
F.J. O'Donoghue et al. Eur Respir J 2003;21:977-984

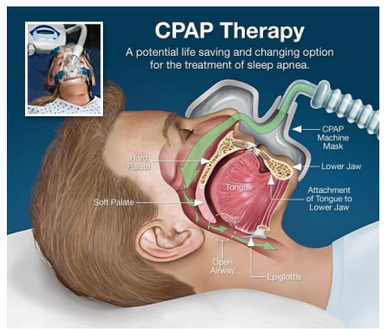
Obstructive Sleep Apnea and Hypoventilation

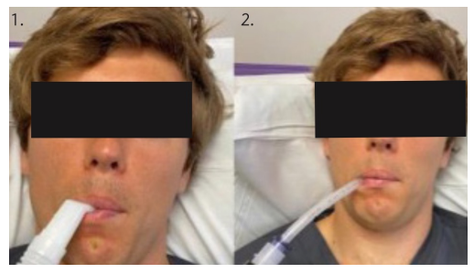


Berger et al. J Appl Physiol 2000;88(1):257-264

Non-invasive Positive Pressure Ventilation







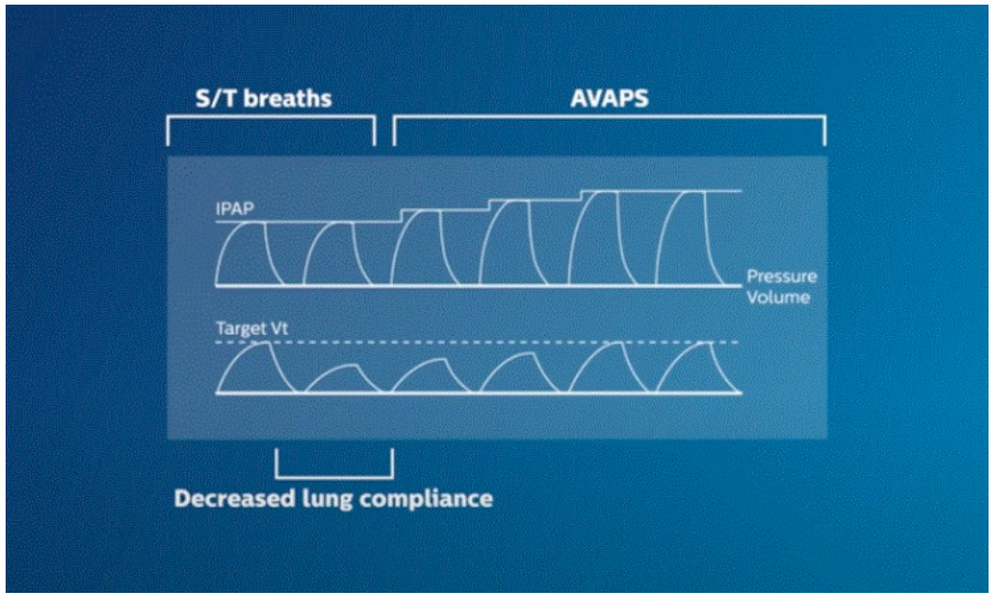
Respiratory Assist Devices

Home Mechanical Ventilators

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 pattern (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 variation in ventilation
- Positional variation in ventilation
- Fluid shifts/changes in lung compliance seen in OHS
- Progression of disease seen in ALS
- Intermittent exacerbations seen in COPD

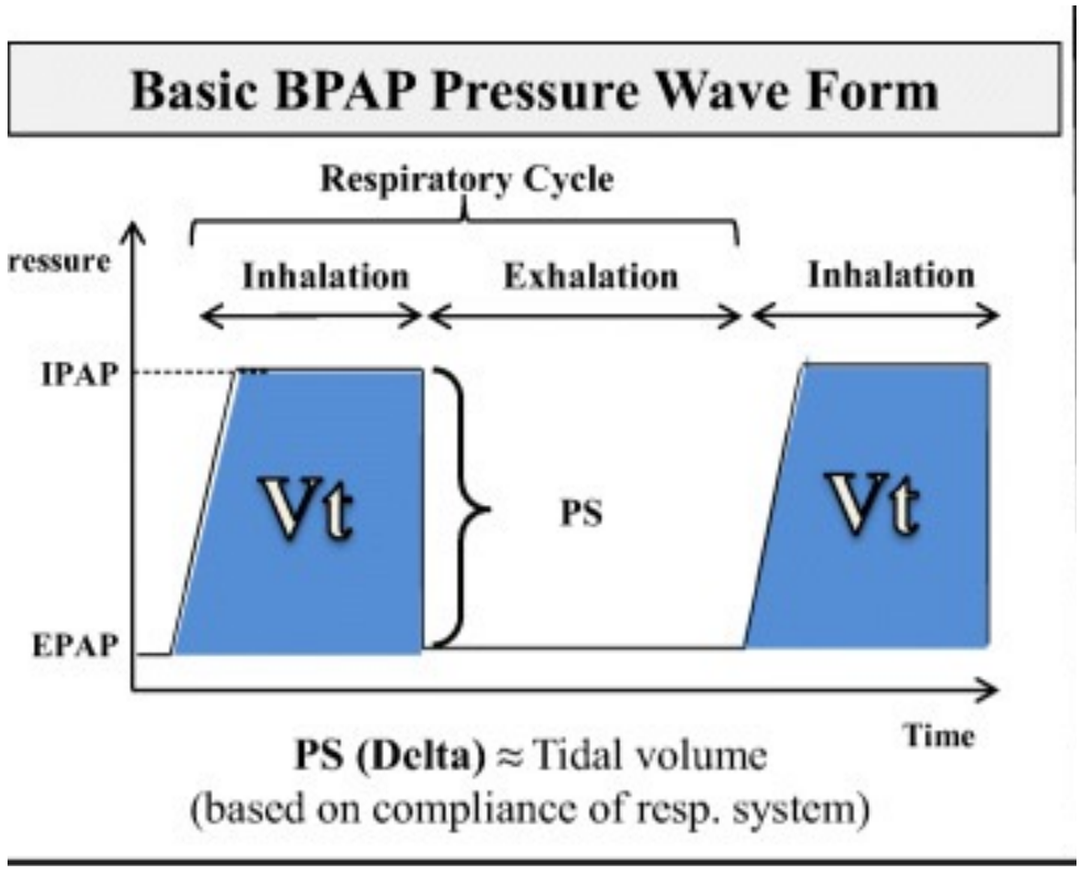
Non-Invasive Ventilation

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

Home Mechanical Ventilators - Comparison Chart

	Ventilator Details	Philips Trilogy 100	Philips Trilogy EVO	Resmed Astral 100	Resmed Astral 150	Breas Vivo 45LS	Breas Vivo 50	Breas Vivo 65	Lowenstein Luisa	Ventec-VOCSN	Vyaire LTV 1150	Inogen TAV	Hillrom Life2000
NIV	Target Tidal Volum	AVAPS-AE	AVAPS-AE	iVAPS-AE	iVAPS-AE	PSV(TgV) - AE	PSV(TgV) - AE	PSV(TgV) - AE	TTV-VAPS-AE	Vol. Targeted - PS	N/A	Tidal Assist	3 Activity Levels
NIV	Target Minute Ventilation	N/A	N/A	✓	✓	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
NIV		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A	N/A
	Special Feature	**AVAPS-AE** Average Volume Assured Pressure Support with Auto EPAP	**AVAPS-AE** Average Volume Assured Pressure Support with Auto EPAP	**iVAPS-AE** Intelligent Volume Assured Pressure Support with auto EPAP	**iVAPS-AE** Intelligent Volume Assured Pressure Support with auto EPAP	**PSV(TgV) - AE** Pressure Support Ventilation (Target Tidal Volume) with Auto EPAP	**PSV(TgV) - AE** Pressure Support Ventilation (Target Tidal Volume) with Auto EPAP	**PSV(TgV) - AE** Pressure Support Ventilation (Target Tidal Volume) with Auto EPAP	**TTV-VAPS-AE, High-Flow Therapy** Targeted Tidal Volume-Vol Assured Pressure Support-Auto EPAP	**5 Therapies in 1** Vent, Oxygen, CoughAssist, Suction and Nebulizer	**SBT** Spontaneous Breathing Trial Mode	**Ambulatory Ventilation** with 5 levels of flow and proprietary interface	**Ambulatory Ventilation** with 3 activity level settings and proprietary interface
	Billing Code	E0465, E0466	E0465, E0466	E0465, E0466	E0465, E0466	E0465, E0466	E0465, E0466	E0465, E0466	E0465, E0466	E0467 script must include at least 1 of the integrated	E0465, E0466	N/A	E0466
	Patient Selection	COPD, NMD, RTD Pediatric/Adult	COPD, NMD, RTD Pediatric/Adult	COPD, NMD, RTD Pediatric/Adult	COPD, NMD, RTD Pediatric/Adult	COPD, NMD, RTD Pediatric/Adul	COPD, NMD, RTD Adult	COPD, NMD, RTD Pediatric/Adult	COPD, NMD, RTD Pediatric/Adult	COPD, NMD, RTD Pediatric/Adult	COPD, RTD Pediatric/Adult	COPD, RTD Adult	COPD Adult
	Weight	11 lbs	11.5 lbs	7.1 lbs	7.1 lbs	5 lbs 4oz	11 lbs 7 oz	11 lbs 14oz	8.3 lbs	up to 18.3 lbs	14.5 lbs	4.7 oz.	1 lb
	Battery Backup	Internal: 3 hrs Detacheable: 3 hrs	Internal: 7.5 hrs Detacheable	Internal: 8 hrs External: up to 24	Internal: 8 hrs External: up to 25	Internal: 2.5 hrs Click-On 6.5 hrs	Internal: 4 hrs Click-On: 8hrs	Internal: 4 hrs Click-On: 8 hrs	Internal: 6 hrs External: up to 18 hrs	Internal: 9 hrs.	5 hrs with SprintPack Dual battery	90 days at 8hrs/day	Internal: 4 hrs
	O2 Input	Up to 15 l/min	Up to 30 l/min	Up to 30 l/min	Up to 30 l/min	Up to 15 l/min	Up to 15 l/min	Up to 15 l/min	Up to 30 l/min	Up to 20 l/min	Up to 80 l/min	High Pressure O2 source	Up to 10 l/min and High Pressure O2 Source
	Compliance Monitoring	✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A	N/A	N/A
	Display Monitoring	SpO2 optional	Optional SpO2, FiO2	Optional SpO2, FiO2	Optional SpO2, FiO2	SpO2, FiO2, EtCO2	SpO2, FiO2, EtCO2	SpO2, FiO2, EtCO2	Optional SpO2, FiO2	FiO2	N/A	N/A	N/A
	Software	Care Orchestrator	Care Orchestrator	Airview	Airview	EveryWare	EverWare	EveryWare	Pending	Multi-View	Hours Only	N/A	Hours only
	Download via...	Wireless Hub or SD CARD	Wireless Hub or SD CARD	Attached Modem	Attached Modem	Attached Modem	Attached Modem	Attached Modem	USB	USB, Wireless	Hyperlink with Cable to PC	N/A	N/A
	Patient Weight	>5kg.	>2.5 kg	>5kg.	>5kg.	>5kg.	>10kg.	>5kg.	Adult	>5kg.	>5kg.	Adult	Adult
	Single Circuit with Leak	✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A	N/A	N/A
	Single Circuit with Valve	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	N/A	N/A
	Dual Limb Circuit	N/A	✓	N/A	✓	N/A	N/A	✓	✓	N/A	N/A	N/A	N/A

Bilevel Positive Airway Pressure



Selim et al, Neurotherapeutics (2021) 18:81–90

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.

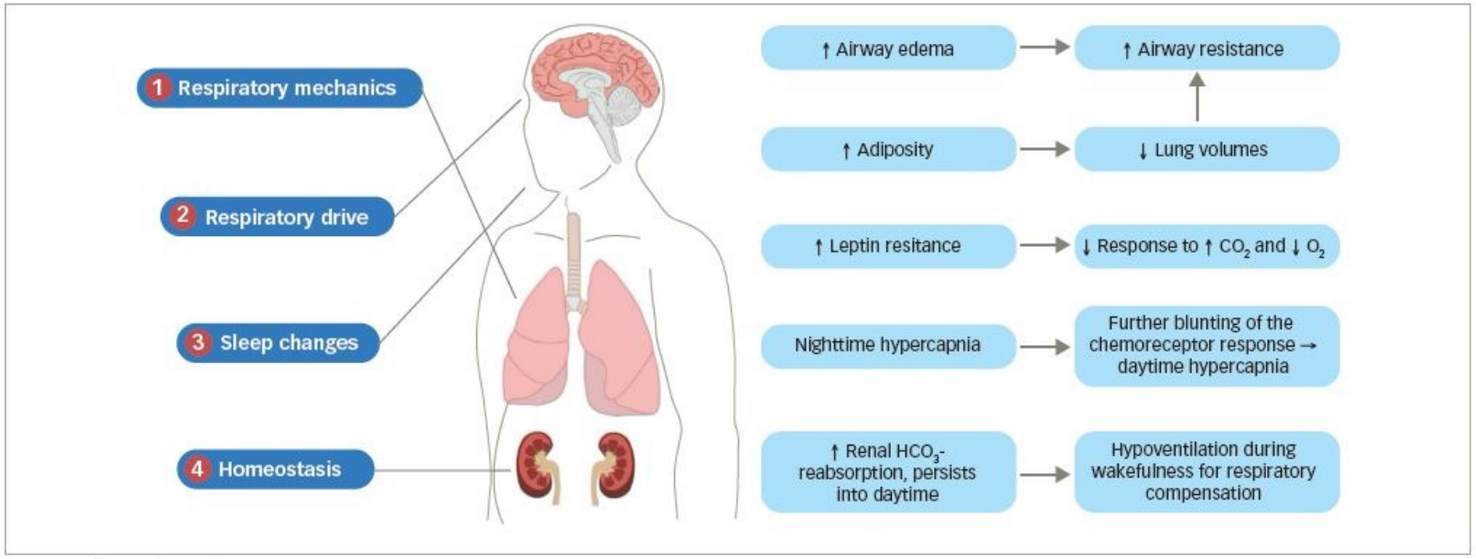
OHS Phenotypes

- 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)

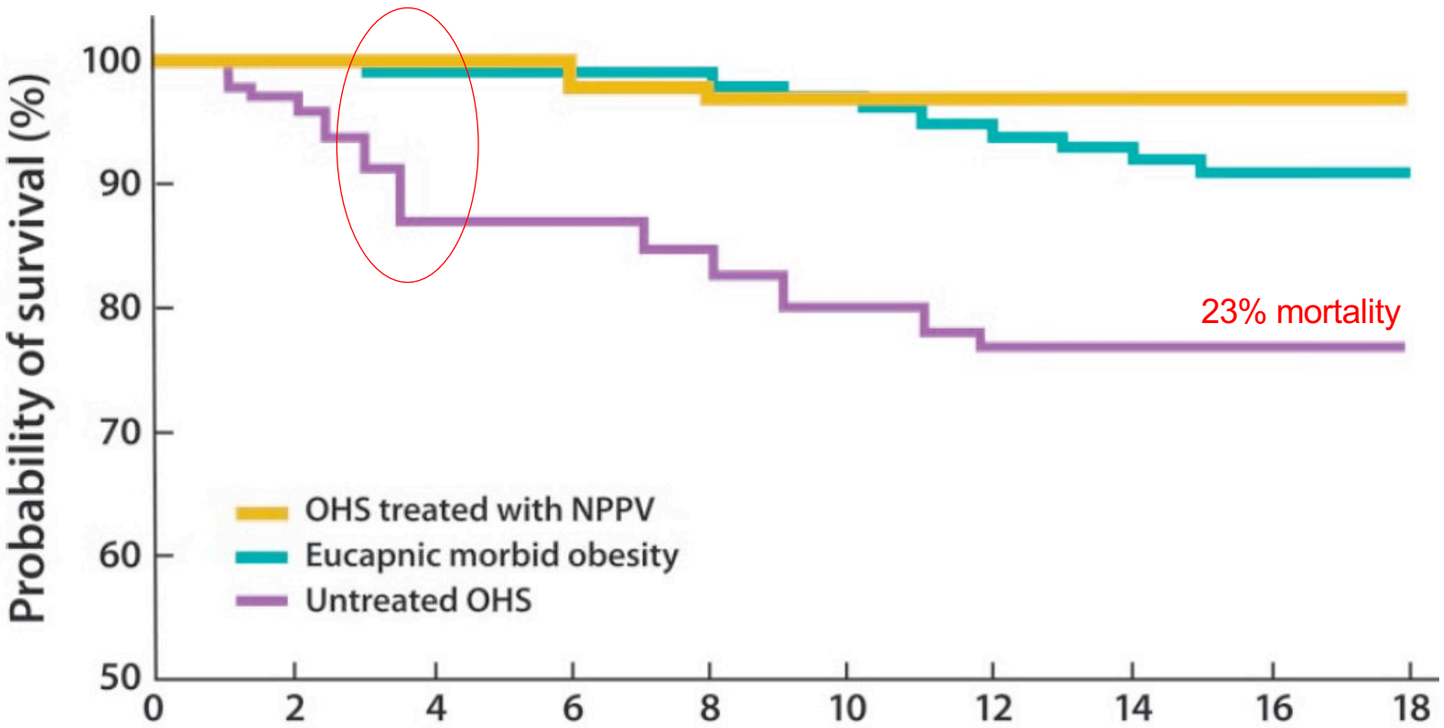
Masa et al. Am J Respir Crit Care Med 2015. Berry et al. J Clin Sleep Med 2012

Pathophysiology



Greer et al. US Respiratory and Pulmonary Diseases. 2020

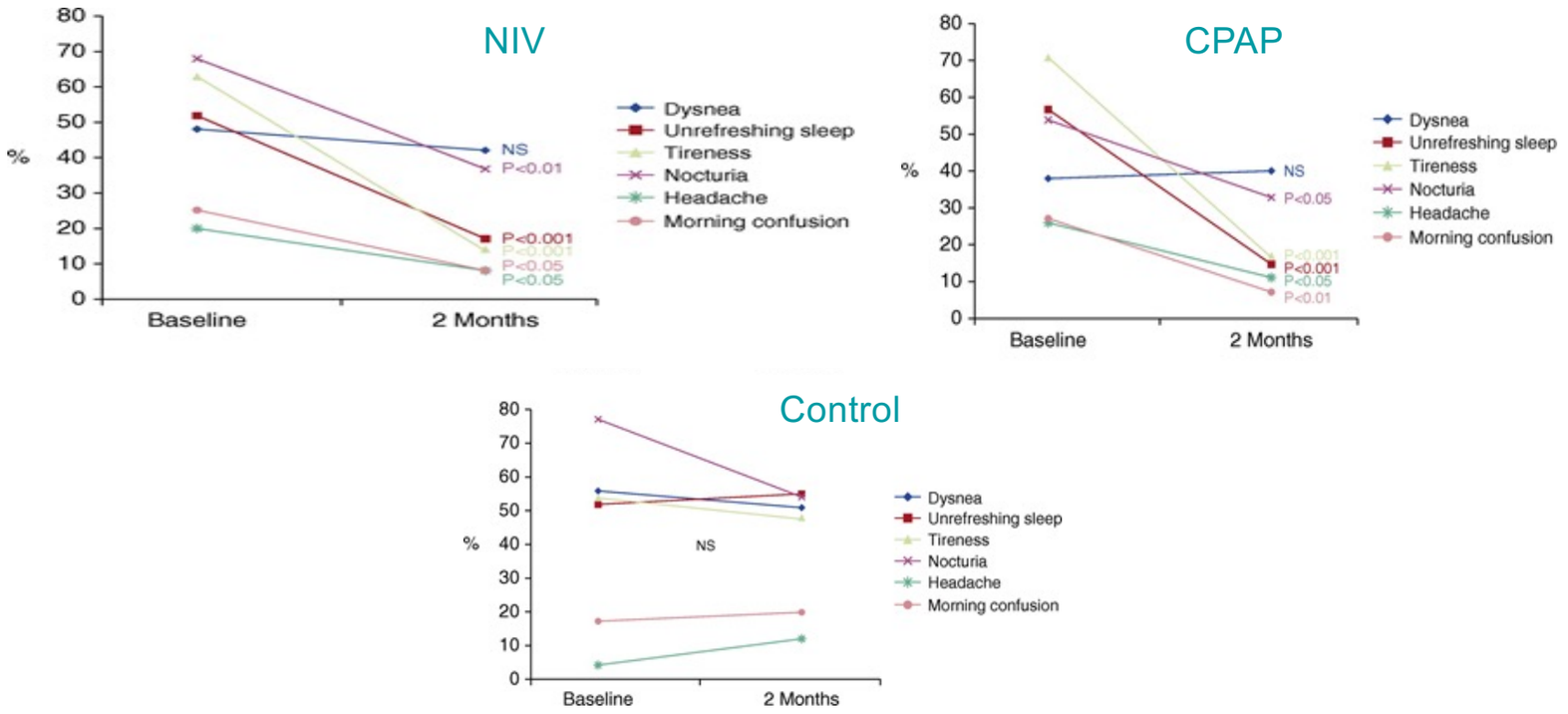
OHS Mortality / NIV Survival



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

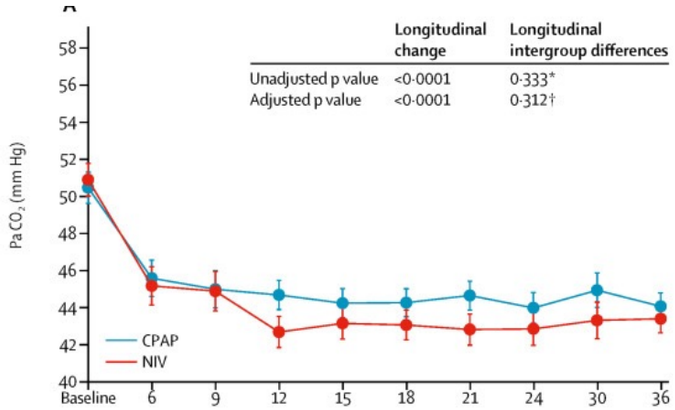
Pickwick Study (N=221)

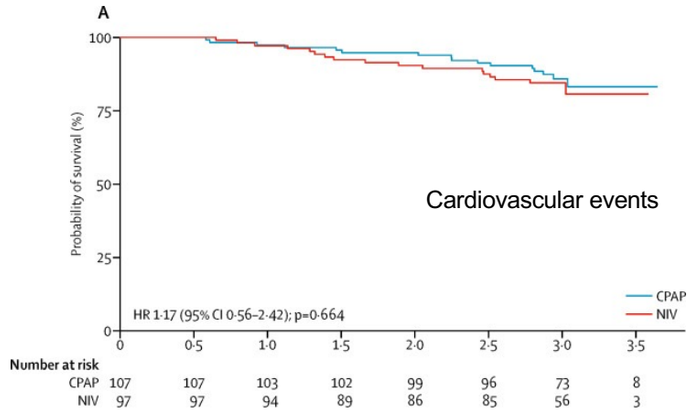


Masa et al. AJRCCM Vol 192;1,July 1 2015

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

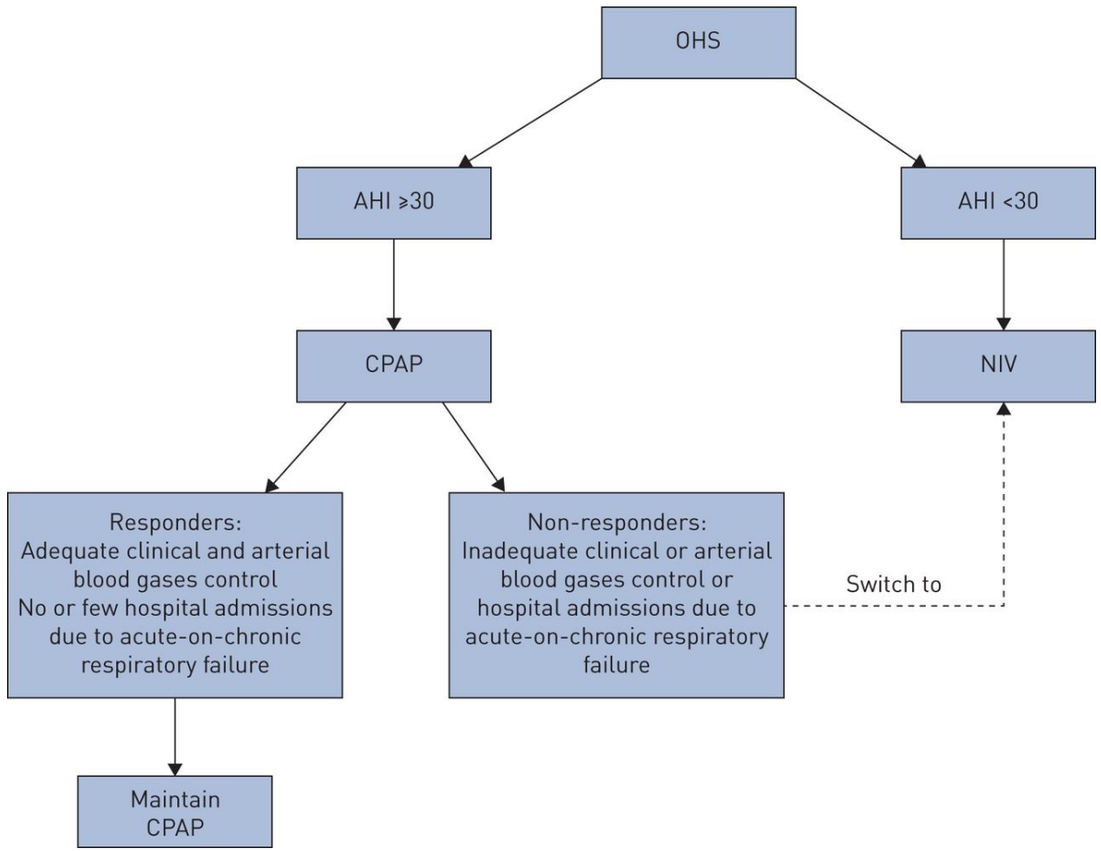
Long-Term Pickwick Randomized Controlled Clinical Trial (N=221)





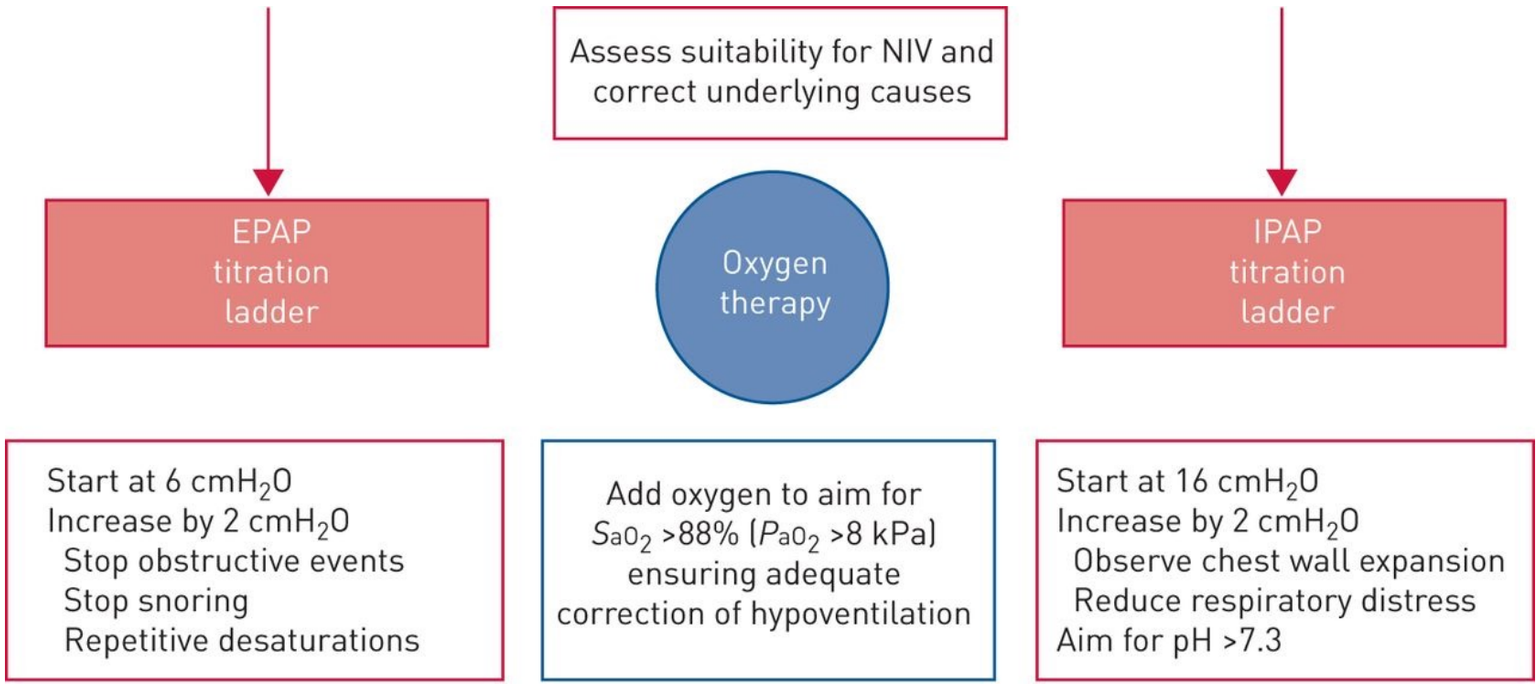
Masa et al. The Lancet, Vol 393, issue 10182, page 17215. Apr 27, 2019

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.
You are contemplating initiation of home NIV.
The patient is all ready for discharge, what should you do?

Go to **www.menti.com** and use the code **2208 5976**

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. Keep the patient one more night and obtain bedside Spirometry.
D. Discharge the patient without NIV and obtain a PSG as soon as you can.

Go to **www.menti.com** and use the code **2208 5976**

Question #1

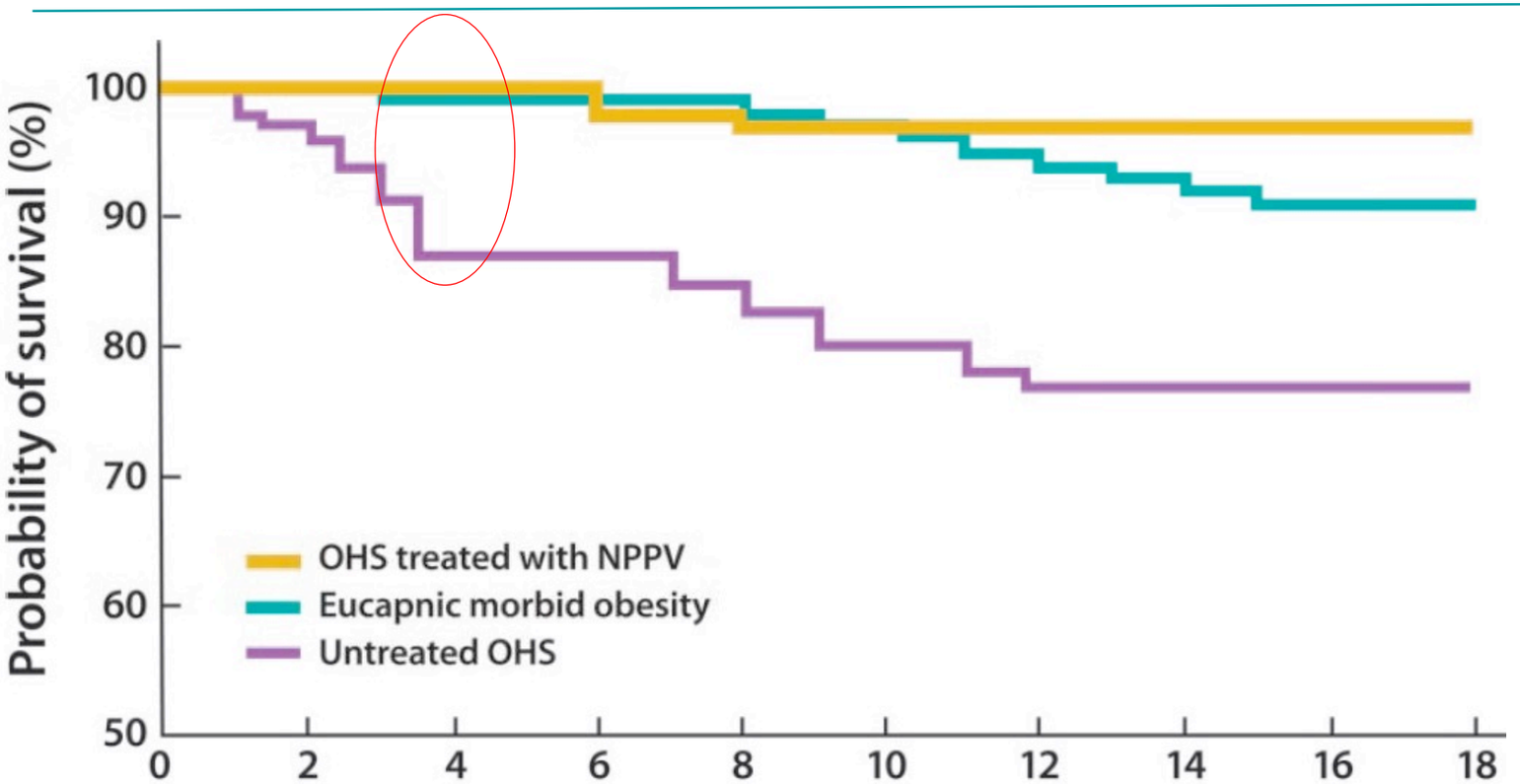
A. Use the patient's diagnosis and ABG results to qualify for NIV, and order an outpatient attended PSG in 2-3 months.
(patient already meets criteria for OHS)

B. Keep the patient one more night and get a portable sleep study off NIV

C. Keep the patient one more night and obtain bedside Spirometry.

D. Discharge the patient without NIV and obtain a PSG as soon as you can.

Benefit of Initiation upon discharge



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

- 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)
- 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
- 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)

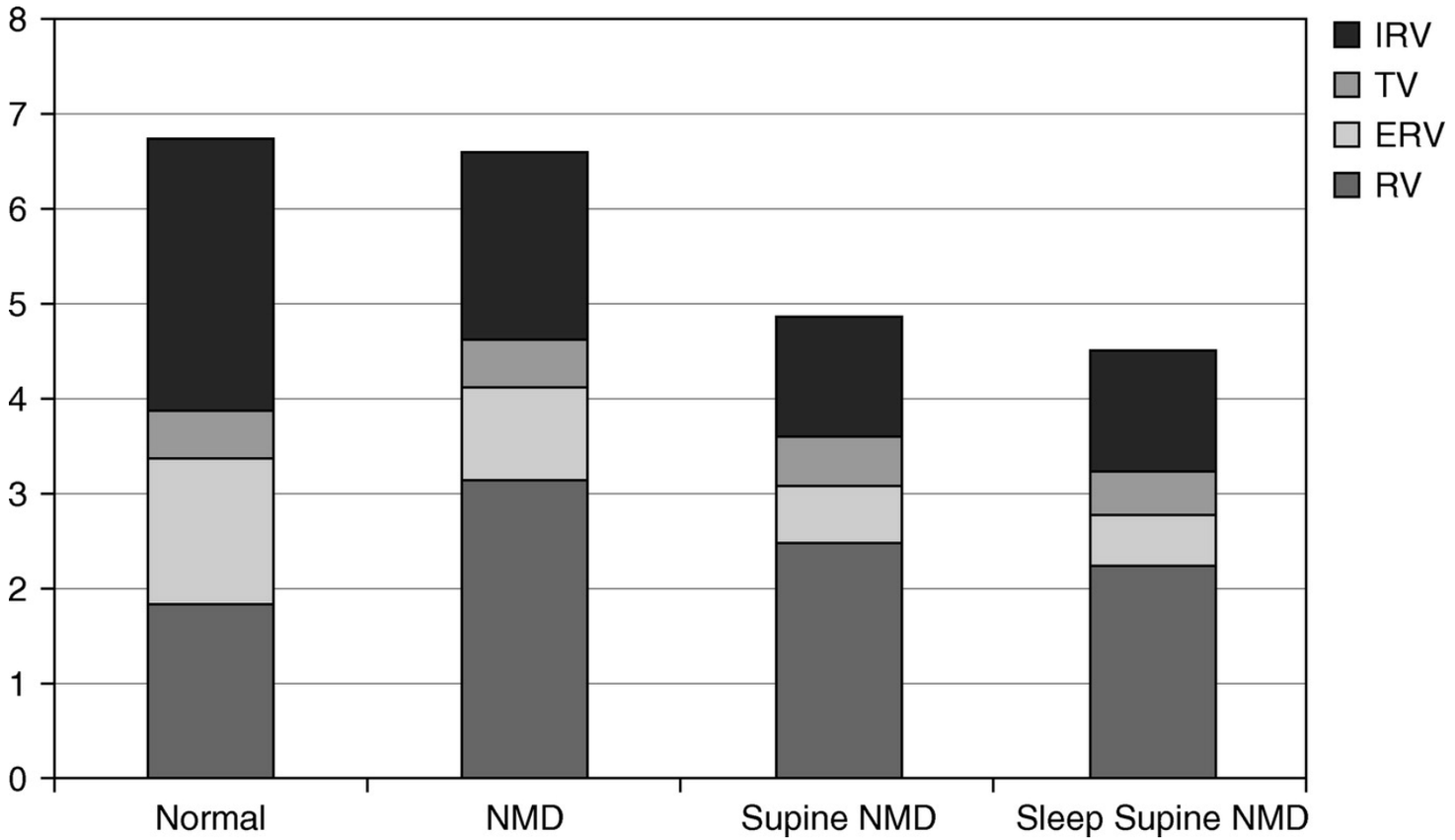
Motor Neuron
- Post-polio syndrome (very slowly progressive)
- Amyotrophic lateral sclerosis (rapidly progressive)
- Spinal muscular atrophy (progressive)

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

Go to **www.menti.com** and use the code **2208 5976**

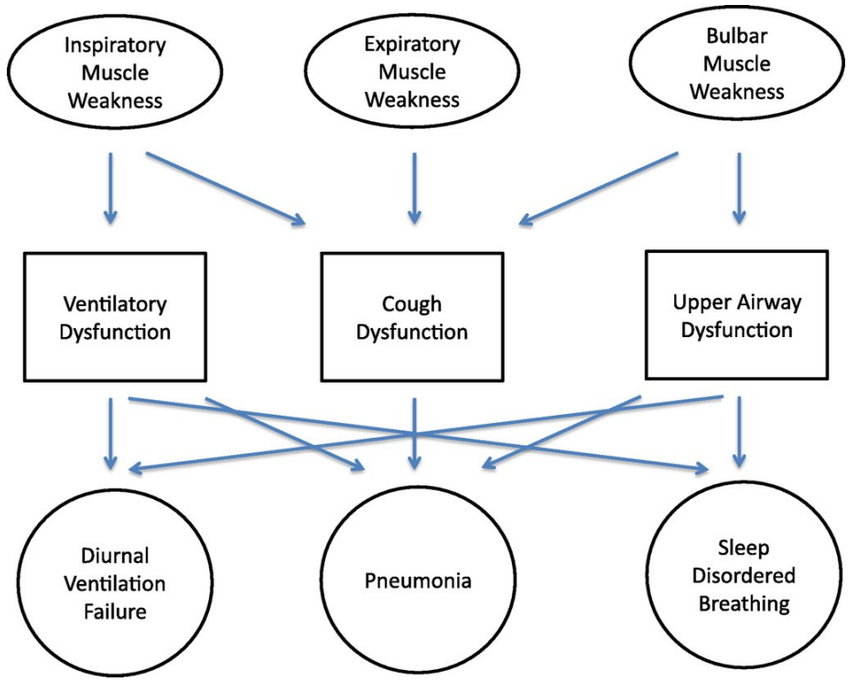
Answer # 2

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

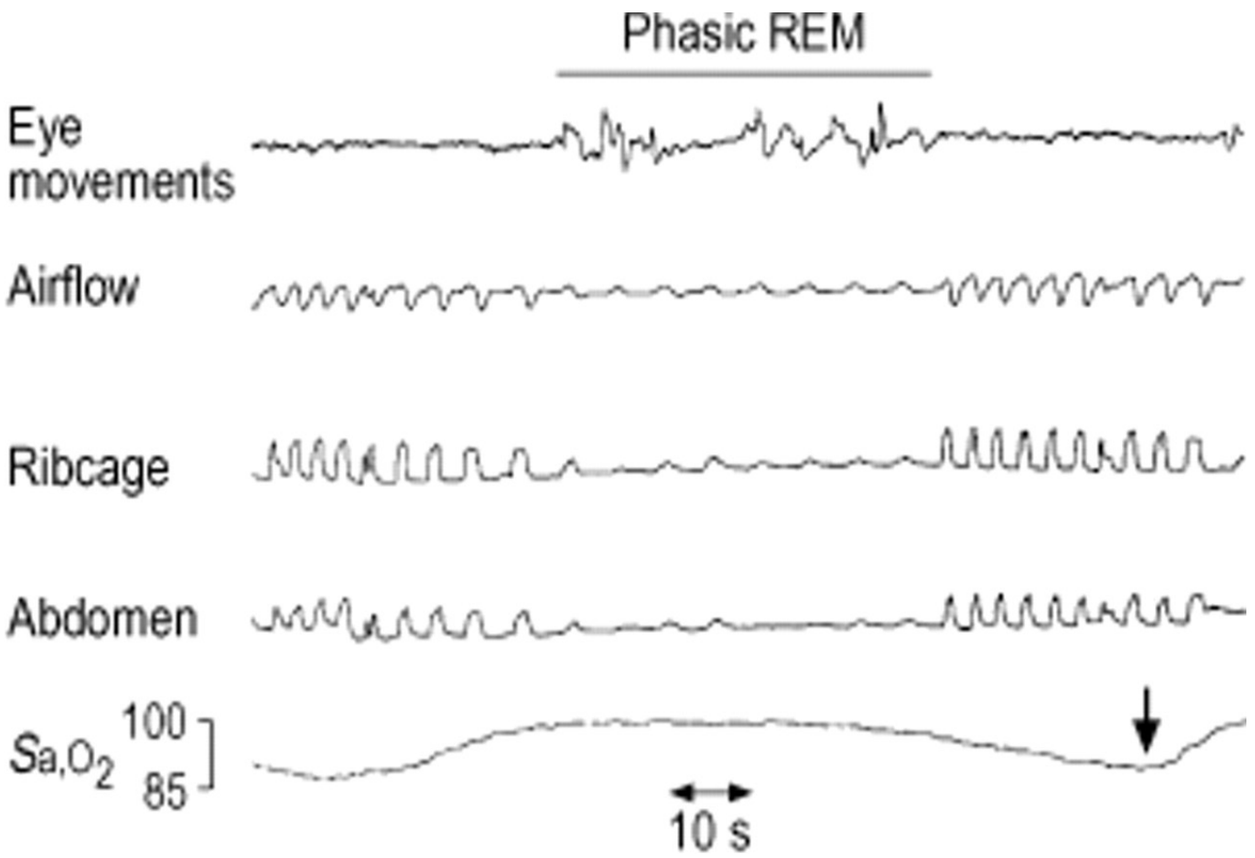
(multiple mechanisms, overnight oximetry might not explain the whole picture)

Neuromuscular Disease and respiratory pathophysiology



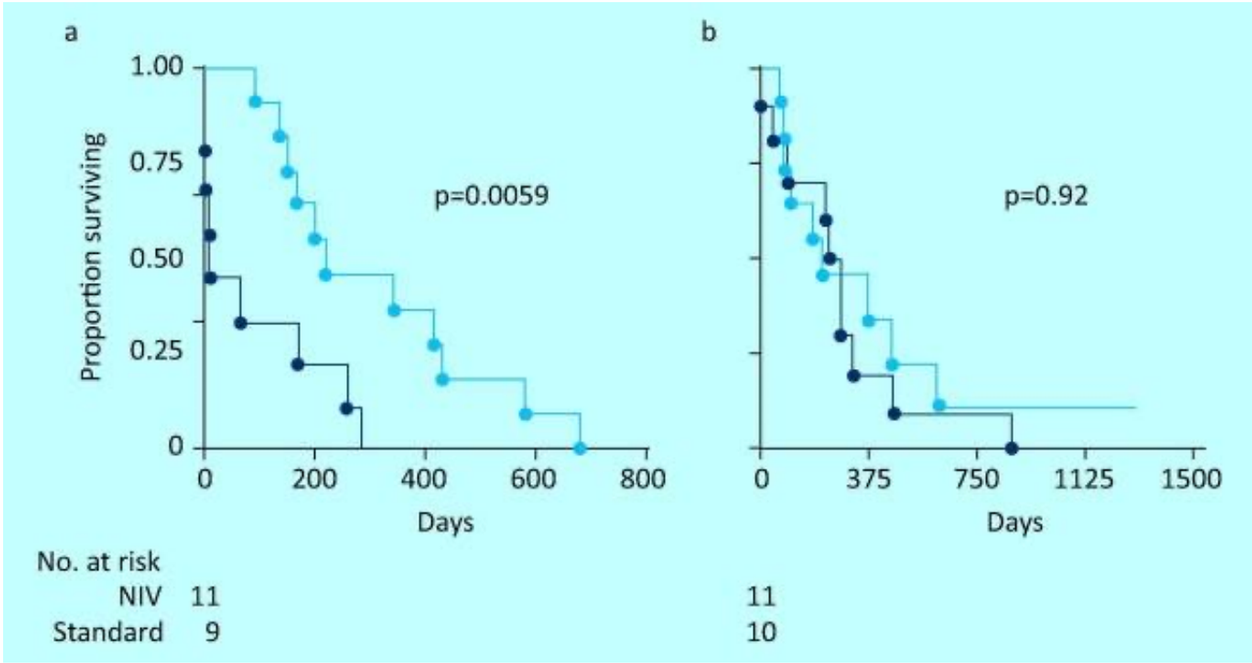
Benditt et al. AJRCCM Vol 187, Iss. 10, pp 1046–1055, May 15, 2013

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 with ALS, admitted with pneumonia, acute on chronic hypercapnia.
Admission $PaCO_2$ was 75 mmHg, pH 7.25 and HCO_3 34
Intubated for 5 days but now extubated and successfully treated with BiPAP 15/5 cmH_2O during sleep.
Morning $PaCO_2$ now is 50 mmHg with a normal pH, and the patient is much more comfortable with more daytime energy.
A bedside spirometry showed an FVC 40% predicted.
You are contemplating sending this patient home on NIV.
The patient is all ready for discharge, what should you do?

Go to **www.menti.com** and use the code **2208 5976**

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.

Go to **www.menti.com** and use the code **2208 5976**

Question # 3

A. Use the patient's current diagnosis and ABG results to qualify for NIV
(Patient already meets criteria for initiation of NIV in ALS)

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

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
- FVC < 50% predicted AND COPD is not contributing to symptoms.

Initiating NIV

When? Symptoms (orthopnea, daytime sleepiness) Vs. PCO2 and PFTs

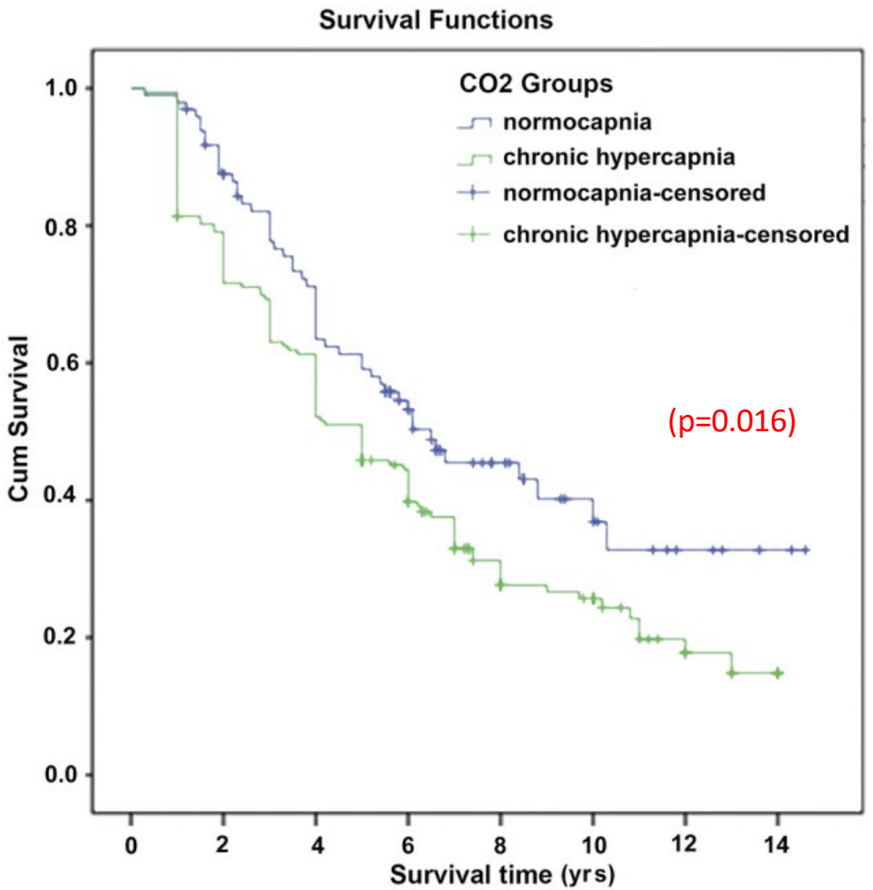
Where? During in-patient admission, outpatient setting or sleep lab

BPAP-ST	VAPS (iVAPs or AVAPS)
- IPAP: 8-10 cmH2O - EPAP: 4-5 cmH2O - BR: 2 below spont RR - Adjust IPAP by 1-2 cmH2O to alleviate dyspnea, decrease RR, and increase tidal volume	- 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 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

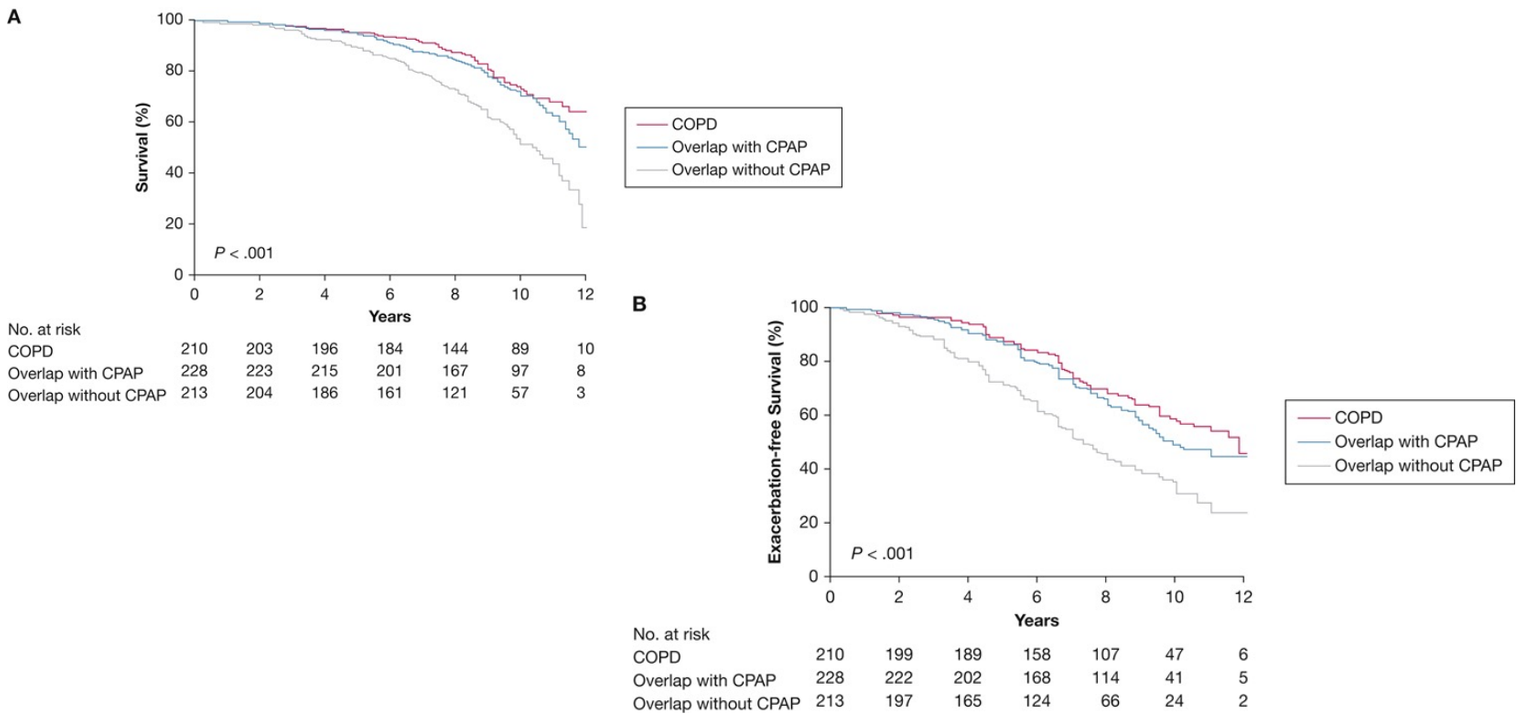
Hypercapnia in COPD and Survival



- Increased Dyspnea
- Decreased QOL
- More frequent hospitalizations

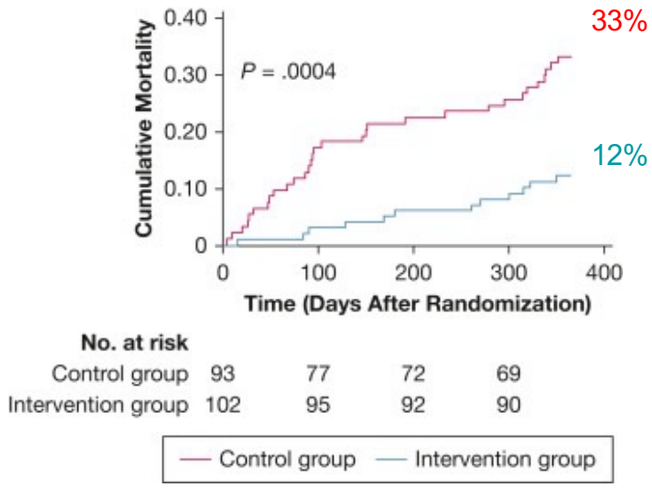
Yang H. et al. BMJ Open 2015;5:e008909

Overlap Syndrome - ↑ Mortality
(COPD + OSA, 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



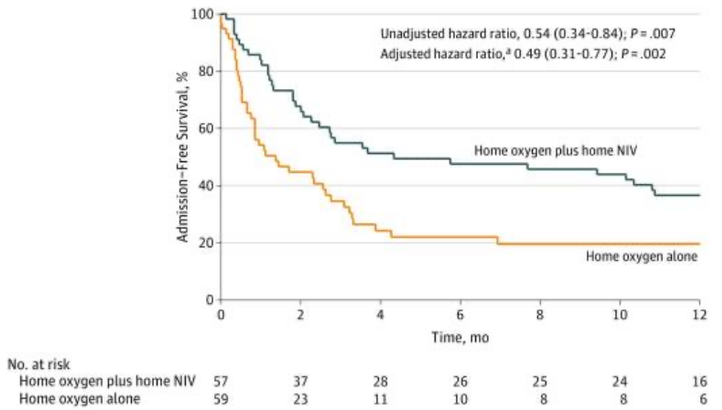
Long Term RCT (N = 201): COPD Gold IV ($PaCO_2$ > 52 and pH > 7.35, stable hypercapnic)

- HI NIV (IPAP 24-28 cmH_2O with back up rate) aimed to reduce $PaCO_2$ to below 48, or >20% from baseline, 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

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 > 52) 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

- 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)
- 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.
- 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
  - OR, Documentation of Chronic respiratory failure secondary to COPD

Take Home Points

- In OHS, both CPAP and NIV improve survival, in addition to sleep quality, and daytime symptoms.
- In ambulatory patients with stable OHS and OSA, CPAP is preferred.
- Use NIV if non obstructive OHS or persistent hypoventilation despite CPAP.
- 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 failing empiric Rx)

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

References

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