Controversies in Sleep Disordered Breathing

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Welcome to

ATS 2020 | VIRTUAL

Objectives

- Discuss the role of home sleep testing
- Understand the benefits of CPAP therapy
- Review indications for non-CPAP treatment options for OSA
- Determine when to start treatment with CPAP vs. NIV in ambulatory patients with OHS

A Case Study

51 yo male with daytime sleepiness:

• Multiple episodes **falling asleep at work, *even during conversations*,** meals

• Snoring so bad, sleeps separately from wife

• PMH notable only for HTN and gout, not on tx

• Exam notable for
   – Ht 5' 11", Wt 330 lbs → BMI 46 kg/m^2
   – Neck size 19"

STOP-BANG Screen for OSA

- **S** • Snoring
- **T** • Tired During Day
- **O** • Observed Apneas
- **P** • High Blood Pressure
- **B** • BMI > 35 kg/m^2
- **A** • Age > 50 yo
- **N** • Neck Circ > 15.75"
- **G** • Male Gender

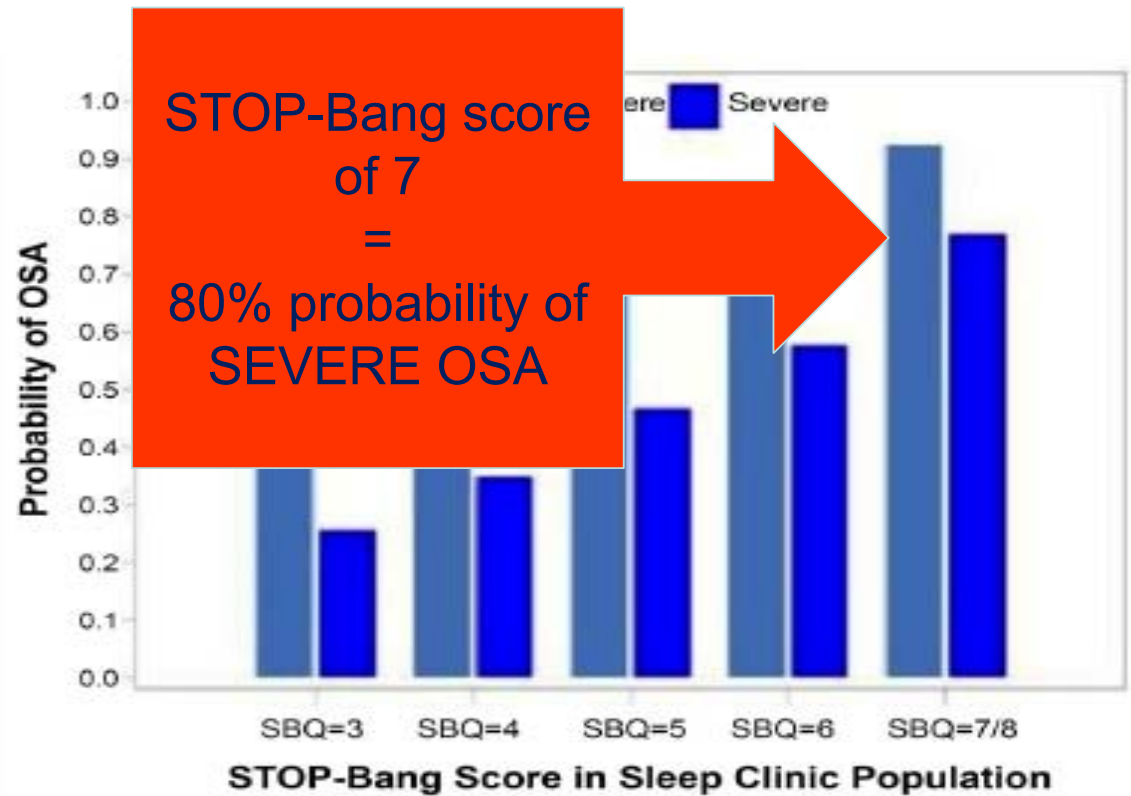Chung F. Anesthesiology. 2008; 108: 812–21

Sleep Apnea- A Case Study

51 yo male with daytime sleepiness:

• Multiple episodes **falling asleep at work, *even during conversations***, meals

• Snoring so bad, sleeps separately from wife

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STOP-Bang
Score = 7/8

STOP-BANG Screen for OSA

S • Snor
T • Tired
O • Obse
P • High
B • BMI
A • Age
N • Neck
G • Male

STOP-Bang score
of 7
=
80% probability of
SEVERE OSA

Probability of OSA

SBQ=3   SBQ=4   SBQ=5   SBQ=6   SBQ=7/8

STOP-Bang Score in Sleep Clinic Population

Severe

Nagappa M, Mokhlesi B, Chung F. PLoS One 2015; 10(12):e0143697

Question 1:
The next step in the management of this sleepy patient should be to:

A. Order an in-laboratory split night polysomnogram
B. Refer the patient to the sleep clinic
C. Start empiric auto-CPAP therapy without a diagnostic test
D. Order a home sleep apnea test

Question 1:
Correct answer

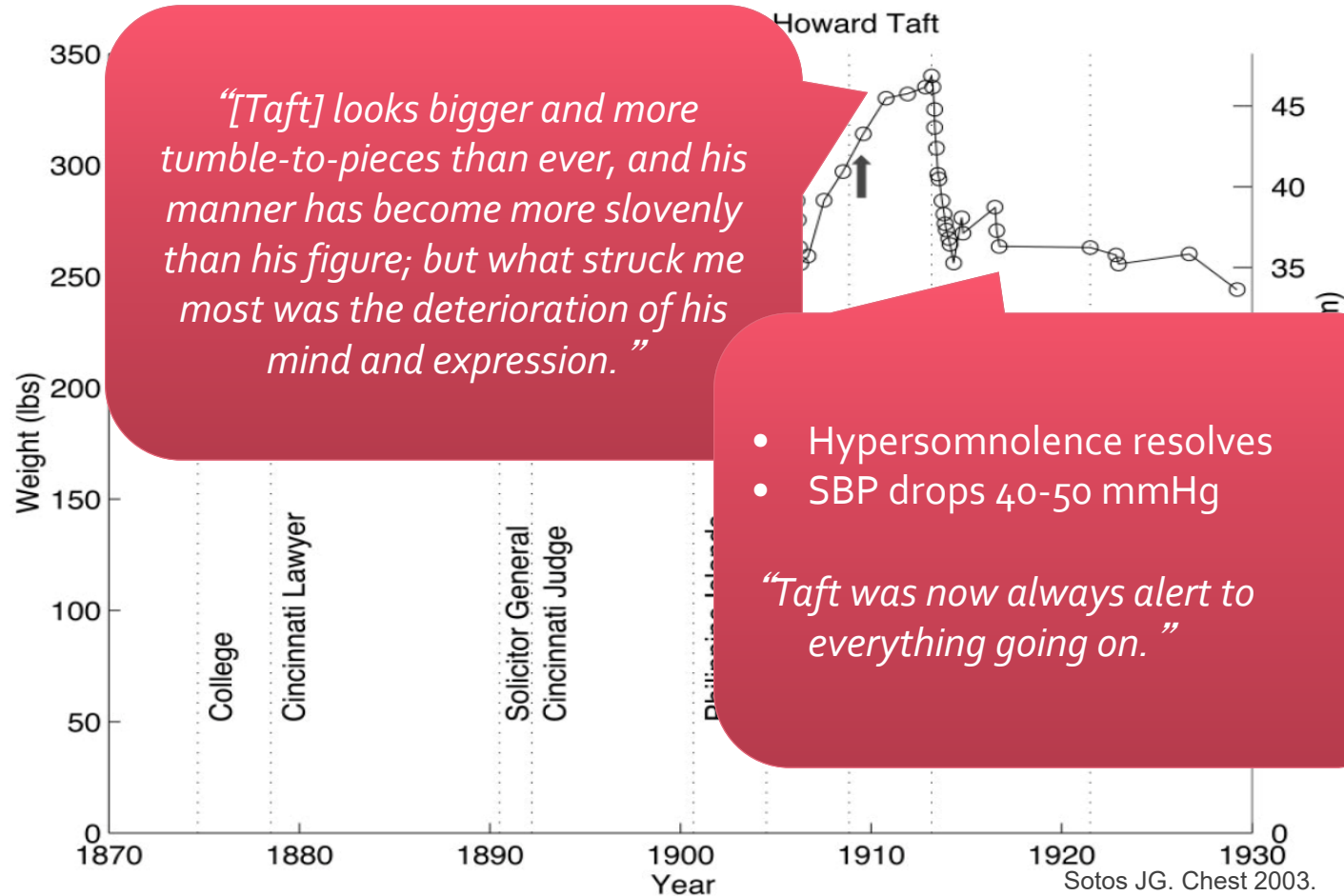**D.** Order a home sleep apnea test

Sleep Apnea- A Case Study

William Howard Taft,
27th President
(1908 – 1912)

"*I am convinced that this undue drowsiness is due to the accumulation of the flesh….*"

Noted to fall asleep:
• During Cabinet meetings
• Meals
• Church
• Playing cards
• While standing

Sotos JG. Chest 2003.

Can screening questionnaires replace diagnostic tests?

- There are a variety of screening tools for OSA
  - STOP-Bang questionnaire
  - Berlin questionnaire
- Screening tools more useful to rule out OSA (high negative predictive value)
- If clinical suspicion for OSA is high, the patient should undergo a diagnostic test
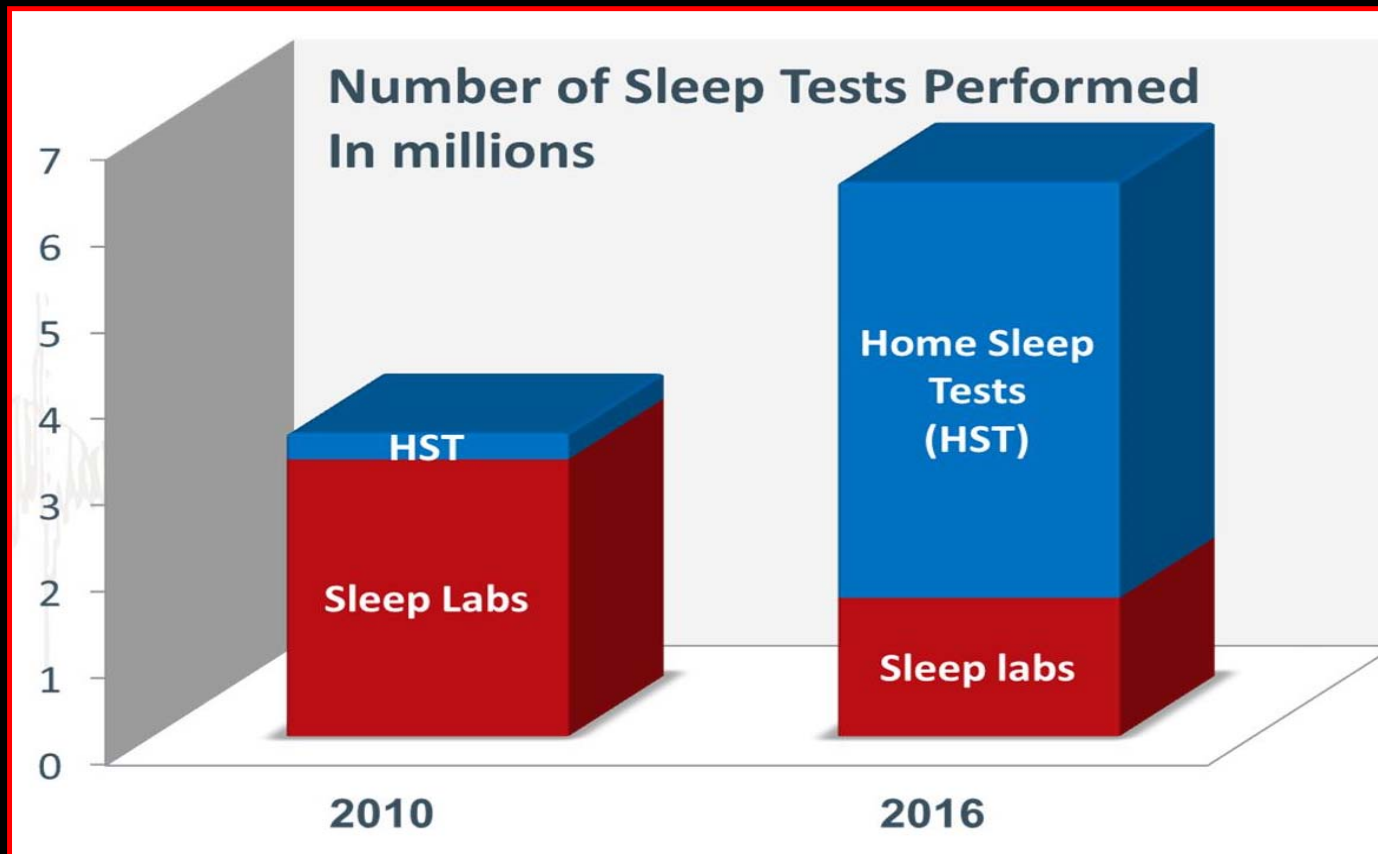
Should you routinely screen your **asymptomatic** patients for OSA?

- The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for OSA in asymptomatic adults.

- There is uncertainty about the accuracy or clinical utility of all potential screening tools.

Sleep market in the US 2010 vs. 2016

Number of Sleep Tests Performed In millions

- HST
- Sleep Labs
- Home Sleep Tests (HST)
- Sleep labs

2010 — 2016

Respiratory polygraphy

Chest + Abd effort belts

Pressure/ flow + Snore sensors

Oximetry/ Heart rate

Leg movement sensors

Peripheral Arterial Tonometry

PAT-derived resp effort

Snore channel

Oximetry / Heart rate

Actigraphy/ Body position

PAT=Peripheral arterial tonometry

Summary- Portable Sleep Monitoring

- Unattended
  - Requires cognitive & manual dexterity
  - Data loss a concern (around 15-20%)

- Less sensitive than in-lab PSG
  - Can't tell when a patient is sleeping, so tends to underestimate AHI

- Validated only in patients without significant comorbidities

- Costs $200-$300/ study

- Primary Care use great but requires education, resource commitment

Diagnosis and management of OSA without in-lab PSG

- Several studies confirmed effectiveness of HSAT
- Studies included patients with:
  - High probability of moderate to severe OSA
  - Sleepy patients
  - No significant comorbid conditions such as CHF, COPD, hypoxia, hypercapnia, NMD, other sleep disorders
- No difference in patient outcomes
- No difference in CPAP adherence
- No difference in patient satisfaction
- Lower costs

Mulgrew AT. Ann Intern Med. 2007; 146:157-66.

Berry RB, Sleep 2008; 31:1423-1431

Corral J. AJRCCM 2017;196:1181-1190

AASM Clinical Practice Guidelines Recommendations

- Screening questionnaires should not be used to diagnose OSA
- PSG or HSAT should be used for diagnosis of OSA in uncomplicated adult cases
- PSG, rather than HSAT, should be used for diagnosis of OSA in complicated cases
  - significant cardiorespiratory disease, neuromuscular condition, hypoventilation, chronic opioid medication use, history of stroke, or severe insomnia
- A split-night PSG is preferred over full night PSG

Kapur VK et al. JCSM 2017; 13:479

Mokhlesi B. JAMA 2017; 318:2035

Primary care vs. sleep specialist

- Two non-inferiority RCTs

- Australian RCT
  - Chai-Coetzer CL et al. JAMA 2013; 309:997
  - N=155 patients

- Spanish RCT
  - Sanchez-Quiroga MA et al. AJRCCM 2018 Apr 17
  - N=303 patients

- No difference in outcomes:
  - Quality of life, improvement in sleepiness, BP
  - CPAP adherence
  - More cost effective

Primary Care vs Specialist Sleep Center Management of Obstructive Sleep Apnea and Daytime Sleepiness and Quality of Life
A Randomized Trial

High risk patients based on a questionnaire and positive nocturnal oximetry (3% ODI >16) were randomized.

Primary Care Management

- PCP + specialist nurse model
- Nurse contact at 2 wks, 1 mo, 3 mo, 6 mo
- PCP contact at 3 mo, 6mo

Sleep Specialist Management

- Referral to 1 of 9 sleep centers
- Follow-up at 1 mo, 3 mo, 6 mo

Chai-Coetzer CL et al. JAMA 2013; 309:997

Primary Care vs Specialist Sleep Center Management of Obstructive Sleep Apnea and Daytime Sleepiness and Quality of Life
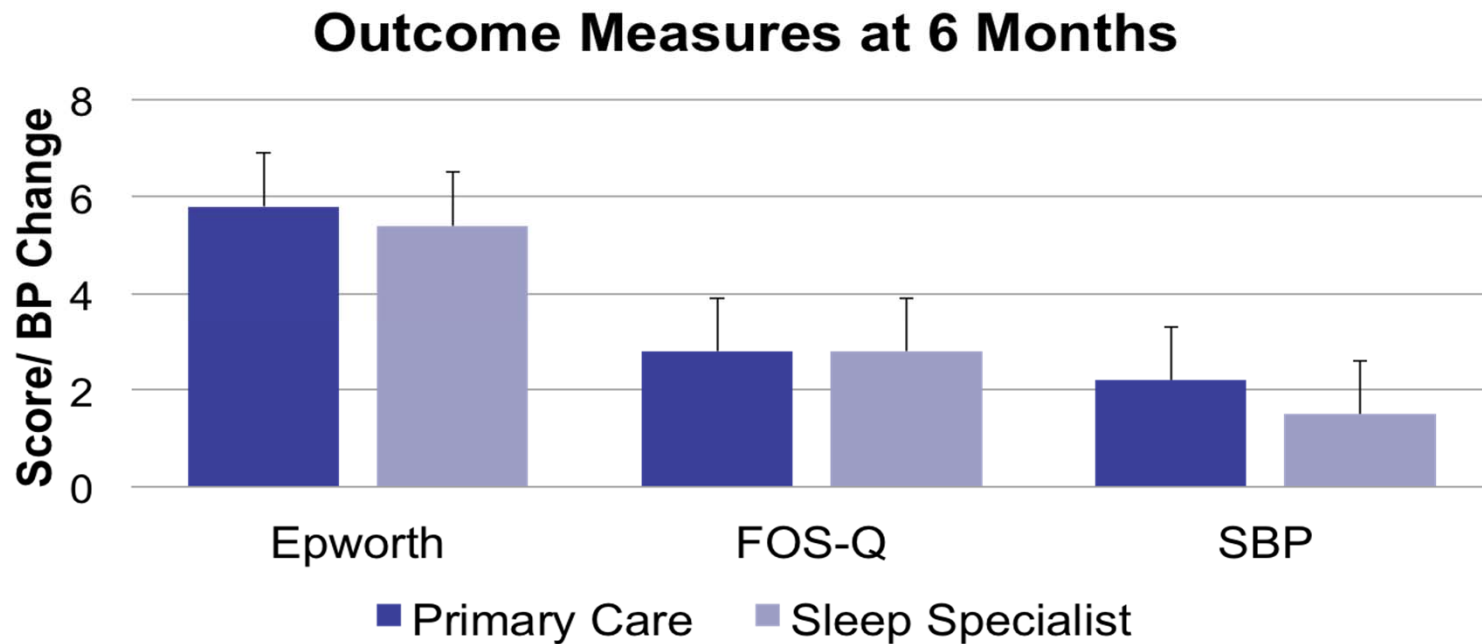## A Randomized Trial

Baseline Subject Characteristics

	Primary Care N=81	Sleep Specialist Care N=74
Male gender (%)	85	77
Age (yrs)	57±10	54±11
Mean BMI (kg/m2)	33±5	33±5
Epworth Score	12.8±4	12.5±4
3% ODI (events/hr)	32±18	35±17

Primary Care vs Specialist Sleep Center Management of Obstructive Sleep Apnea and Daytime Sleepiness and Quality of Life
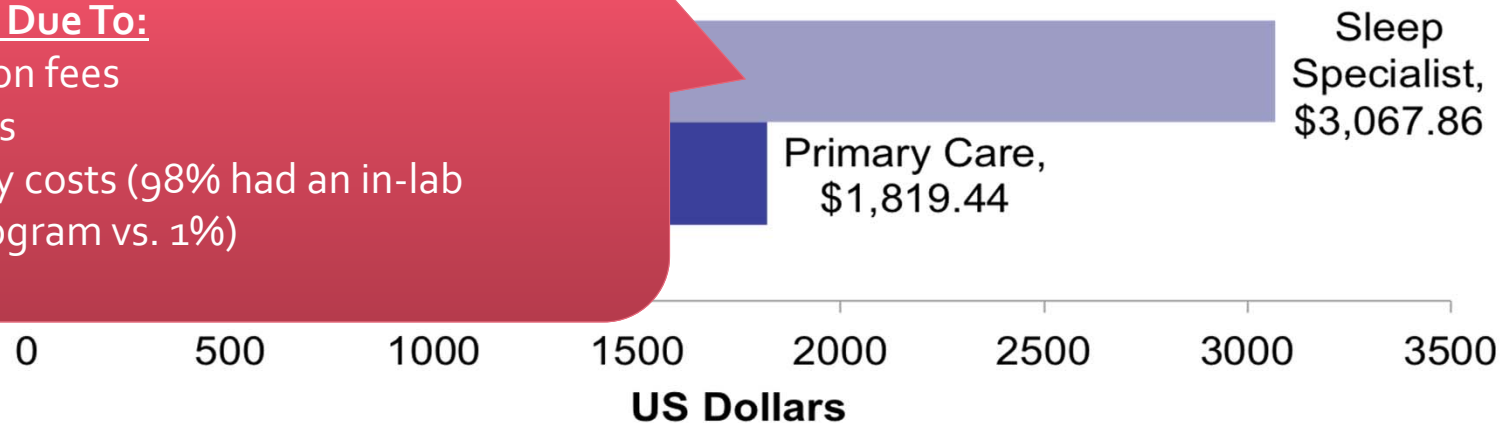## A Randomized Trial

Outcome Measures at 6 Months

Chai-Coetzer CL et al. JAMA 2013; 309:997

Primary Care vs Specialist Sleep Center Management of Obstructive Sleep Apnea and Daytime Sleepiness and Quality of Life
A Randomized Trial

Average Diagnostic + Treatment Cost Per Subject

Cost Increase Due To:
- Consultation fees
- Travel costs
- Sleep study costs (98% had an in-lab polysomnogram vs. 1%)

Sleep Specialist, $3,067.86

Primary Care, $1,819.44

0   500   1000   1500   2000   2500   3000   3500

US Dollars

Chai-Coetzer CL et al. JAMA 2013; 309:997

Primary Care vs Specialist Sleep Center Management of Obstructive Sleep Apnea and Daytime Sleepiness and Quality of Life
A Randomized Trial

- Non-inferiority study
  - Sleep specialists more likely to prescribe alternative non-CPAP therapy (28% vs. 3%)
  - Less withdrawal from study with sleep specialist (8% vs. 21%)
  - Less CPAP discontinuation with sleep specialist

- With intensive education and nursing support, a primary care model is a reasonable approach
  - Time & Resources needed
  - Education needed:
    - 6 hours education of PCPs and nurses
    - Nurses spent 5 days of in-service training in sleep clinics with specialist

Chai-Coetzer CL et al. JAMA 2013; 309:997

Question 2:

A 55 years old woman is referred to you because she underwent a home sleep apnea study (HSAT) and was diagnosed with moderate OSA (apnea-hypopnea index 20). Complaints that led to HSAT were loud snoring and witnessed apneas. She was also recently diagnosed with hypertension which is currently untreated. BMI is 36 kg/m^2 and BP is 155/95 mmHg. She reports sleeping habitually 6.5 hours per night and denies excessive daytime sleepiness, but does complain of mild daytime fatigue.

Question 2:

Which of the following recommendations will be the most likely to improve her long-term cardiovascular outcomes?

A. Start CPAP therapy to normalize blood pressure
B. Extend sleep to 8 hours per night
C. Start oral antihypertensive therapy to normalize blood pressure
D. Treat OSA with CPAP to improve daytime symptoms in order to facilitate weight loss

Question 2:
Correct answer

C. Start oral antihypertensive therapy to normalize blood pressure

# The Impact of OSA Treatment on Blood Pressure
A Network Meta-Analysis

	No. of Trials	Sample Size	Type of Meta-analysis	Blood Pressure Difference (SE) [95% CI], mm Hg	P Value
Systolic Blood Pressure					
CPAP vs inactive control	47	4533	Pairwise	−2.6 (0.5) [−3.6 to −1.6]	<.001
			Network	−2.5 (0.5) [−3.5 to −1.5]	<.001
Diastolic Blood Pressure					
CPAP vs inactive control	46	4488	Pairwise	−2.1 (0.3) [−2.8 to −1.4]	<.001
			Network	−2.0 (0.4) [−2.7 to −1.3]	<.001

Bratton DJ, et al. JAMA 2015; 314:2280

Comparison of CPAP and valsartan in hypertensive patients with OSA

- 8-week randomized controlled crossover trial
- 23 hypertensive patients
  - office systolic BP/diastolic BP: 155±14/102±11 mmHg)
  - age: 57±8 years
  - AHI: 29±18/h
  - BMI: 28±5 kg/m^2
- Randomized first to either CPAP or valsartan 160 mg followed by 4-week washout period and then crossed over to the second 8-week period of the alternative treatment

Pepin JL, et al Am J Respir Crit Care Med 2010; 182 (7):954

Comparison of CPAP and valsartan in 23 patients with newly diagnosed hypertension and moderate to severe OSA
An 8 week randomized cross-over trial
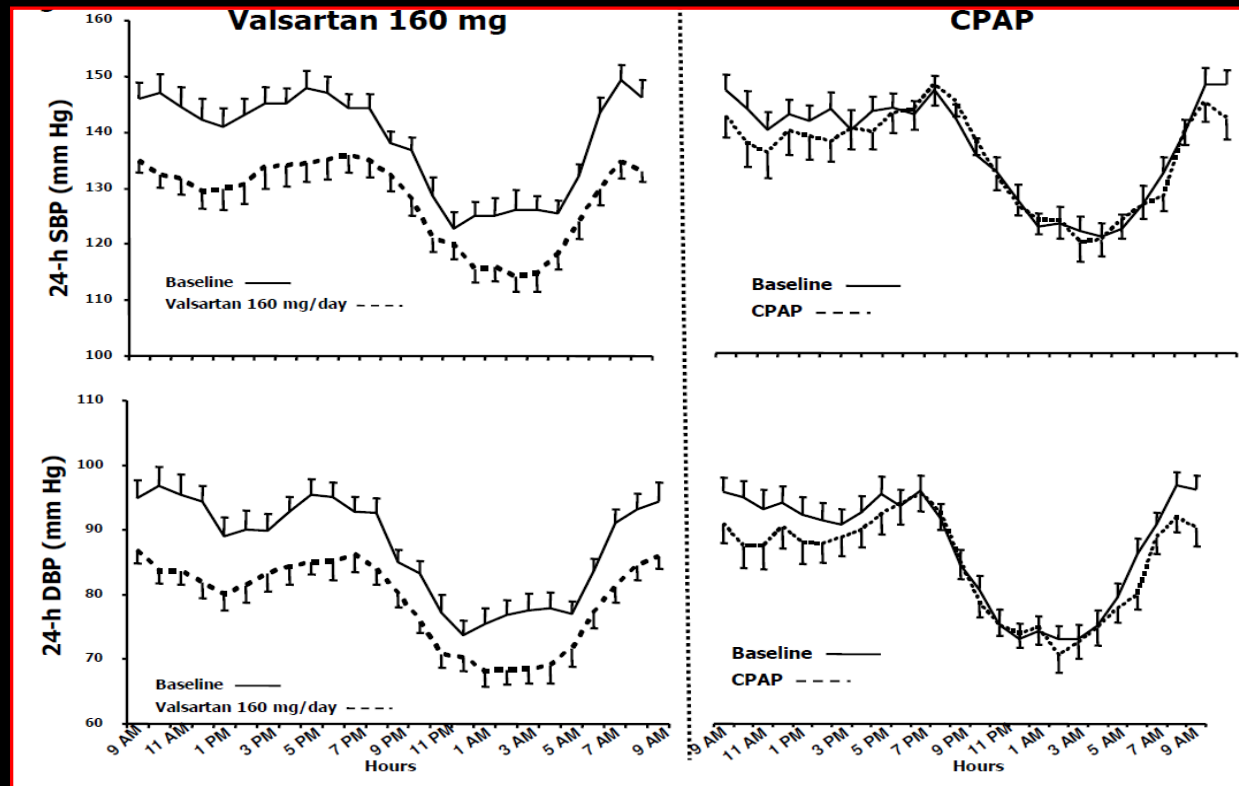
Pepin JL, et al Am J Respir Crit Care Med 2010; 182 (7):954

CPAP for primary prevention of HTN and CV events in nonsleepy OSA

- Multicenter RCT of moderate-severe OSA
  - Median follow up of 4 years
    - 357 randomized to CPAP (median AHI 35)
    - 366 to usual care (median AHI 42)
    - Median CPAP use was 5 h/night (IQR 2.2-6.3)
  - No difference in outcomes
    - In CPAP group 68 patients with new hypertension and 28 CV events
    - In control group 79 patients with new hypertension and 31 CV events

Barbe F, et al. JAMA 2012; 307:2161

CPAP for primary prevention of HTN and CV events in nonsleepy OSA
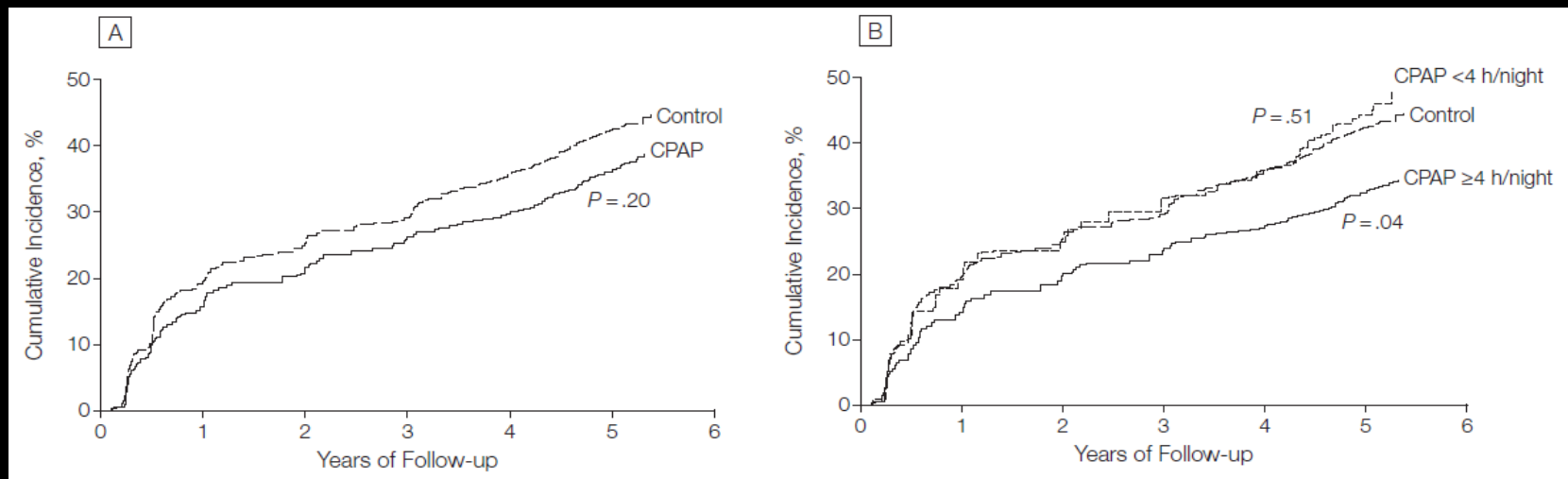
Barbe F, et al. JAMA 2012; 307:2161

Effect of CPAP on BP in patients with OSA and resistant HTN

- Multicenter RCT of moderate-severe OSA
  - Mean AHI 40, on average taking 3.8 antihypertensives, baseline BP 144/83 mm Hg
  - Follow up after 12 weeks
    - 98 randomized to CPAP (median AHI 35)
    - 96 to usual care (median AHI 42)
    - 72% used CPAP > 4 h/night
    - Larger drop in mean BP with CPAP (3.1 mm Hg; p=0.02) and diastolic BP (3.2 mm Hg; p=0.005)

| | No. (%) | | | | | |
| | CPAP Group (n = 98) | | Control Group (n = 96) | | | |
	Baseline	Follow-up	Baseline	Follow-up	OR (95% CI)[a]	P Value
Prevalence dipper pattern	25 (25.5)	35 (35.9)	25 (26.0)	21 (21.6)	2.4 (1.2-5.1)	.02
Prevalence riser pattern	27 (27.6)	20 (20.5)	34 (35.4)	35 (36.8)	0.45 (0.23-0.91)	.03

Martinez-Garcia, MA, et al. JAMA 2013; 310:2407

<u>S</u>leep <u>A</u>pnea Cardio<u>V</u>ascular <u>E</u>ndpoints (SAVE study)

- Multicenter RCT for secondary prevention of CV events after a mean of 3.7 years
  - moderate-severe OSA (4% ODI > 12/h on ApneaLink) and h/o coronary disease or stroke
    - 1359 randomized to CPAP
    - 1358 to usual care
    - Mean CPAP use was only 3.3 h/night
    - Excluded ESS > 15, SpO2 <80% for >10% TRT, resting hypoxemia, severe COPD
  - No difference in cardiovascular endpoints
  - <u>Significant improvement in quality of life, mood and work productivity</u>
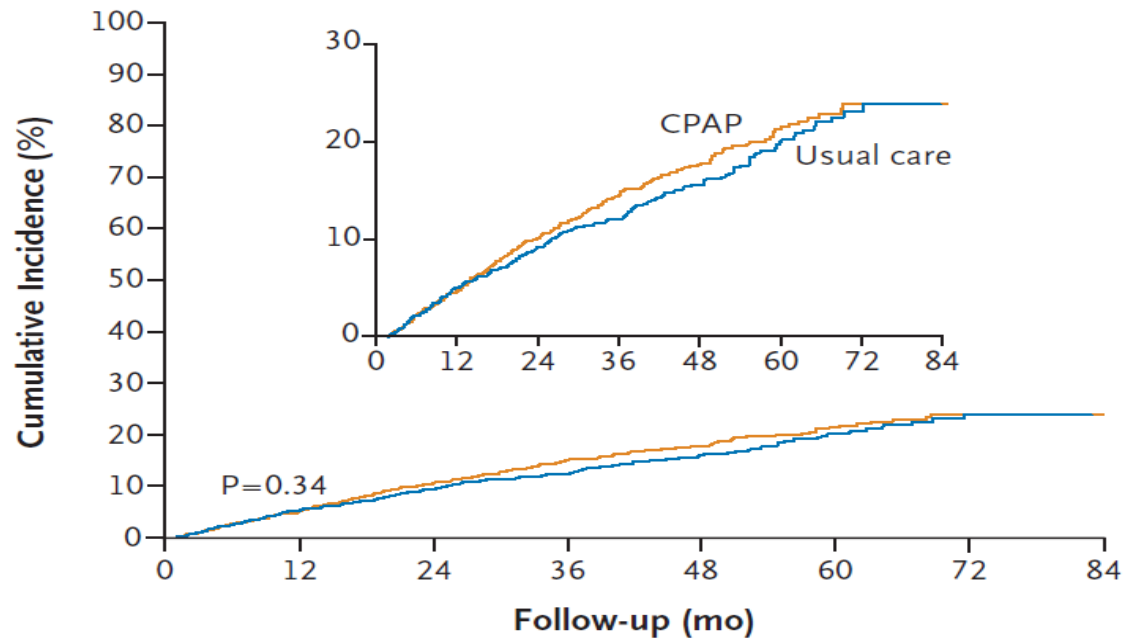
McEvoy RD, et al. NEJM 2016; 375:919

Sleep Apnea CardioVascular Endpoints (SAVE study)

SAVE Study
Average CPAP Adherence

Average nightly adherence in hours (Mean and 95%CI) over time
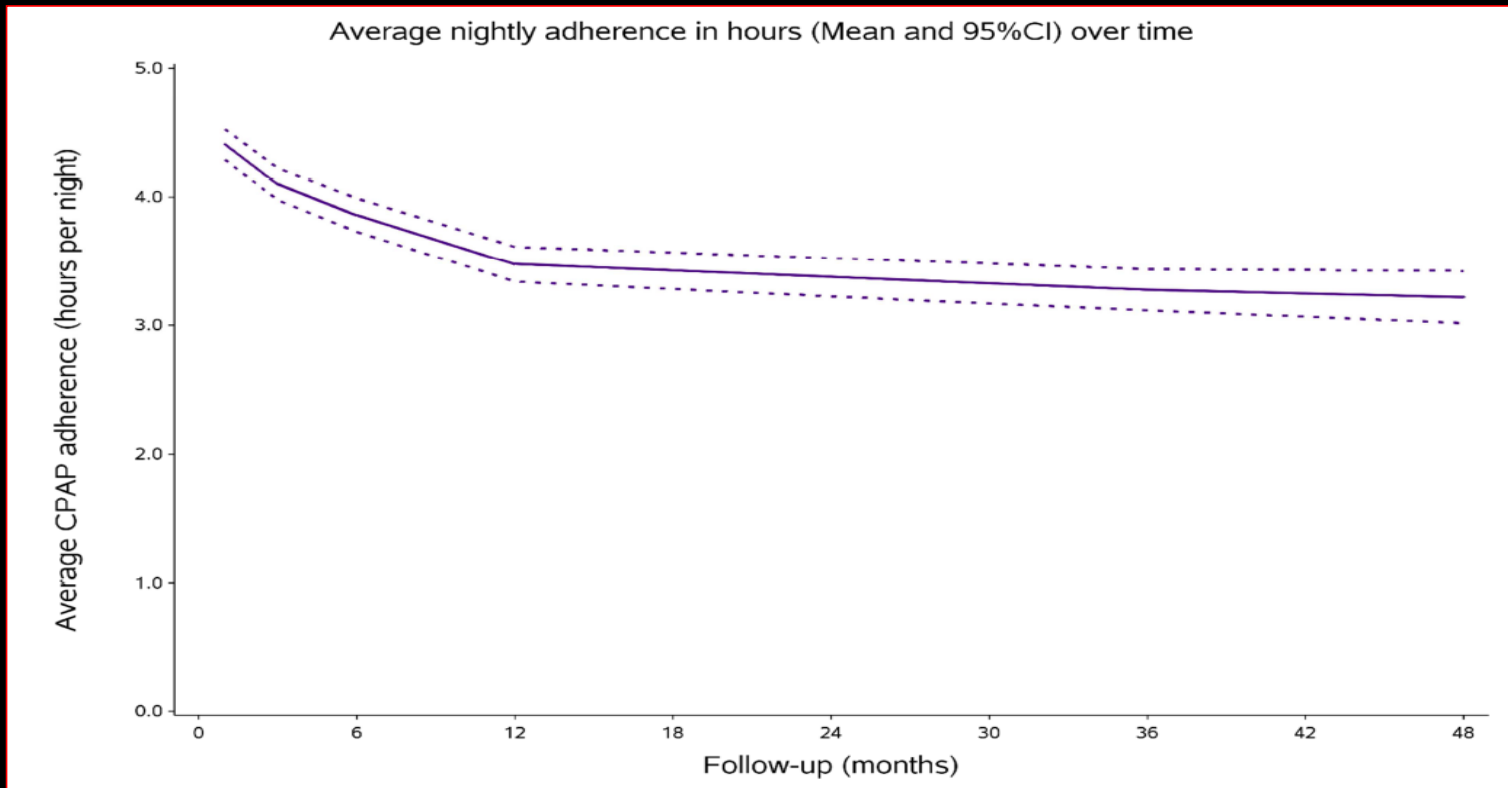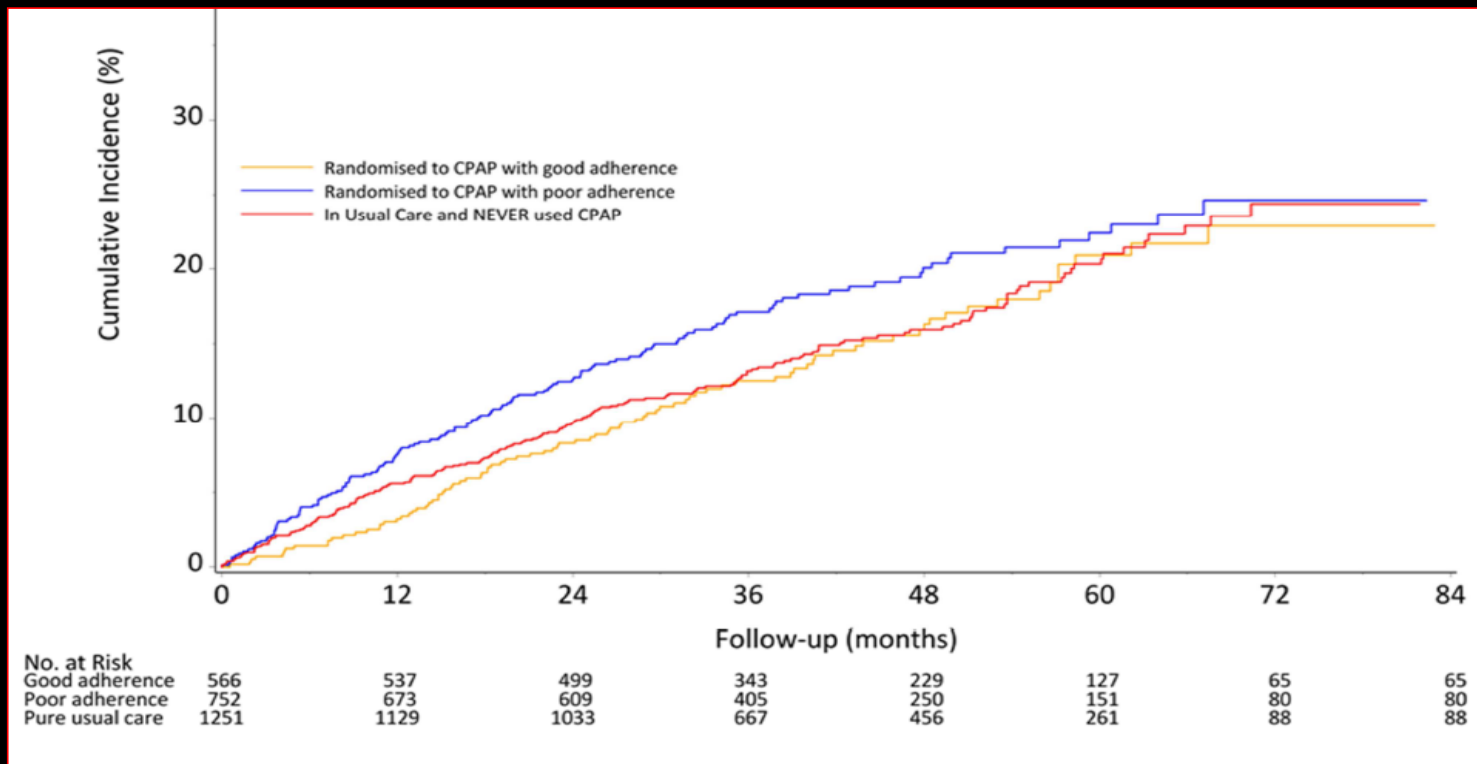
McEvoy RD, et al. NEJM 2016; 375:919

SAVE Study
Outcomes based on CPAP adherence

McEvoy RD, et al. NEJM 2016; 375:919

Question 3:

Our 55 year old woman from question 2 decides to start treatment for OSA to decrease snoring and witnessed apneas so that her husband can sleep in the same bedroom with her. She undergoes a brief trial of CPAP in the clinic and feels it will be difficult for her to tolerate any type of interface/mask on her face.

Question 3:

Which of the following recommendations will be the most accurate in the treatment of OSA?

A. CPAP has greater efficacy than mandibular advancement devices in treating OSA

B. Mandibular advancement device has lower clinical effectiveness than CPAP for mild to moderate OSA

C. Referral to ENT for hypoglossal nerve stimulator

D. Uvulopalatopharyngoplasty (UPPP) is more effective in treating OSA than CPAP

Question 3:
Correct answer

A. CPAP has greater efficacy than mandibular advancement devices in treating OSA

CPAP Therapy

- Overwhelming evidence from RCTs that compared to control or sham CPAP, CPAP improves:

  - Daytime sleepiness
  - Snoring
  - Quality of life (including bed partners)
  - Apnea-hypopnea index
  - Intermittent hypoxemia during sleep
  - Sleep fragmentation
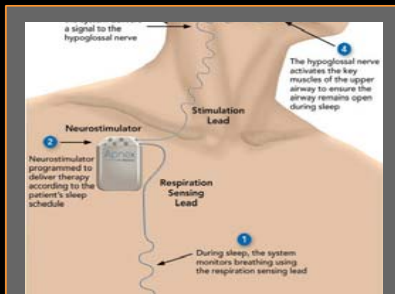
Treatment options for OSA

Treatment options for OSA
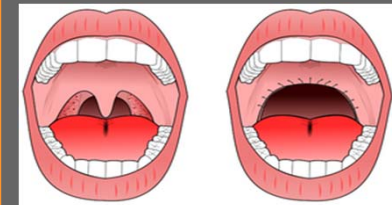
Other Therapy Options for OSA

Body Position

ProVent™

Hypoglossal Nerve Stimulator


Didgeridoo/
oropharyngeal
exercise

Upper airway
surgery/UPPP

Oral appliance vs. CPAP for 1 month in moderate-severe OSA
Randomized cross-over trial (n=108)

Oral Appliance Therapy:

- Greater efficacy for CPAP vs. greater clinical effectiveness for oral appliance
- Great option for mild-moderate OSA
- Good salvage option for severe OSA where CPAP is not going to be used
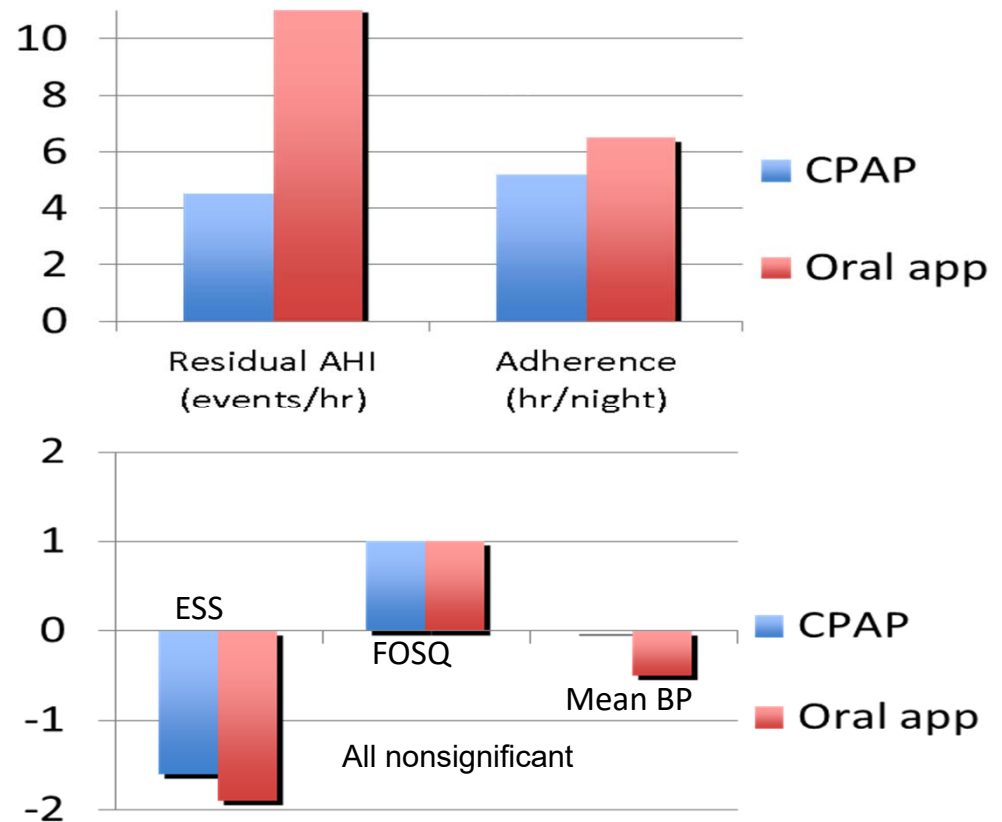
Adapted from Phillips CL et al. AJRCCM 2013; 187: 1879

Question 4:

60 years old severely obese man was recently hospitalized for acute-on-chronic hypercapnic respiratory failure and was successfully treated with NIV during the hospitalization. He was discharged from the hospital 6 weeks ago and is now following up in your pulmonary clinic. He complains of hypersomnia and dyspnea on exertion. He has PMH of hypertension and gout.

On exam his blood pressure is 148/86 mmHg and BMI is 55 kg/m^2. SpO$_2$ on room air while resting is 93%. Respiratory rate is 25. He undergoes office spirometry which reveals mildly reduced FVC and a normal FEV$_1$ and FEV$_1$/FVC. Room air ABG reveals a pH of 7.34, PaCO$_2$ of 53 mmHg and PaO$_2$ of 60 mmHg. You order a split night PSG which reveals severe hypoxemia during sleep (30% of total sleep time below 90% SpO$_2$) and very severe OSA (AHI of 90).

Question 4:

You decide to initiate positive airway pressure therapy. The best treatment option is to start:

A. CPAP
B. Bilevel PAP in spontaneous mode (no backup rate)
C. Bilevel PAP ST (with a backup rate)
D. Volume targeted pressure support (AVAPS or iVAPS)

Question 4:
Correct answer

A. CPAP

Efficacy of Different Treatment Alternatives for Obesity Hypoventilation Syndrome: Pickwick Study
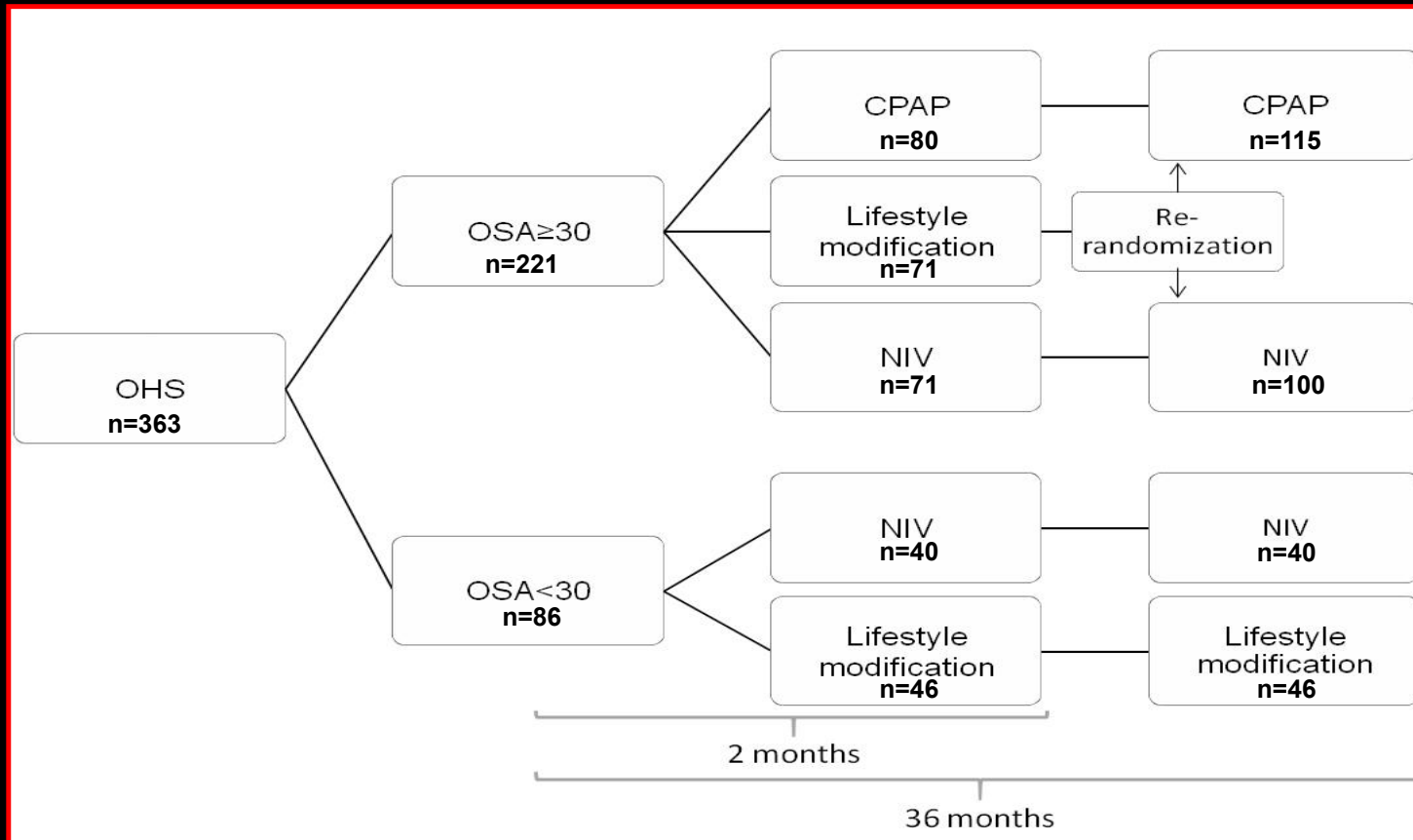
Masa JF et al. AJRCCM 2015

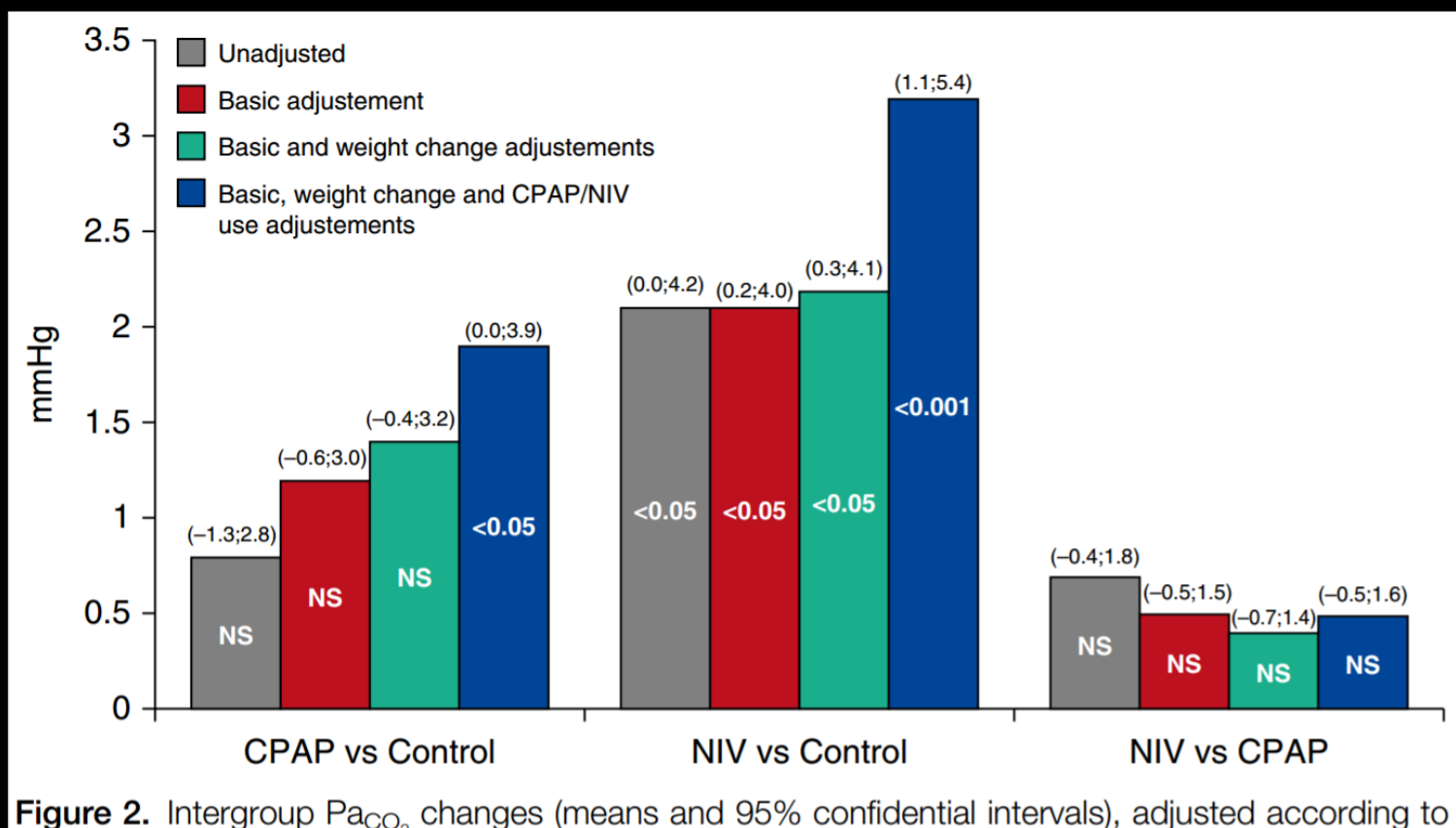# Efficacy of Different Treatment Alternatives for Obesity Hypoventilation Syndrome: Pickwick Study
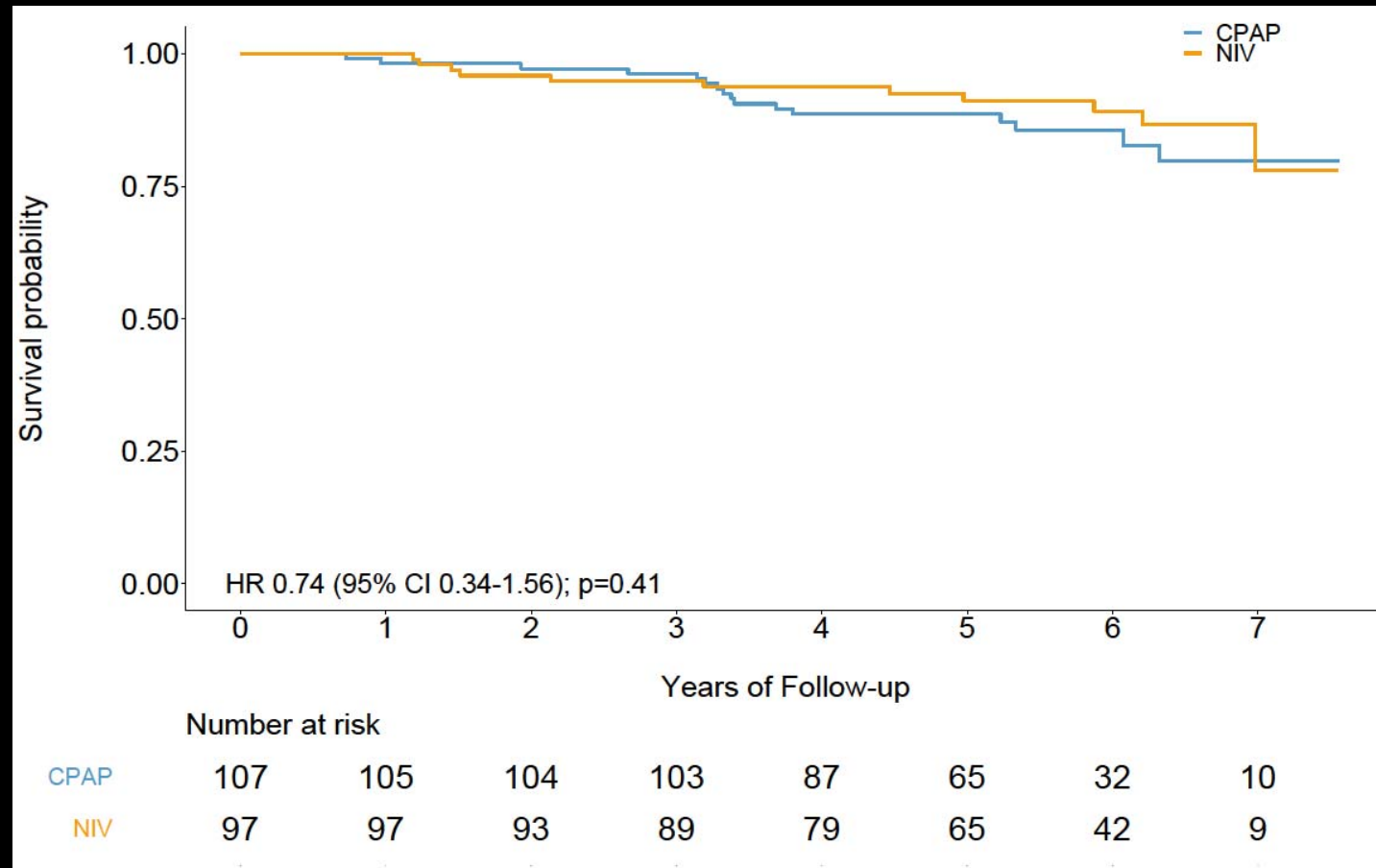

Figure 2. Intergroup Pa_{CO_2} changes (means and 95% confidential intervals), adjusted according to
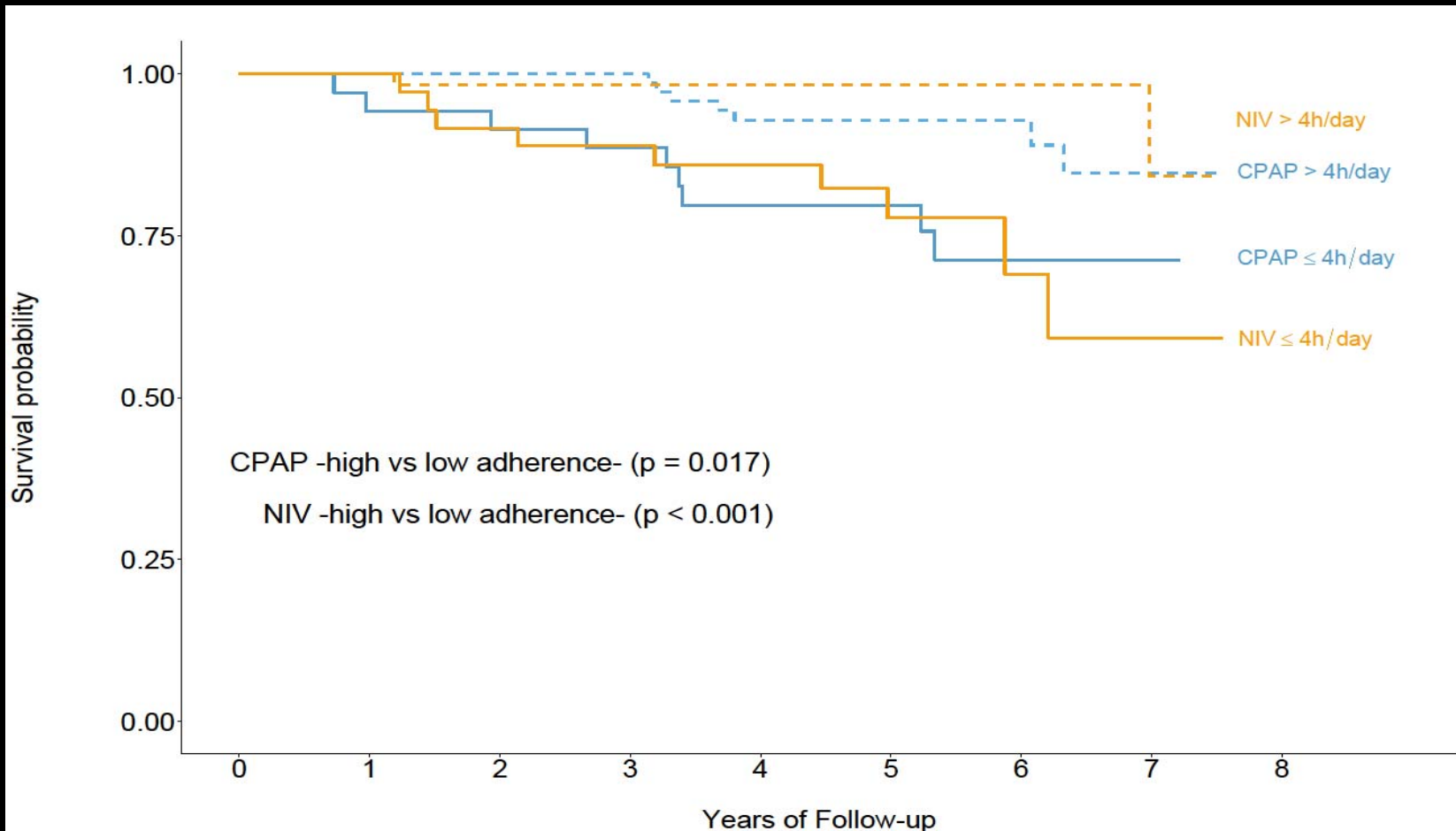
Results of Pickwick trial:
Long term outcomes

- Median follow-up of 5.4 years
  - Mean CPAP pressure 10.7±2.6 cm H_2O
  - Median (25th, 75th percentile) CPAP use 6 (3, 7) h/night
  - Mean NIV pressure 19.7/8.2 cm H_2O, backup rate 14
  - Median (25th, 75th percentile) NIV use 6 (1.3, 7.2) h/night
- Hospital days/year 1.63 for CPAP and 1.44 for NIV; adjusted p=0.56
- Incident cardiovascular events was 15% for CPAP and 17% for NIV; adjusted p=0.66
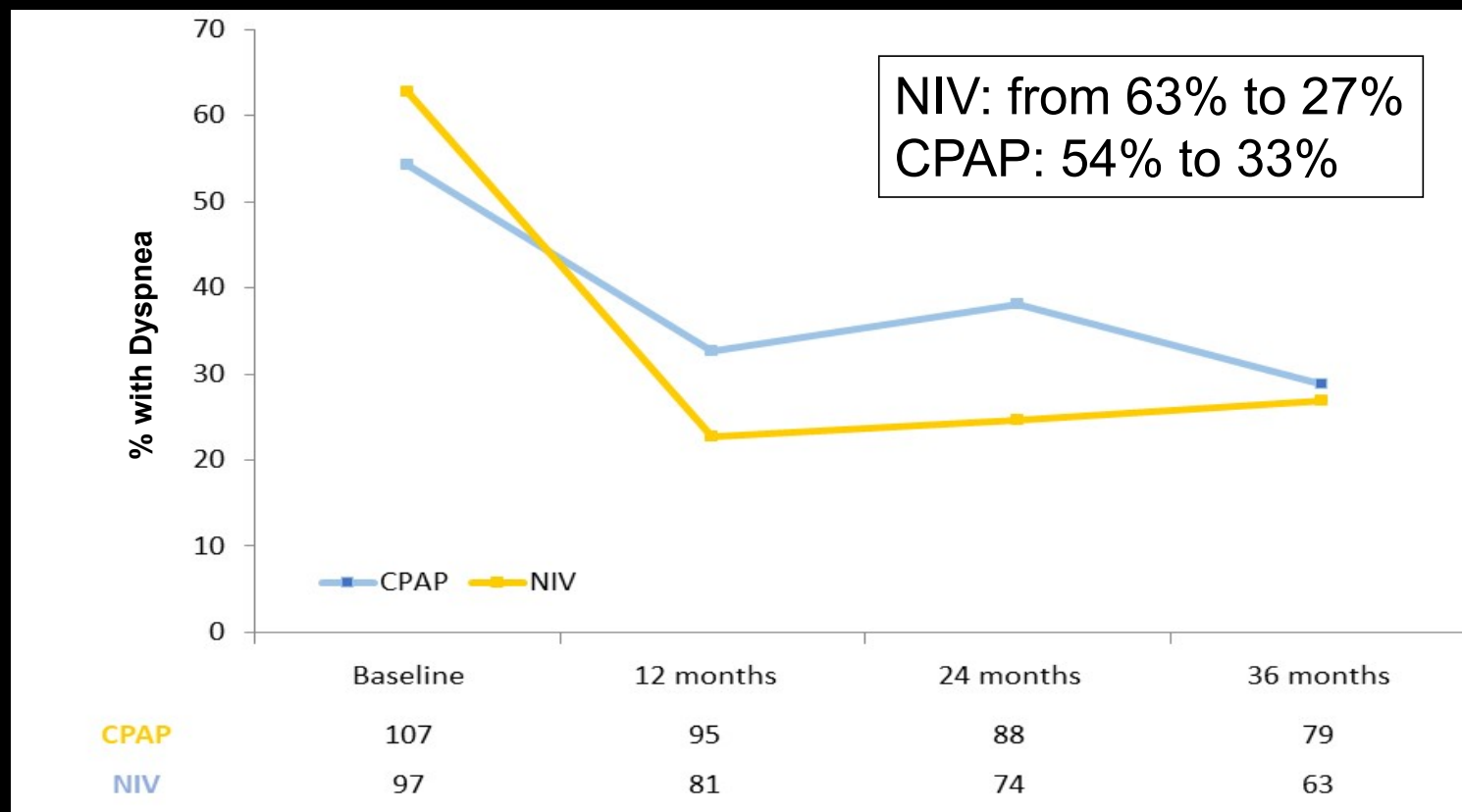- Mortality rate was 15% for CPAP and 11% for NIV; adjusted p=0.63

Masa JF, Mokhlesi B, et al. Lancet 2019; 393:1721

Long-term survival CPAP vs. NIV

Long-term survival CPAP vs. NIV based on adherence

Long-term Change in Dyspnea

NIV: from 63% to 27%
CPAP: 54% to 33%

	Baseline	12 months	24 months	36 months
CPAP	107	95	88	79
NIV	97	81	74	63

Need for daytime supplemental oxygen

- Both NIV and CPAP groups experienced a progressive and significant reduction in the need for daytime supplemental oxygen therapy
- CPAP:
  - 29 (27%) at baseline to 12 (13%) at 36 months (p=0.01)
- NIV:
  - 21 (22%) at baseline to 9 (11%) at 36 months (p=0.04)

So when do you consider using NIV?

Consider when

➢ Decompensated acute-on-chronic hypercapnic respiratory failure

➢ No documented OSA or in cases of mild OSA

➢ Failure of CPAP

 ➢ $PaCO_2$ does not improve after 1-2 months despite adequate adherence

 ➢ Intolerant of higher pressures

➢ Other co-existing indications for NIV

Conclusions

- OSA is highly prevalent in the community
- CPAP is highly effective in improving daytime sleepiness, quality of life, reducing risk of motor vehicle accidents and improving sleep fragmentation and intermittent hypoxemia during sleep
- CPAP reduces daytime blood pressure by 2-3 mmHg
  - Anti-hypertensives are more effective than CPAP
- Oral appliances are not inferior to CPAP in reducing BP or reducing symptoms
  - Not as efficacious as CPAP but similar clinical effectiveness because of higher adherence
- It remains unclear whether CPAP improves cardiovascular morbidity and mortality