

# Non-Invasive Ventilation (NIV) in Chronic Obstructive Pulmonary Disease (COPD)

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# Disclosures

- I have no disclosure at this time

# Objectives

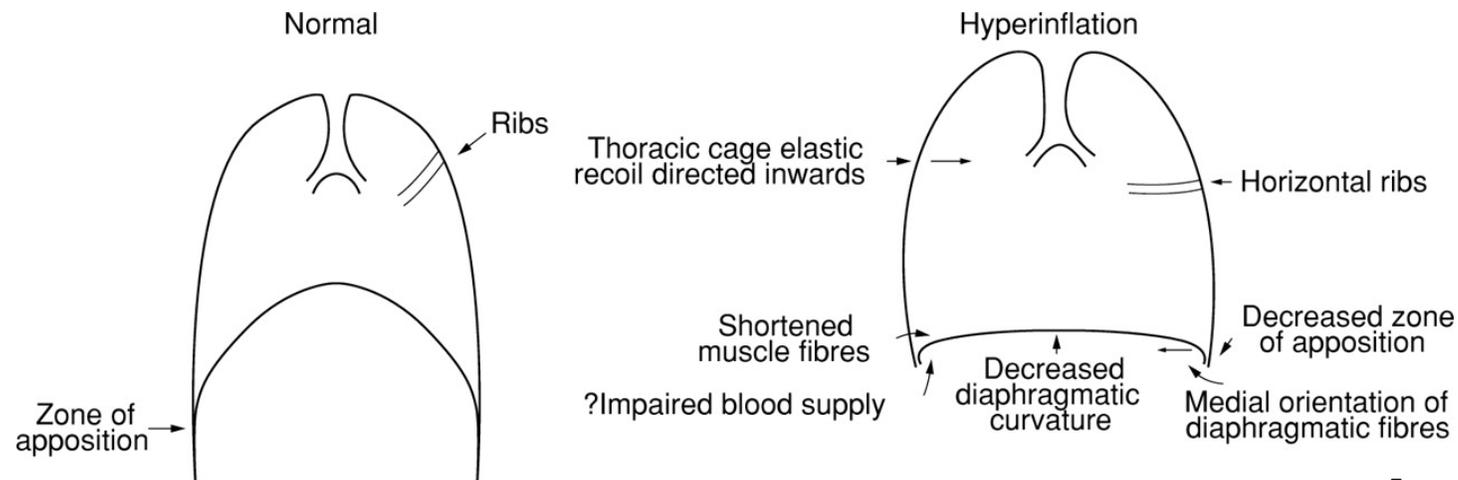
- Epidemiology and Physiology
- Early NIV failures
- Change in the Paradigm: High Intensity Pressure Support
- How to actually treat your patients

# COPD Burden

- COPD is the 4<sup>th</sup> leading cause of death in the US
- 3<sup>rd</sup> most common cause of hospital readmission among Medicare beneficiaries
- High burden of disease both in quality of life and financially, which contribute a strain on the current US healthcare system
- This lead to exploration beyond traditional pharmacotherapies, pulmonary rehab and oxygen, specifically the use of noninvasive positive pressure ventilation (NIV)

# Hypothesis

- The role of NIV in COPD is to decrease the work of breathing and improve respiratory mechanics, focusing on hypercapnia.
  - Hyperinflation from emphysema, this increases lower airway resistance, decreases the muscle capacity of the diaphragm, leading to diaphragm muscle atrophy.
  - Combination of diaphragm muscle atrophy and the increased airway resistance leads to an increase muscle load for patients, which contributes to dyspnea.



Ferguson GT et al. Proc Am Thorac Soc. 2006;3:176-179.

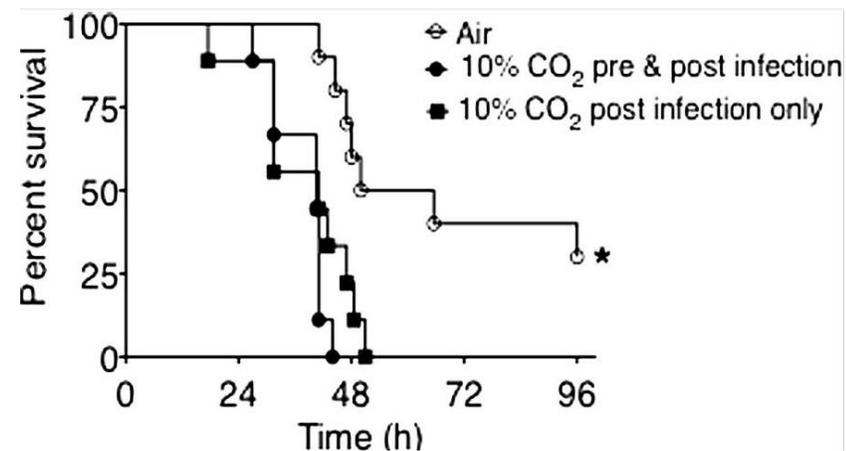
Ottenheim CA et al. Am J Respir Crit Care Med. 2007;175:1233-1240.

Similowski T et al. N Engl J Med. 1991;325:917-923.

N M Sifakas et al. Thorax 1999;54:458-465

# Hypothesis

- The target of NIV in COPD is to offset this diaphragm dysfunction and achieve control of spontaneous breathing with near abolition of diaphragm activity, thus reducing hypercapnia.
  - Chronic hypercapnia can induce skeletal muscle dysfunction
  - Suppresses innate immunity, reduction in CO<sub>2</sub> levels may reduce COPD exacerbations, and thus hospital admissions



Brochard L et al. N Eng J Med. 1995;333:817-822.

Foucher P et al. Chest. 1998;113:1580-1587.

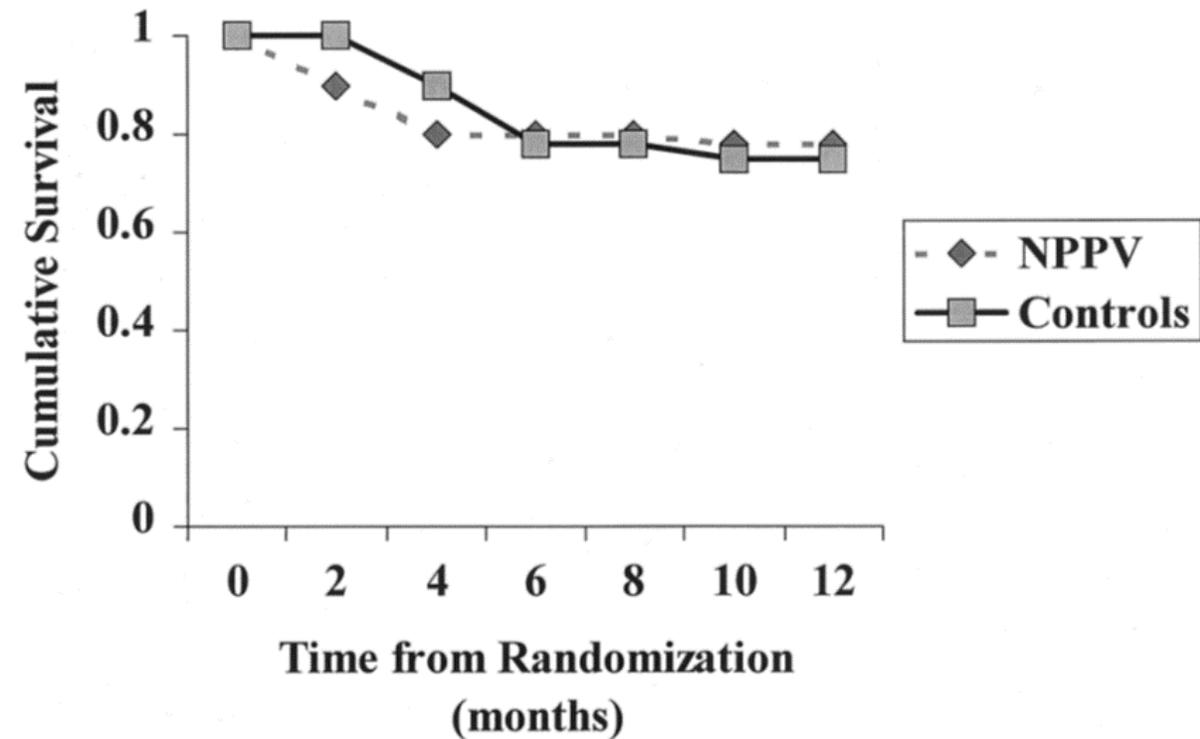
Gates et al. Am J Respir Cell Mol Biol. 2013;49(5):821-828.

# What does the data show?

# Severe COPD

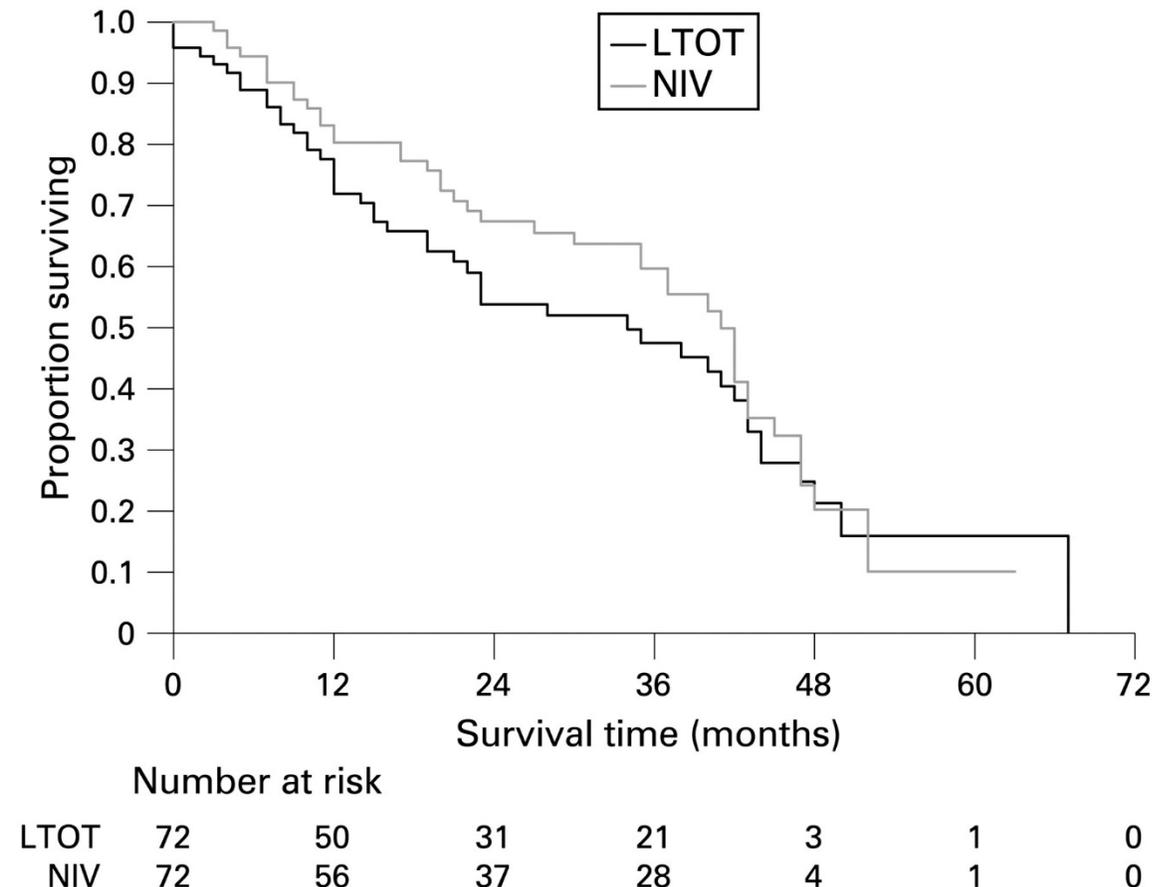
## The story of CO<sub>2</sub>

- Hypothesis
  - Role of NIV in stable severe COPD vs LTOT
  - RCT
  - 52 participants
  - NIV (spontaneous – no back up rate)
  - Severe COPD (FEV<sub>1</sub><45%)
- Outcomes
  - Rate of COPD Exacerbation
  - Hospitalization (Intubation and Mortality)



# The Next Chapter

- Multicenter RCT (144 pts)
- NIV+LTOT vs LTOT
- Inpatient hospitalization
- Baseline CO<sub>2</sub> >46
  - Average CO<sub>2</sub> = 53
- Average PAP = 13/5
- Morning CO<sub>2</sub>
  - LTOT – raised ~19 points
  - NIV +LTOT – raised ~13 points
- Decline in QoL



# A lot of trials, not a lot of success

	Low-Intensity Noninvasive Ventilation		
	Casanova <i>et al.</i> (10)	Clini <i>et al.</i> (11)	McEvoy <i>et al.</i> (12)
Design	RCT	RCT	RCT
N	44	86	144
Age, yr	24 vs. 20	47 vs. 39	72 vs. 72
BMI, kg/m <sup>2</sup>	68 vs. 64	66 vs. 64	69 vs. 67
FEV <sub>1</sub> , % predicted	25 vs. 25	25 vs. 26	25.4 vs. 25.5
PaO <sub>2</sub> , mm Hg	31 vs. 29	31 vs. 27	23.1 vs. 25
PaCO <sub>2</sub> , mm Hg	57.5 vs. 55.7	49.5 vs. 50	52.5 vs. 54.8
Mode	53 vs. 50	55.5 vs. 54	54.4 vs. 52.6
IPAP/EPAP, cm H <sub>2</sub> O	Bilevel-S	Bilevel-S/T	Bilevel-S
Adherence, (h/day)	12/4	14/2	13/5
Acclimatization	5.9	9.2	4.5
Outcome	2 d	10 d	3–4 d
	No improvement in acute COPD exacerbations, hospital admissions, intubations, or mortality	No improvement in hospitalizations or readmissions	Improved sleep quality and overnight hypercapnia, decrease in QoL

# A New Paradigm for Severe COPD and NIV

- Larger inspiratory pressure, leading to a wider pressure support difference
- Increase tidal volume
- Large tidal volume improve alveolar ventilation, improving gas exchange and CO<sub>2</sub> levels
- Ultimately resting the diaphragm
- Development of High Intensity

# Building the foundation of High Intensity NIV

- High Intensity NIV, targets high inspiratory pressure as well as mandatory respiratory rate higher than spontaneous
- Retrospective case study
- 73 patients with severe stable COPD (FEV1 30% predicted)
- Target: Normalize PaCO<sub>2</sub> and improve oxygenation
- Mean IPAP: 28 +/- 5.4 cm H<sub>2</sub>O
- Mean EPAP: 4.6 +/- 1.3 cm H<sub>2</sub>O
- Mean RR: 21 +/- 2.8 BPM
- PaCO<sub>2</sub> levels decreased ~7 mmHg
- PaO<sub>2</sub> increased ~6 mmHg

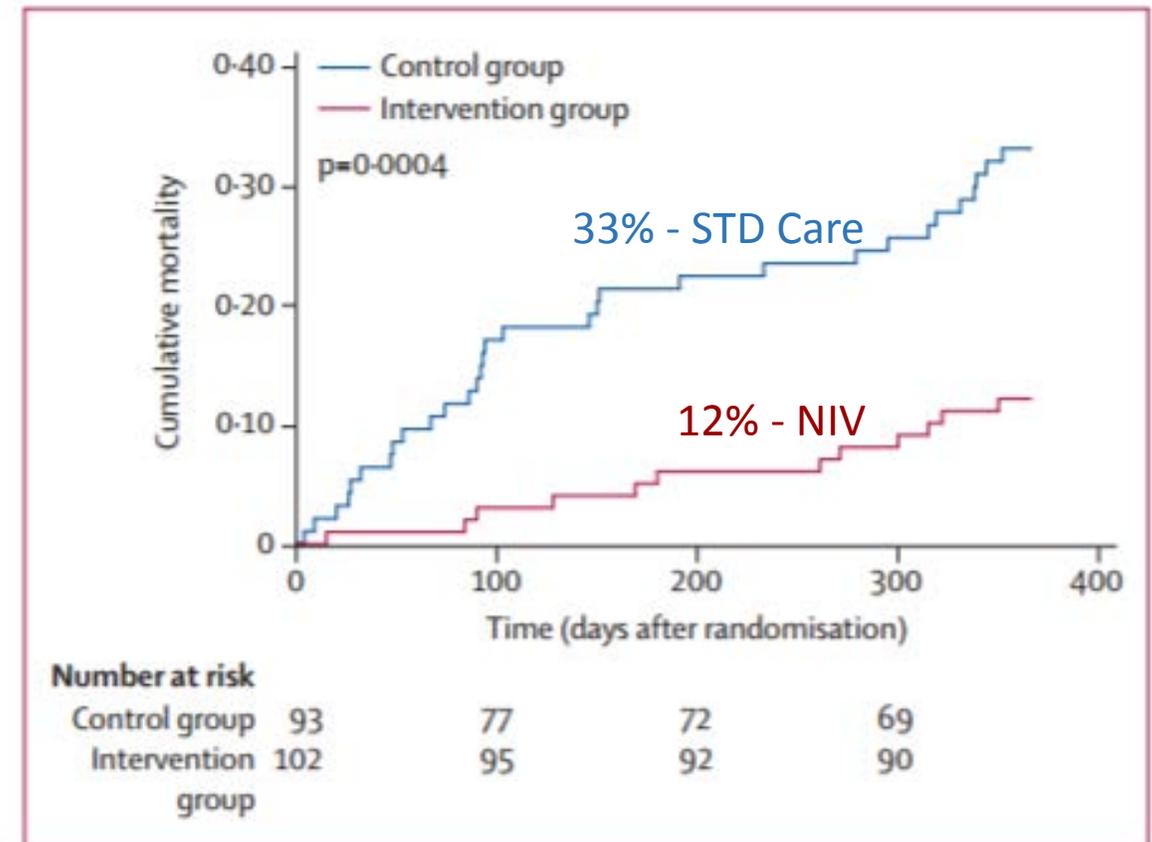
# Building the foundation of High Intensity NIV

- HI vs. LI PS
- RCT 17 patients, chronic hypercapnia
- HI 28/5 x 17 vs LI 14/4 x 8
- Increased Vt in HI (mean 96ml)
- Mean reduction in PaCO<sub>2</sub> in HI (-9.2)
- Improvements in dyspnea, FEV<sub>1</sub>, VC, QoL
- More drop outs with LI
- PSG Data
- RCT 13 patients
- Polysomnography of long term NIV users with COPD
  - More drop outs with LI
- No change in SWS
- PaCO<sub>2</sub> was lower (-6.4) in HI

# Severe COPD: High Intensity vs STD Care

## Mortality

- Severe COPD: High Intensity vs no NIV
- Multicenter RCT (36 centers)
- 195 patients (93 vs. 102)
  - 12 month follow-up
- $PCO_2 \geq 52$
- GOLD stage IV
  - $FEV_1/FVC < 70\%$  and  $FEV_1 < 30\%$
- NIV: 22/4 x 16
  - set to reduce  $PaCO_2$
  - admitted patients electively for a mean of 5.6 days
- QoL
  - Improved SF-36, St. George

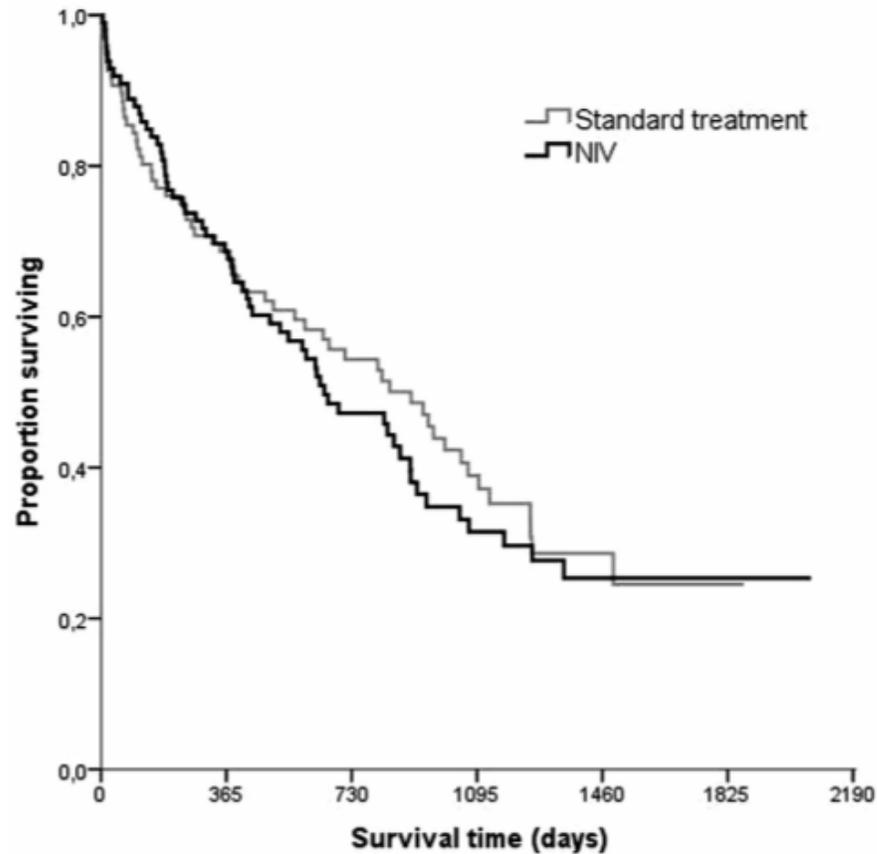


# Severe COPD: High Intensity vs STD Care Post-Exacerbation (RESCUE Trial)

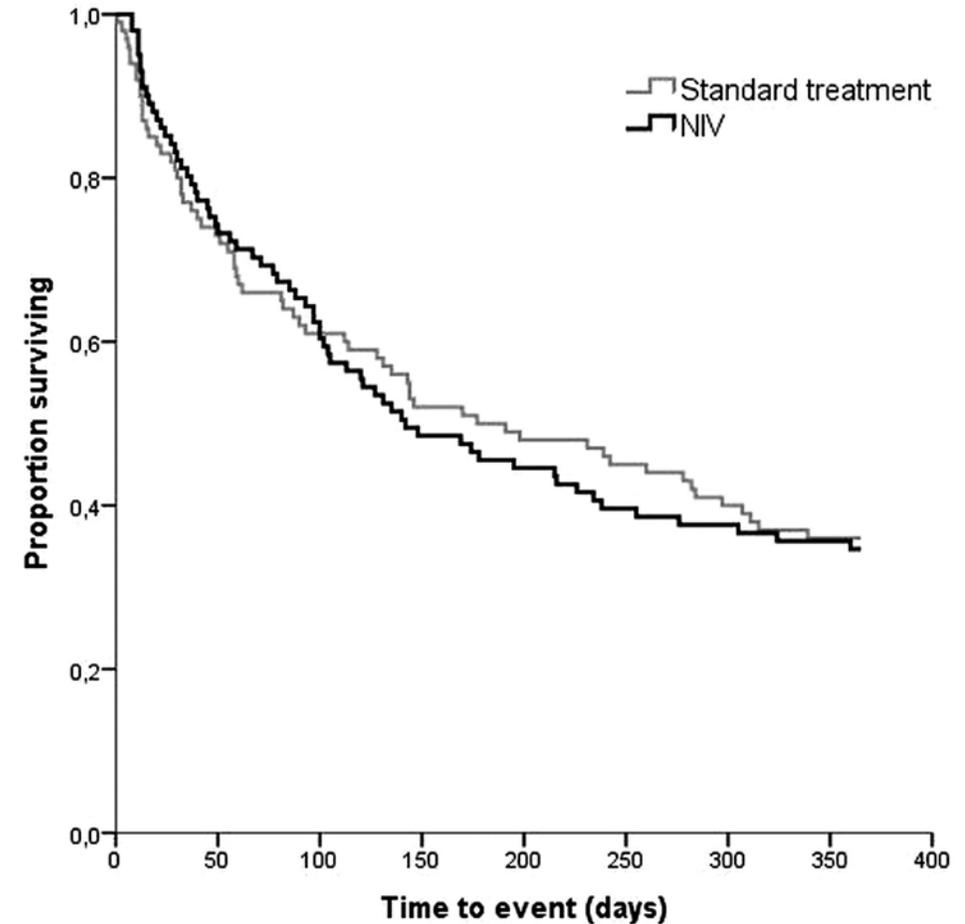
- Multicenter RCT (n=201)
- Severe COPD (Gold 3-4)
- Persistent hypercapnia (pCO<sub>2</sub>>52) 48 hours post exacerbation (NIV/MV)
- NIV: 19/5 x15
- Mortality – no difference
- PCO<sub>2</sub> – (base ~58) ↓ by 3.75 mm Hg
- TcCO<sub>2</sub> – ↓ by 4.5 mm Hg
- Spiro - no difference (FEV<sub>1</sub>=27%)
- HRQoL – trend (not significant) to NIV
- Mood - no difference
- Dyspnea- no difference

# Severe COPD: High Intensity vs STD Care Post-Exacerbation (RESCUE Trial)

## Survival



## Readmission

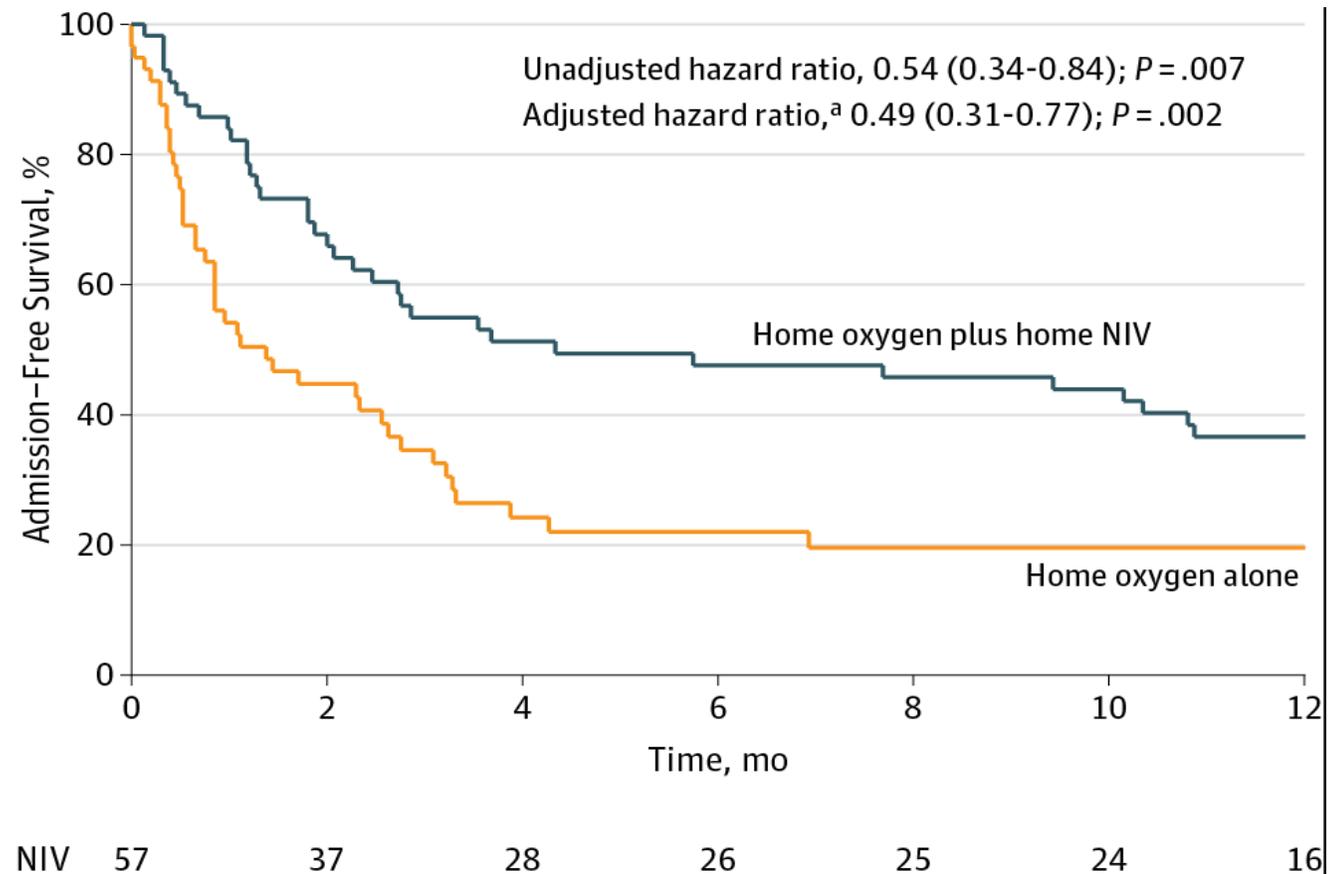


# HOT-HMV: RCT of NIV in hypercapnia due to COPD post acute exacerbation

- Multicenter RCT
- 116 (59 HOT vs. 57 HOT-HMV)
- Hypoxia ( $\text{PaO}_2 < 55$  mmHg) and Hypercapnia ( $\text{PaCO}_2 > 53$  mmHg)
- Mean  $\text{PaCO}_2 \sim 59$  mmHg
- FEV1 23%
- BMI 22

## Summary of Primary Settings:

- IPAP =  $\sim 24$  cmH<sub>2</sub>O (22 to 26)
- EPAP =  $\sim 4$  cmH<sub>2</sub>O (4 to 5)
- BUR =  $\sim 14$  (14 to 16)



# HOT-HMV Economics: U.S. Dollars

	HOT-HMV	HOT	Cost savings
<b>Total Costs</b>	24,458	28,386	<b>-3,928</b>
<b>Devices</b>	4,298	1,582	<b>2,716</b>
<b>MD Visits</b>	10,805	15,033	<b>-4,228</b>
<b>Meds</b>	758	1,088	<b>-330</b>
<b>Exacerbations</b>	8,598	10,683	<b>-2,085</b>

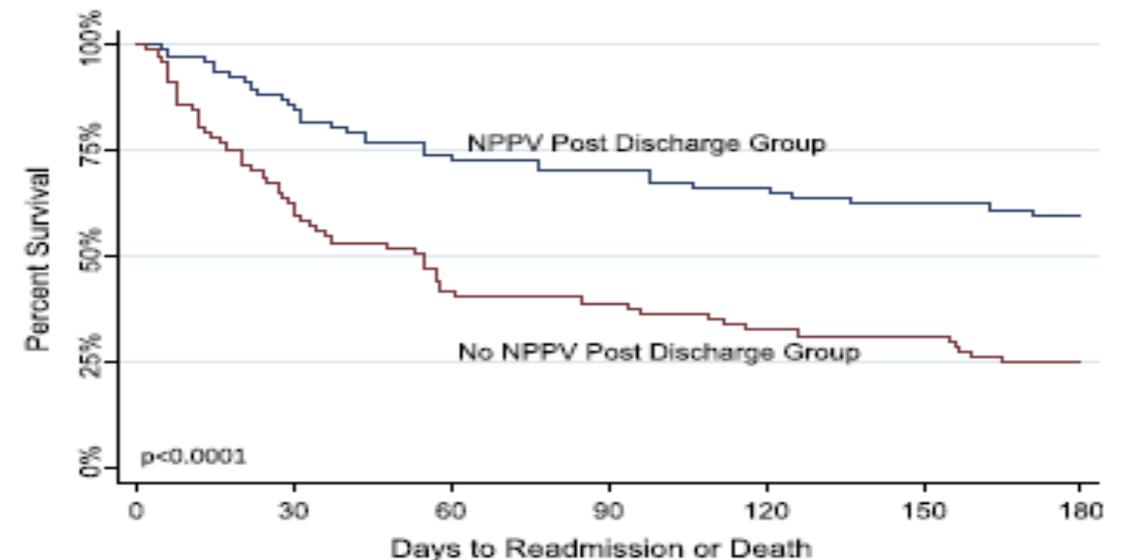
- Potential cost savings of more than \$3,900 per patient in the U.S.
- HOT-HMV could be effective both in terms of saving patients money and improving quality of life when compared to HOT alone

**It works in Europe, but will it work  
in the U.S.?**

# The U.S. Experience #1

180 days of monitoring

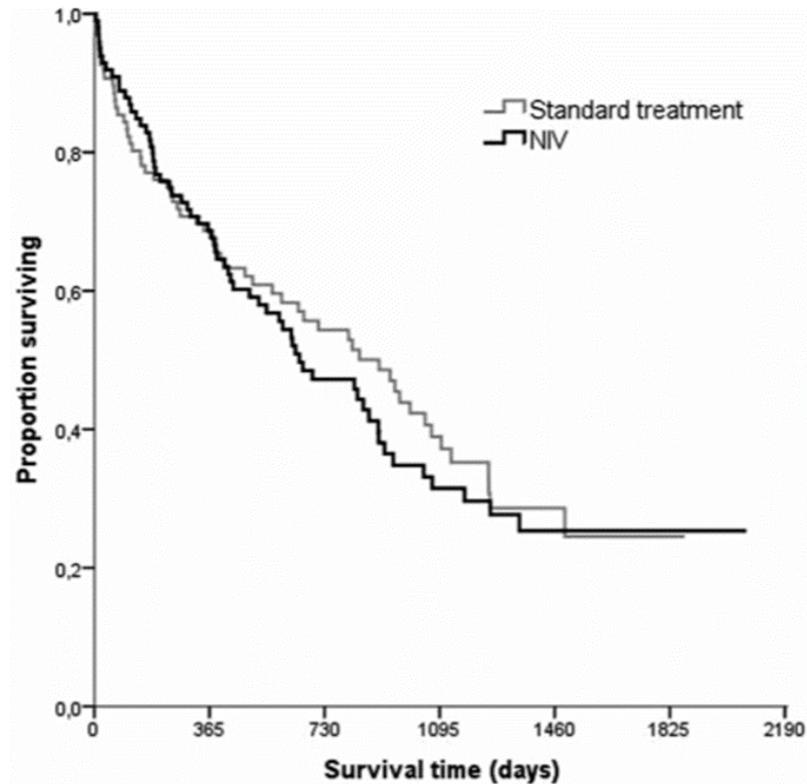
- Single center retrospective study
- 166 patients (88 No NIV vs. 78 NIV) with chronic hypercapnia ( $\text{PaCO}_2 > 45$  mmHg)
- Average settings 22/6
- Continued from ICU settings
- **RESULTS**
  - Reduction in hospital readmissions
    - 40% vs 75%,  $p < 0.0001$
  - Improved mortality



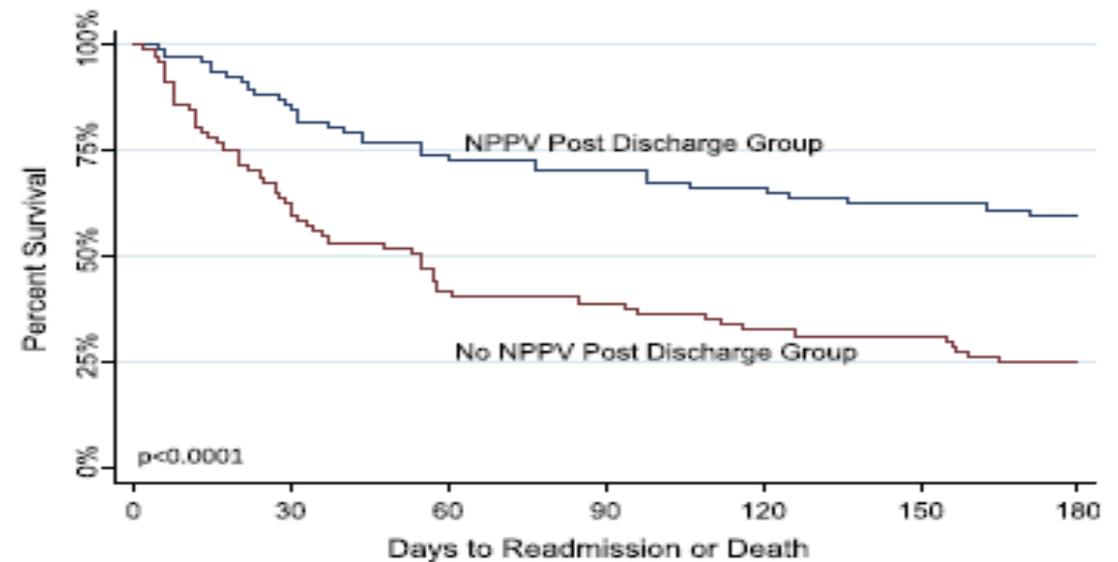
**Figure 2** Kaplan Meier curve of event-free survival comparing patients who used NPPV post discharge versus patients who did not use NPPV post discharge.

# Similar Trials, Different Results

## RESCUE Trial



## Galli and Criner



**Figure 2** Kaplan Meier curve of event-free survival comparing patients who used NPPV post discharge versus patients who did not use NPPV post discharge.

# The U.S. Experience #2

- Retrospective study (N=397) 2010-2014
- History of 2 or more hospitalizations for acute COPD exacerbation in last year
- Population
  - GOLD 2-4
  - BODE Index Score  $\geq 5$
  - Either
    - PaO<sub>2</sub>  $\leq 60$
    - PaCO<sub>2</sub>  $\geq 52$
- Bundled program
  - *Pharmacist* for med teaching
  - *RT* for
    - NIV/VAPS support
    - Home O<sub>2</sub>
    - Care Co-Ordination
      - Visits q30 d X 3 visit then q90 d
    - Stop smoking plans

**Table 2: Hospital Re-admissions following initiation of quality improvement program:**

Number of COPD-related Admissions	Patients with admission in the year prior to program initiation (n [%])	Patients with admission in the year post program initiation (n[%])
0	0 (0%)	348 (87.7%)
1	0 (0%)	40 (10.1%)
$\geq 2$	397 (100%)	9 (2.2%)

# Europe vs United States

- **Europe**

- RCT and prospective trials
- Benefits in pts with chronic hypercapnia
- Severe stable COPD (not in setting of acute exacerbation)

- **United States**

- Retrospective studies
- Improvement in readmission after acute exacerbation (OSA tx?)
- Bundle therapy (NIV, RT, home visit)

## Common Hurdles:

- Pressure Intolerance
- Mask intolerance

## European Models

- Prolonged acclimation, increase adherence to NIV
- Effectively reduced chronic stable CO<sub>2</sub>

	Low-Intensity Noninvasive Ventilation			High-Intensity Noninvasive Ventilation		
	Casanova <i>et al.</i> (10)	Clini <i>et al.</i> (11)	McEvoy <i>et al.</i> (12)	Struik <i>et al.</i> (21)	Köhnlein <i>et al.</i> (20)	Murphy <i>et al.</i> (22)
Design	RCT	RCT	RCT	RCT	RCT	RCT
N	44	86	144	201	195	116
	24 vs. 20	47 vs. 39	72 vs. 72	100 vs. 101	93 vs. 102	59 vs. 57
Age, yr	68 vs. 64	66 vs. 64	69 vs. 67	63.5 vs. 63.9	64.4 vs. 62.2	67.1 vs. 66.4
BMI, kg/m <sup>2</sup>	25 vs. 25	25 vs. 26	25.4 vs. 25.5	24.8 vs. 24.6	24.5 vs. 24.8	22.2 vs. 21.5
FEV <sub>1</sub> , % predicted	31 vs. 29	31 vs. 27	23.1 vs. 25	26 vs. 26	27 vs. 26	22.9 vs. 24
PaO <sub>2</sub> , mm Hg	57.5 vs. 55.7	49.5 vs. 50	52.5 vs. 54.8			48 vs 48
PaCO <sub>2</sub> , mm Hg	53 vs. 50	55.5 vs. 54	54.4 vs. 52.6	57.8 vs 59.3	57.8 vs. 58.5	59 vs. 59
Mode	Bilevel-S	Bilevel-S/T	Bilevel-S	Bilevel-S/T	Bilevel-S/T	Bilevel-S/T
IPAP/EPAP, cm H <sub>2</sub> O	12/4	14/2	13/5	19.2/4.8	21.6/4.8	24/4
Adherence, (h/day)	5.9	9.2	4.5	6.3	5.9	4.7
Acclimatization	2 d	10 d	3–4 d	3–4 d	5–6 d	5–6 d
Outcome	No improvement in acute COPD exacerbations, hospital admissions, intubations, or mortality	No improvement in hospitalizations or readmissions	Improved sleep quality and overnight hypercapnia, decrease in QoL	No change in exacerbations, improvement in daytime PaCO <sub>2</sub>	Improvement in mortality, PaCO <sub>2</sub> , SaO <sub>2</sub> , and FEV <sub>1</sub>	Decrease COPD readmissions

*Definition of abbreviations:* Bilevel-S = no backup rate; Bilevel-S/T = backup rate; BMI = body mass index; COPD = chronic obstructive pulmonary disease; EPAP = expiratory positive airway pressure; FEV<sub>1</sub> = forced expiratory volume in 1 second; IPAP = inspiratory positive airway pressure; PaCO<sub>2</sub> = carbon dioxide tension; PaO<sub>2</sub> = arterial oxygen tension; QoL = quality of life; RCT = randomized controlled trial; SaO<sub>2</sub> = arterial oxygen saturation.

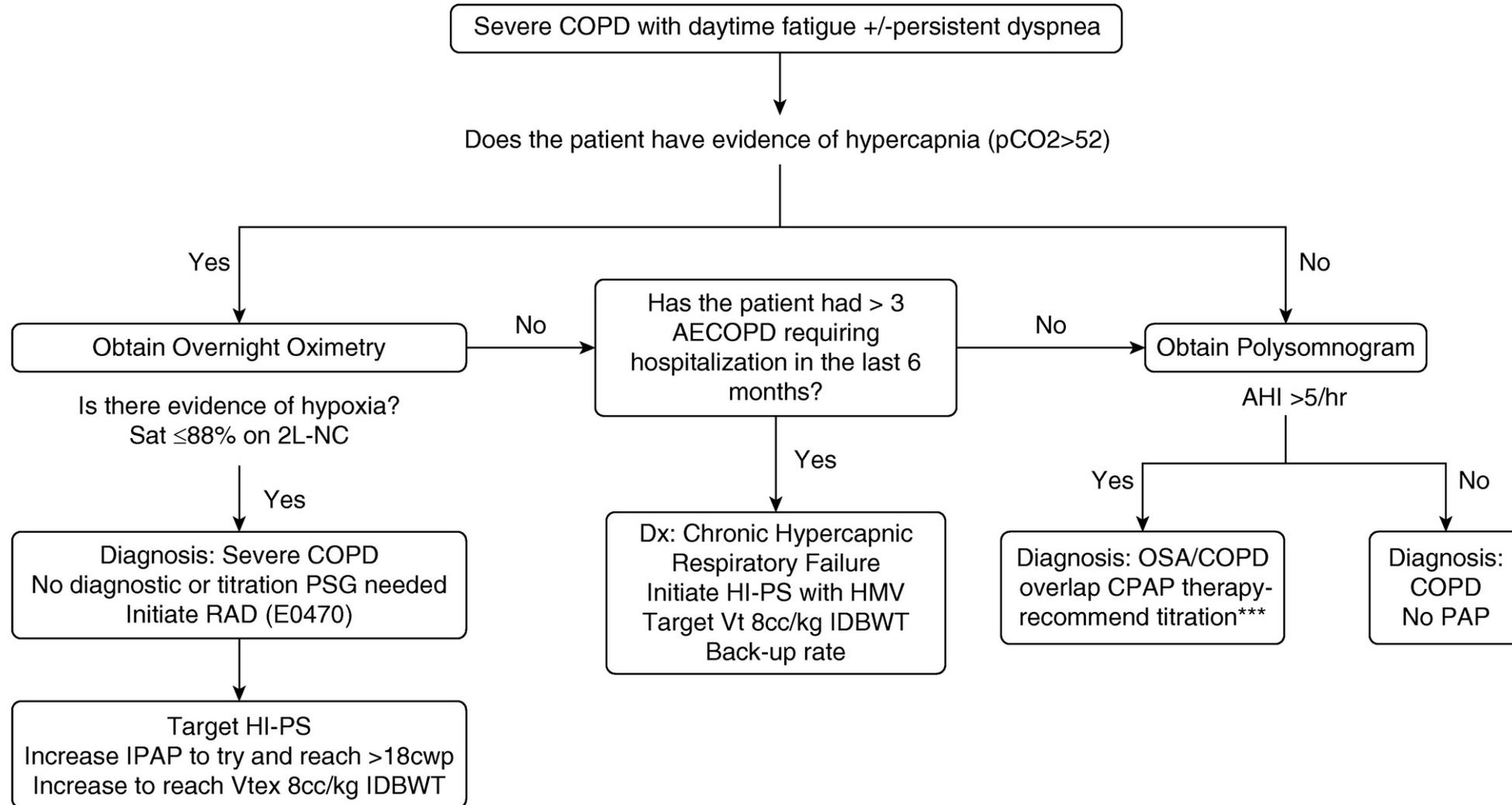
**NIV is beneficial, but how do you get your patients set up and pick the correct settings???**

# RAD Criteria

- Based on both hypoxia ( $\text{SaO}_2 < 88\%$ ) and hypercapnia ( $\text{pCO}_2 > 52 \text{ mmHg}$ )
- Does not require spirometry to prove obstructive lung disease
  1. Arterial Blood Gas while awake and on prescribed  $\text{FiO}_2$  with  $\text{pCO}_2 \geq 52 \text{ mmHg}$  **AND**
  2. Overnight oxygen saturation  $\leq 88\%$  for over 5 minutes, with a minimum of 2 hours of nocturnal recording on 2 lpm supplemental  $\text{O}_2$  or the patient's prescribed  $\text{FiO}_2$ , whichever is higher **AND**
  3. OSA and CPAP treatment has been considered and ruled out (formal testing is not required)

# RAD Criteria with back-up rate (Full support)

1. Must document the patient is using therapy over 4 hours a night over a 3 months period and progression of symptoms.
2. Arterial Blood Gas while awake and on prescribed FiO<sub>2</sub> with pCO<sub>2</sub> ≥ 52 mm Hg
3. Overnight oximetry on NIV showing oxygen saturations < 88% for more than 5 minutes with a minimum of 2 hours of nocturnal recording on 2 lpm supplemental O<sub>2</sub> or the patient's prescribed FiO<sub>2</sub>, whichever is higher.



# What is the cost of therapy?

CMS Name	Common Name	Monthly Costs USD	Diagnosis	Qualifying Data
Ventilator E0464	Invasive Mechanical Ventilator Home Ventilator	~1500	Respiratory Failure	Unclear?????
Respiratory Assist Device E0470 E0471	BilevelPAP(S) BiLevelPAP(ST)	~400	Severe COPD	PaCO <sub>2</sub> ≥ 52 <b>AND</b> O <sub>2</sub> sat ≤ 88% for >5min on 2 LNC
CPAP Device E0601	CPAP autoCPAP	~100	OSA	AHI > 5 with sx

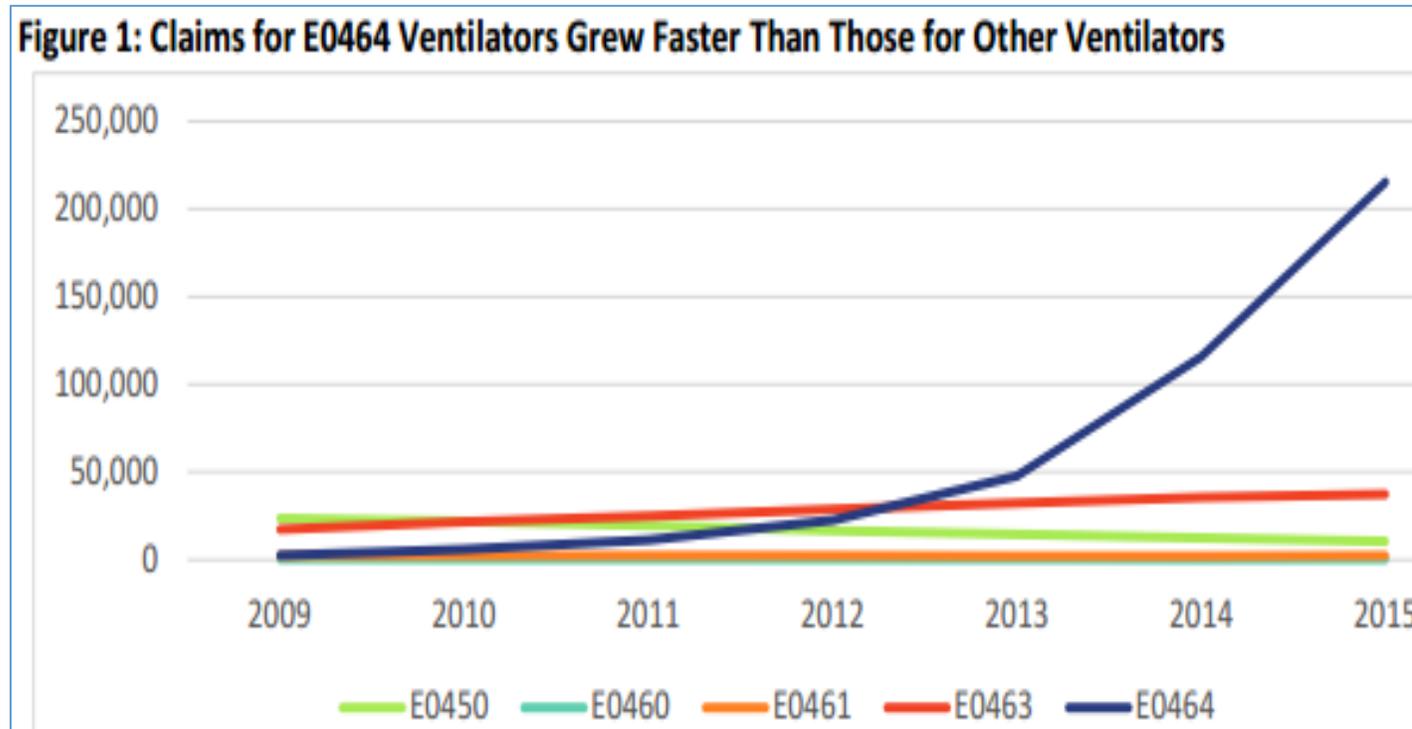
# Why do we care?



U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES  
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## Escalating Medicare Billing for Ventilators Raises Concerns

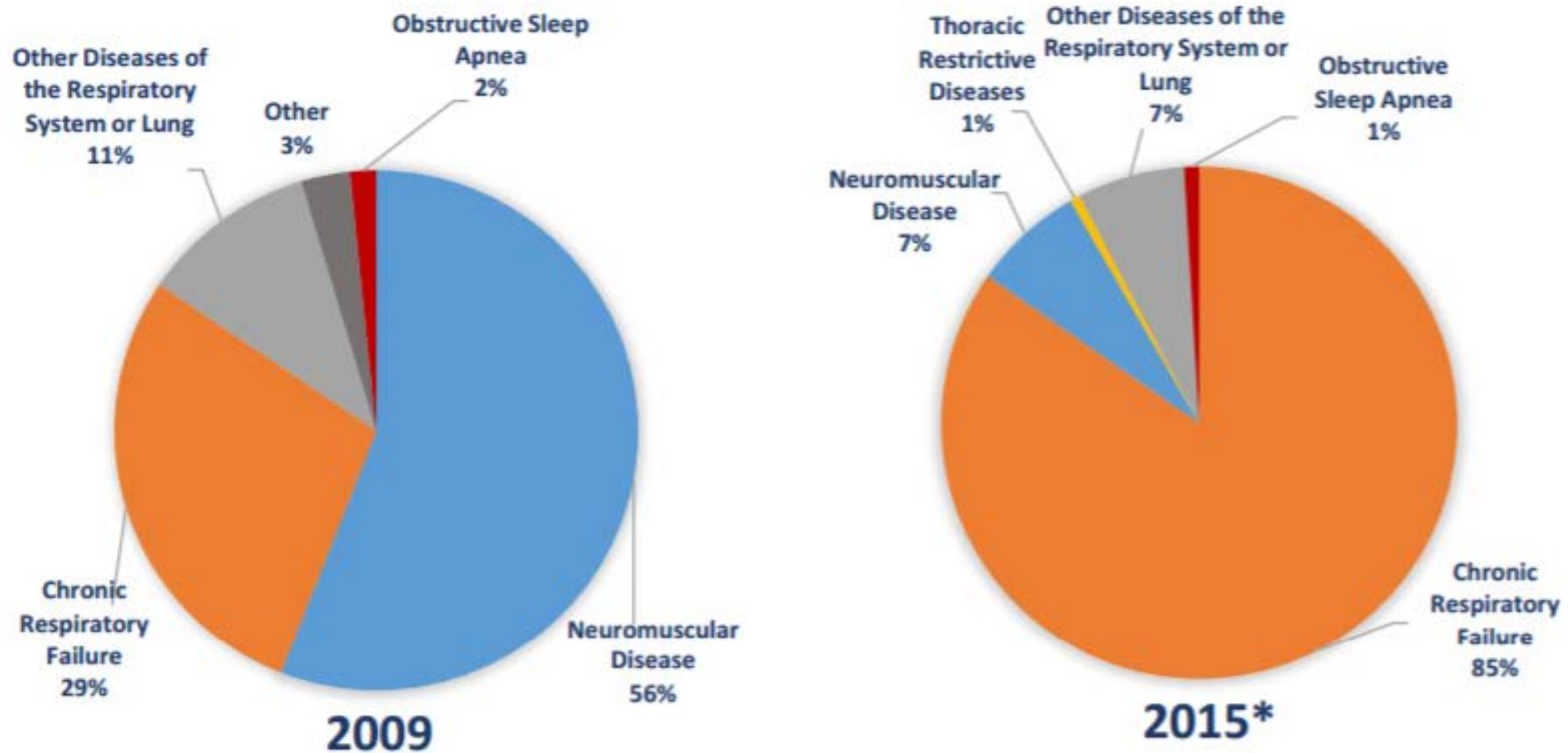




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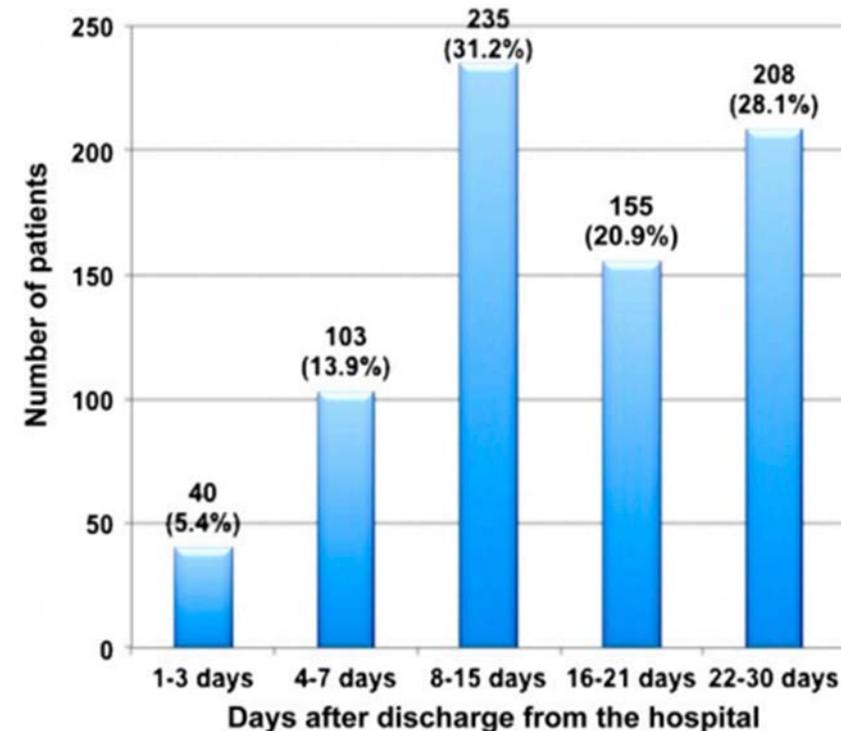
### Escalating Medicare Billing for Ventilators Raises Concerns

**Figure 4: Distribution of Top Diagnoses for E0464 – All Suppliers**



# Why are physicians spending all this money?

- Current RAD guidelines/Criteria are too stringent to meet
- Assure RT care for the patient at home
- Increased pressure on physicians (PCP, IM) to prevent hospital readmissions
  - 1 in 12 adults (40–64 yr old) hospitalized for COPD are readmitted to the hospital within 30 days of discharge.
  - In 2012, The 2012 Affordable Care Act established strong financial incentives for hospitals and physicians to reduce readmissions, including COPD
- ↑ risk of re-exacerbations within the first few weeks after discharge



# Where do we go from here?

- While limited to European trials, there are several RCT that show benefit with the use of NIV with back-up rate in reducing hospital readmissions and mortality.
- The target for NIV should be hypercapnia, not hypoxia
- Under current RAD guidelines it is extremely difficult to qualify a patient for NIV under COPD criteria, especially with a back-up rate, as proven in the reviewed data
- This has led to increased use of HMV, at a much higher price point and less stringent criteria

# Where do we go from here?

- There needs to be revision to current RAD guidelines to simplify the ability to obtain devices that can provide high intensity pressure support with back-up rate
- These revised guidelines should be based on chronic stable hypercapnia ( $p\text{CO}_2 > 52$  mm Hg) AND not include hypoxia

Thank You  
Questions?