Sleep Apnea in patients with CHF

Dr. Seth Yandell M.D., FACP

Board certified in Sleep Medicine by the ABIM

Cardiovascular changes in NREM & REM sleep

- – NREM Sleep:
  - – ↓ Sympathetic and ↑ Parasympathetic Activity
  - – ↓ HR & BP
  - – ↓ Ventilation
- Phasic REM sleep ↑ HR and BP
- NREM sleep is peaceful for CV system
- Phasic REM sleep is not peaceful for CV system

Prevalence of Heart Failure in U.S.

- 2.3% of US population (6.7 million)
- 12-15% of population >65 y old
- Leading cause of hospitalization in people > 65
- >1 million US hospitalizations yearly due to CHF

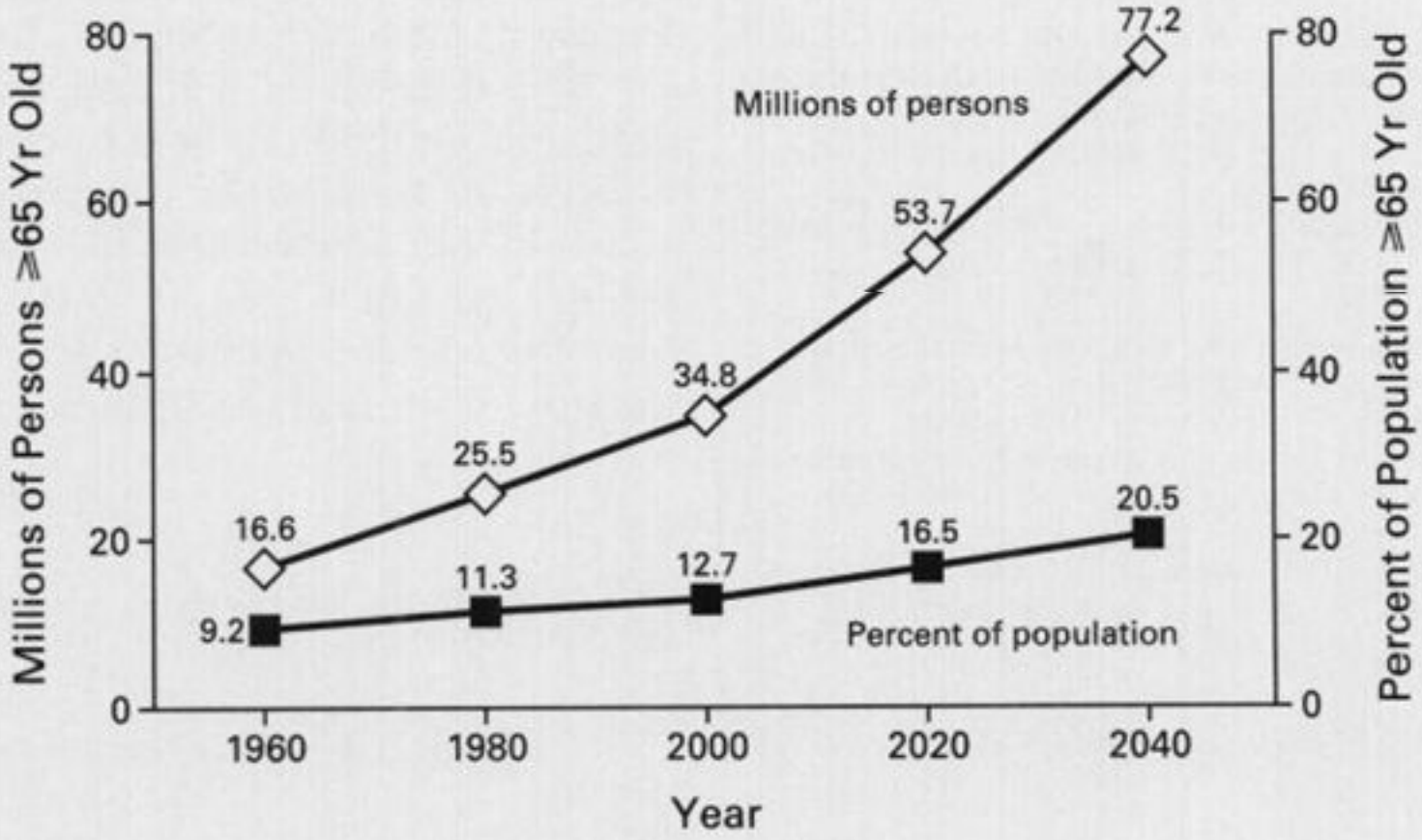
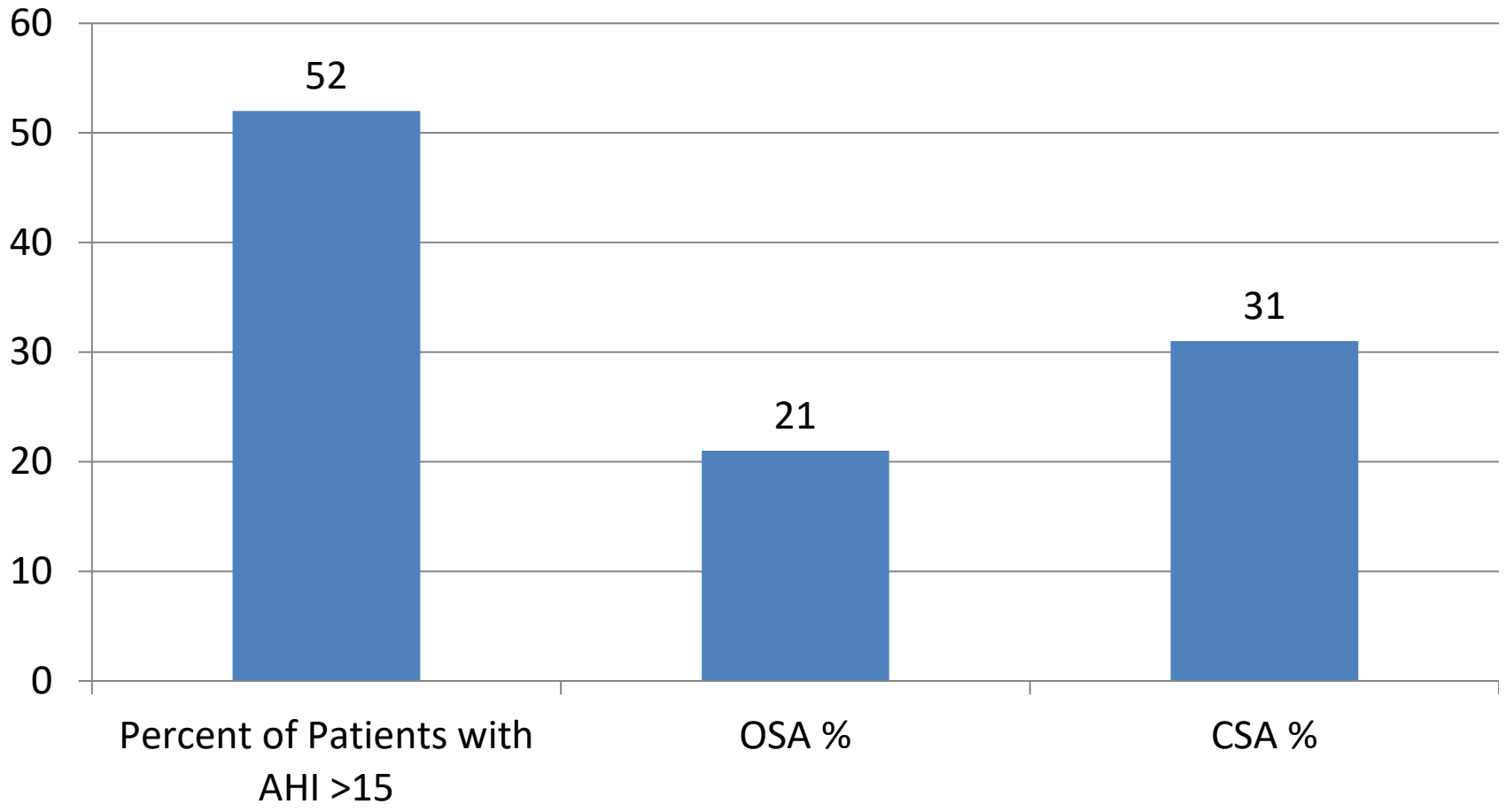


Figure 1. Projected Increases in the U.S. Population 65 Years of Age or Older. Data are from the U.S. Census Bureau.[16]

Prevalence of sleep apnea in systolic heart failure

Author, Country, Year	Number of patients	% Patients with AHI >15
Javaheri, US 2006	100	49
MacDonald, US 2008	108	61
Wang, Canada 2007	287	47
Vazir, UK 2007	55	53
Oldenburg, Germany 2007	700	52

Prevalence of sleep apnea in 1250 consecutive patients with SHF

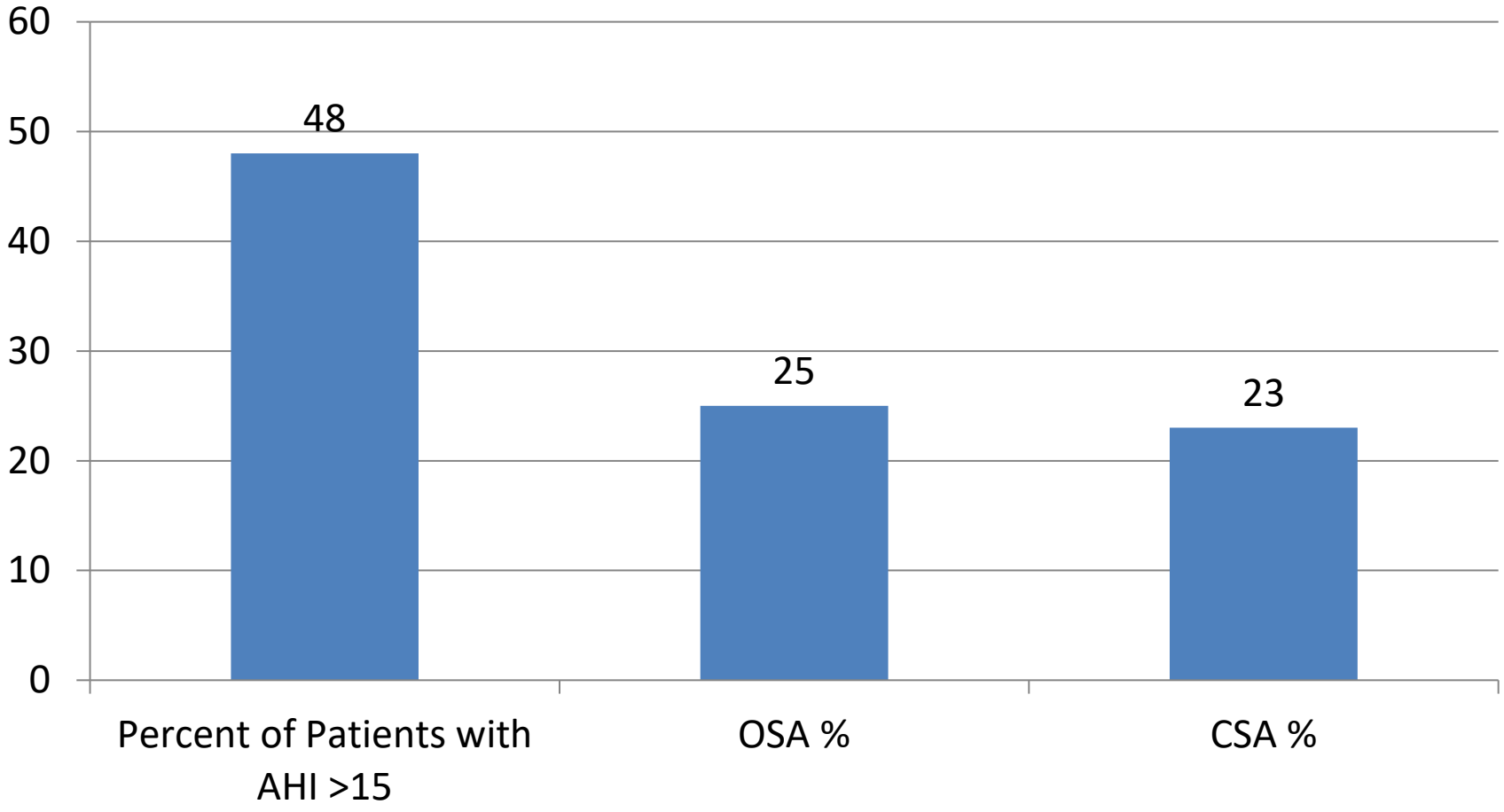


Prevalence of sleep apnea in Diastolic Heart Failure

- n = 244 consecutive patients (87 women)
- • Mean age 65
- Echocardiogram, Polysomnography, and R and L heart catheterization
- Cause of DHF:
  - HTN (44%)
  - CAD (33%)
- Hypertrophic/Restrictive (23%)

Bitter T, et. al. Sleep-disordered breathing in heart failure with normal left ventricular ejection fraction. Eur J Heart Fail. 2009 Jun;11(6):602-8.

Prevalence of Sleep Apnea in Diastolic Heart Failure(n=244)



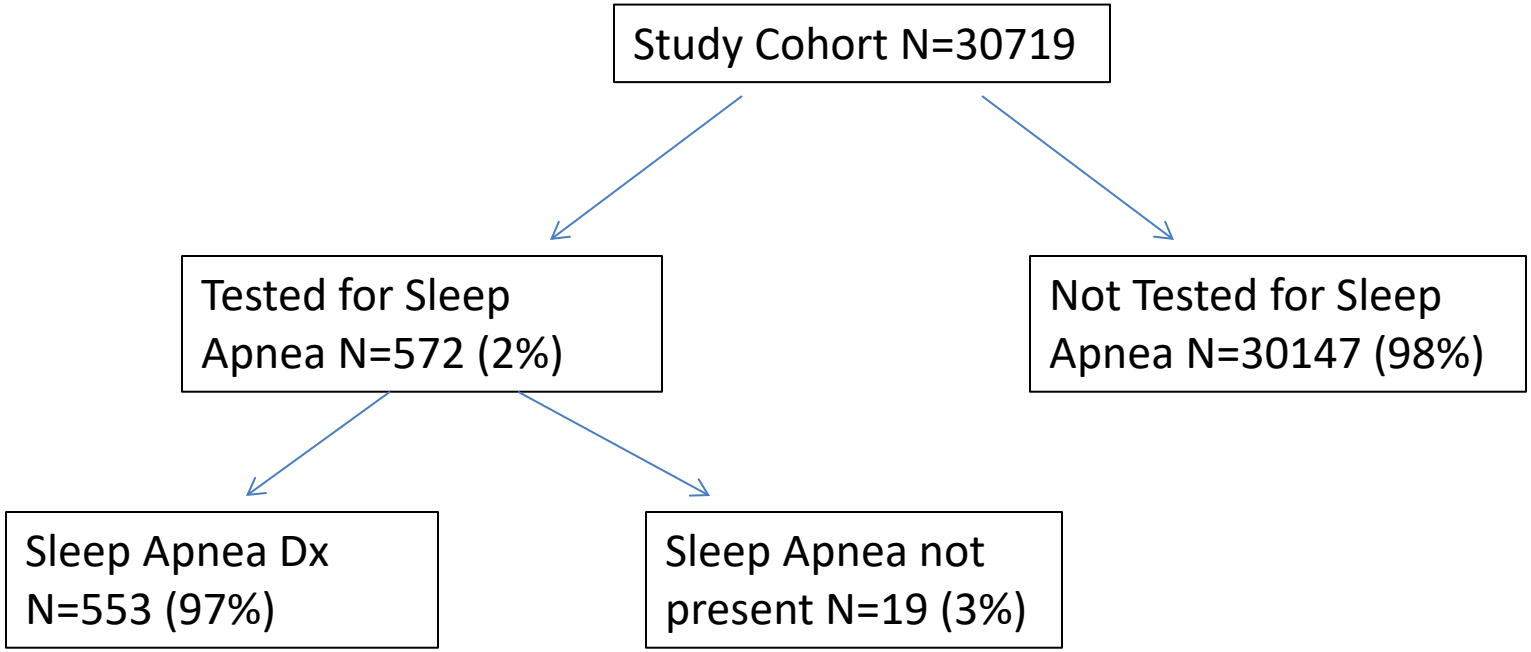
Deleterious effects of sleep apnea in patients with diastolic heart failure

- Patients with SA performed worse on exercise test and 6 minute walk
- With increasing impairment of diastolic dysfunction
  - the prevalence of SA, and CSA in particular increased
  - Patients with CSA had lower PCO_2, higher NT-proBNP, LVEDP, PCWP, and PAP

How frequently are patients with CHF tested for sleep apnea?

- A retrospective cohort study used the 2004-2005 Medicare Standard Analytical Files (SAFs).
- SAFs contain a 5 % sample of randomly selected Medicare beneficiaries.
- The study population included newly diagnosed HF patients in the first quarter of 2004 without prior diagnosis of SA.

- Among a population of 30,719 newly diagnosed HF patients, only 1,263 (4%) were clinically suspected to have SA.
- Of these, only 2% of the total cohort were tested for SA.



Javaheri S, et.al. Sleep apnea testing and outcomes in a large cohort of Medicare beneficiaries with newly diagnosed heart failure. Am J Respir Crit Care Med. 2011 Feb 15;183(4):539-46.

Why are heart failure patients undertested and underdiagnosed

- How do we usually screen for sleep apnea
- Common tool is the Epworth Sleepiness Scale in primary care and clinical practice
- Differences in symptoms for CHF patients with OSA vs patients with OSA without CHF

Epworth Sleepiness Scale

Using the following scale, circle the *most appropriate number* for each situation.

0 = would doze *less than once a month*
1 = *slight* chance of dozing
2 = *moderate* chance of dozing
3 = *high* chance of dozing

Situation	Chance of Dozing
Sitting and reading	0 1 2 3
Watching TV	0 1 2 3
Sitting, inactive in a public place (in a theater or in a meeting)	0 1 2 3
As a passenger in a car for an hour without a break	0 1 2 3
Lying down to rest in the afternoon (when circumstances permit)	0 1 2 3
Sitting and talking to someone	0 1 2 3
Sitting quietly after a lunch without alcohol	0 1 2 3
In a car, while stopped for a few minutes in the traffic	0 1 2 3

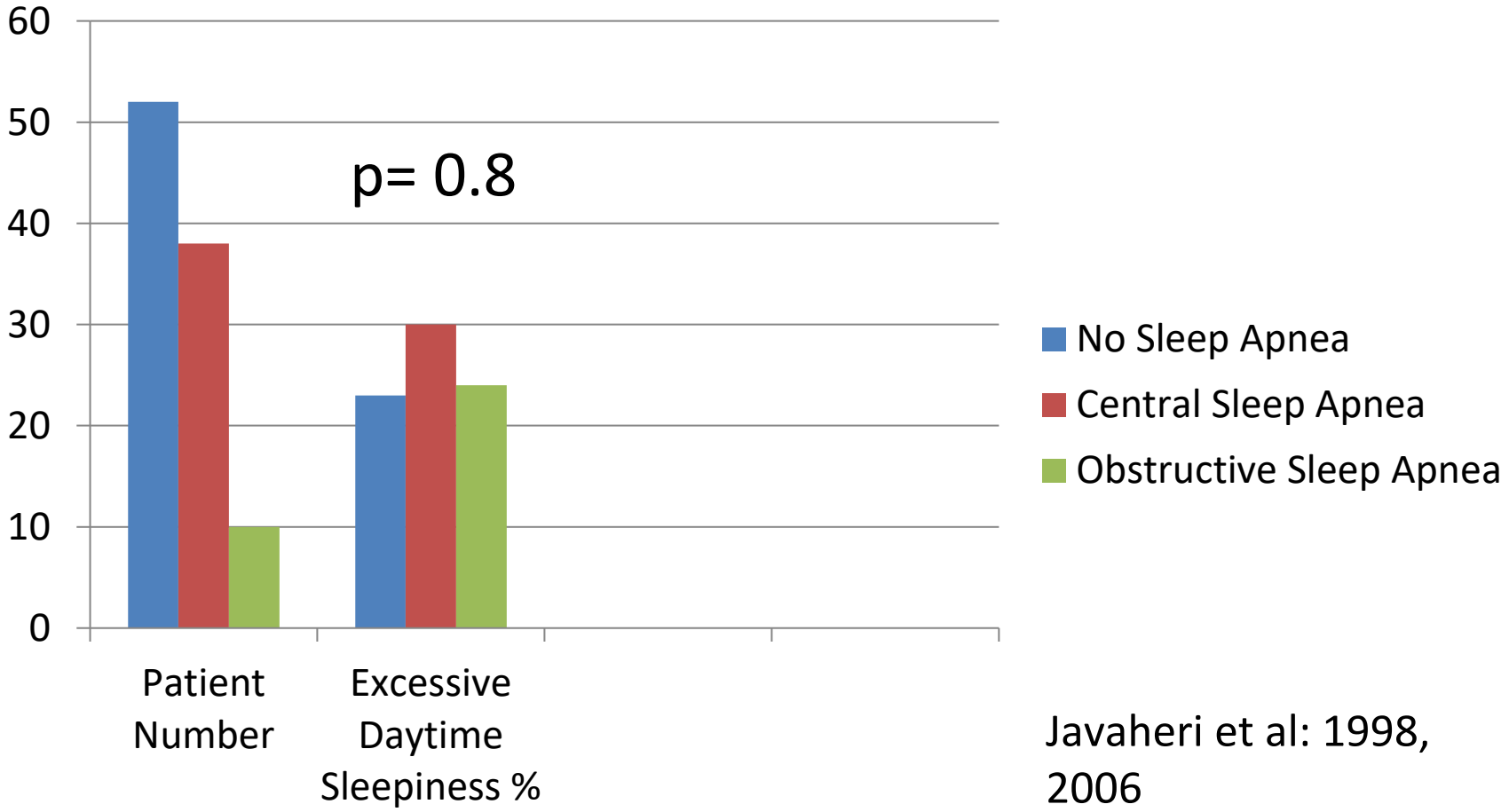
Add the 8 numbers you have circled **TOTAL** _____

0-9 normal range, ≥ 10 abnormal

The mystery of the lack of subjective excessive daytime sleepiness (EDS) in patients with CHF

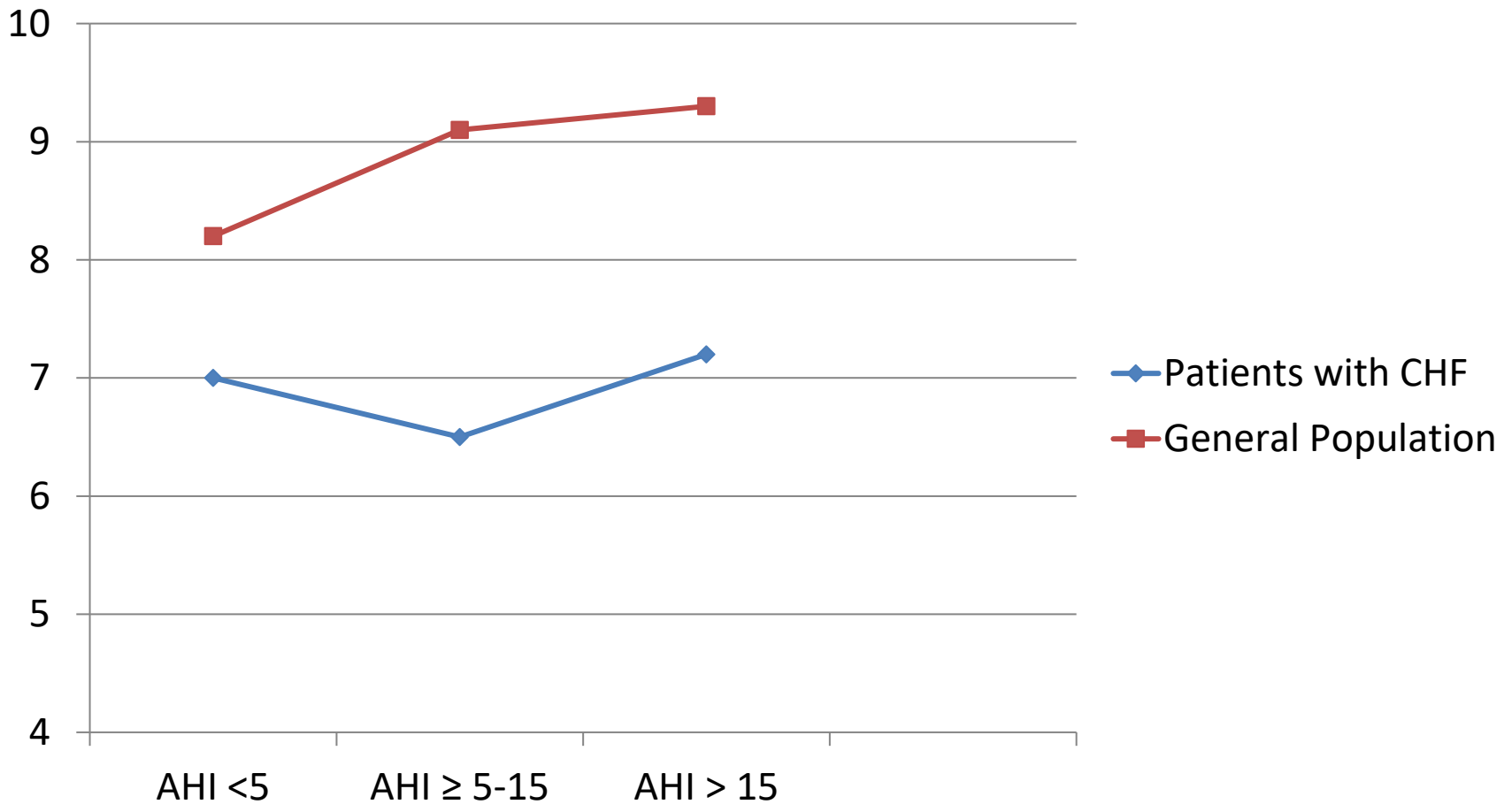
- Most studies show no difference in subjective EDS in patients with systolic heart failure with or without sleep apnea.
- However, when tested objectively, by MSLT or Osler test, heart failure patients with sleep apnea are sleepier than those without sleep apnea.

Excessive Daytime Sleepiness ratings in patients with heart failure



Javaheri et al: 1998, 2006

Differences of ESS Score between HF patients (University of Toronto) and the GP (Madison Sleep Cohort) according to the AHI



Clinical impact of lack of subjective sleepiness in patients with heart failure

- Under diagnosis of sleep apnea in heart failure
- Inadequate long-term CPAP adherence could diminish its effectiveness in maximizing LVEF and survival both for OSA and CSA

Treatment of OSA in CHF

- Promote sleep hygiene
- Avoid ETOH, benzodiazepines,and opioids
- Weight loss
- Positive airway pressure devices: CPAP/BIPAP
- Nocturnal use of supplemental oxygen

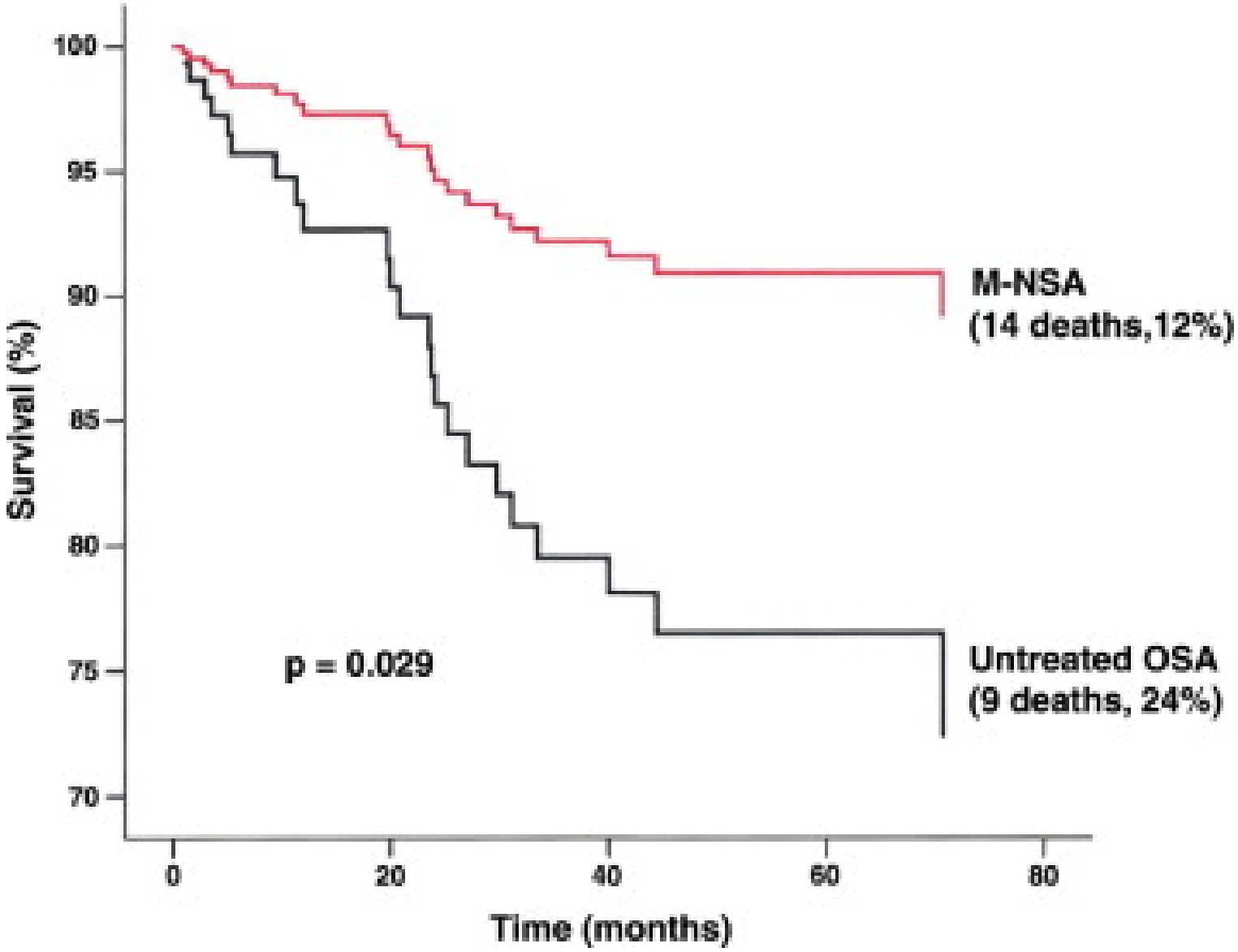
Effects of PAP on LVEF in RCT of OSA in Systolic CHF

	Kaneko Non blinded	Mansfield Non blinded	Egea Double blinded	Smith Double blinded	Khayat Non blinded	Khayat Non blinded
# Patients	12	19	20	23	11	13
AHI	40	25	44	36	30	34
LVEF	25	35	29	30	29	26
Change in LVEF	+9*	+5*	+2.2*	0.0	+0.5	+8.5*
Duration	4 weeks	3 months	3 months	6 weeks	3 months	3 months
PAP Titration	CPAP Yes	CPAP Yes	CPAP Yes	Auto pap No	CPAP Yes	Bipap Yes
PAP compliance In Hours/Night	6.2	5.6	Not measured	3.5	3.6	4.5

OSA as Cause of Mortality in CHF

- 218 patients with LVEF<45%
- 45 with CSA (21%), excluded from analysis
- 113 control group with treatment of OSA, AHI **<** 15, mean = 7/h
- 41 untreated OSA AHI ≥15/hr mean = 33/h

Wang H et al. *J Am Coll Cardiol.* 2007; 49: 1632


100
95
90
85
80
75
70
Survival (%)
0
20
40
60
80
Time (months)
p = 0.029
M-NSA
(14 deaths,12%)
Untreated OSA
(9 deaths, 24%)

Multivariate Hazards Ratios for Mortality Rate

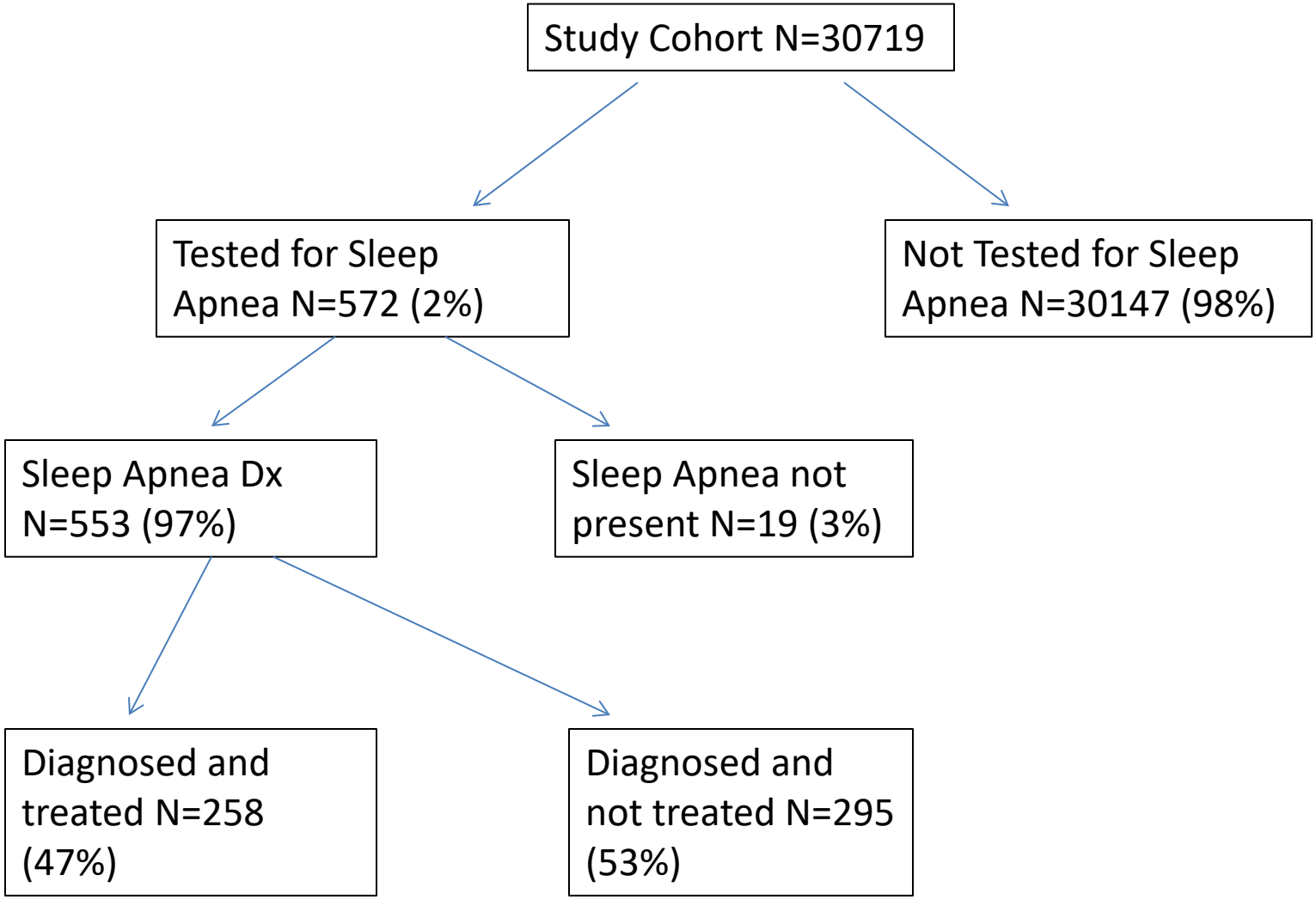
Variables	Hazard Ratio	p Value	95% Confidence Interval	
			Lower	Upper
Untreated OSA	2.81 	0.029	1.11	7.10
LVEF	0.93	0.006	0.88	0.98
NYHA functional class	2.30 	0.037	1.04	5.08
Age	1.05	0.005	1.02	1.09

Wang H et al. *J Am Coll Cardiol.* 2007; 49: 1632

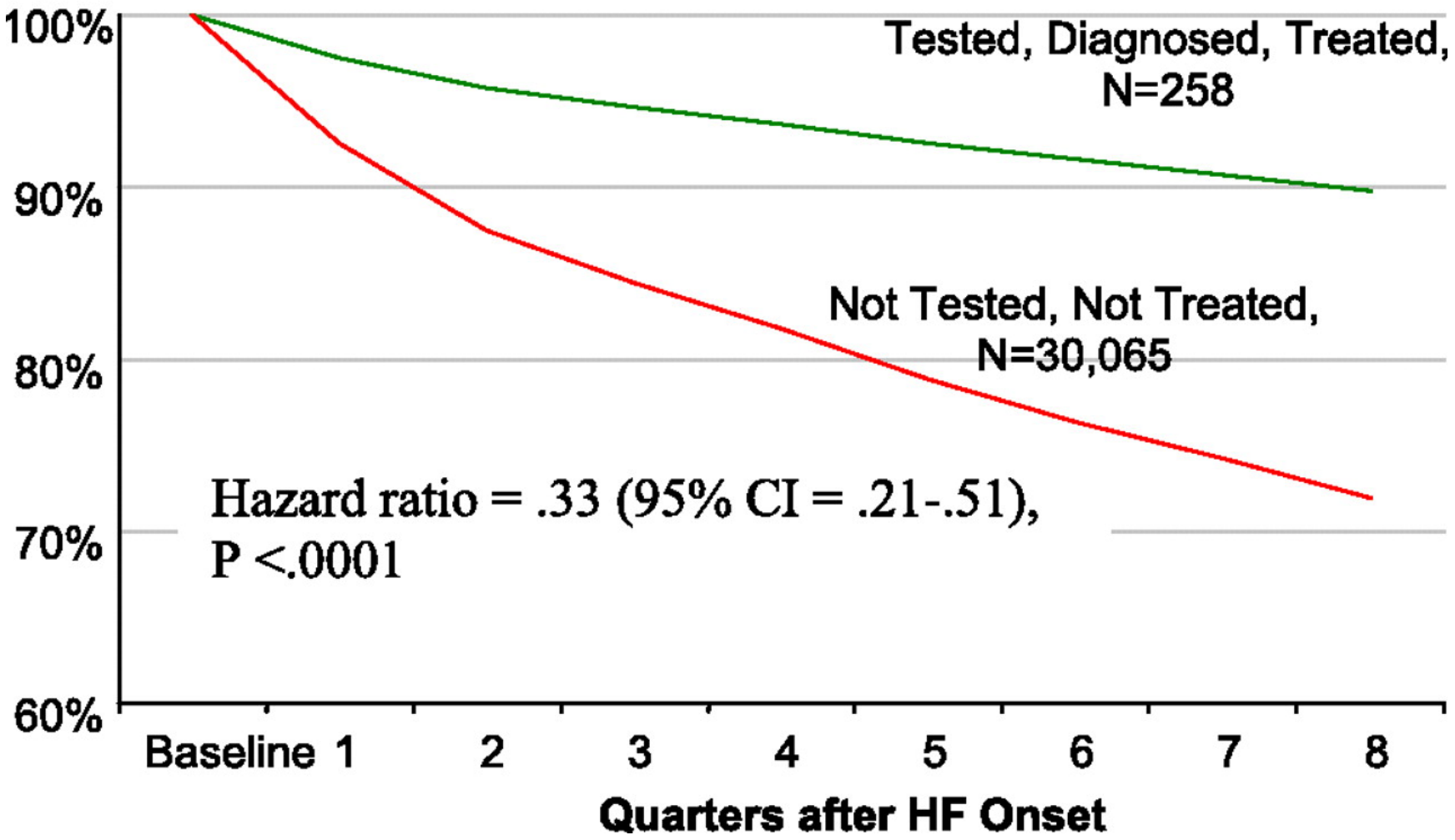
Sleep apnea testing and outcomes

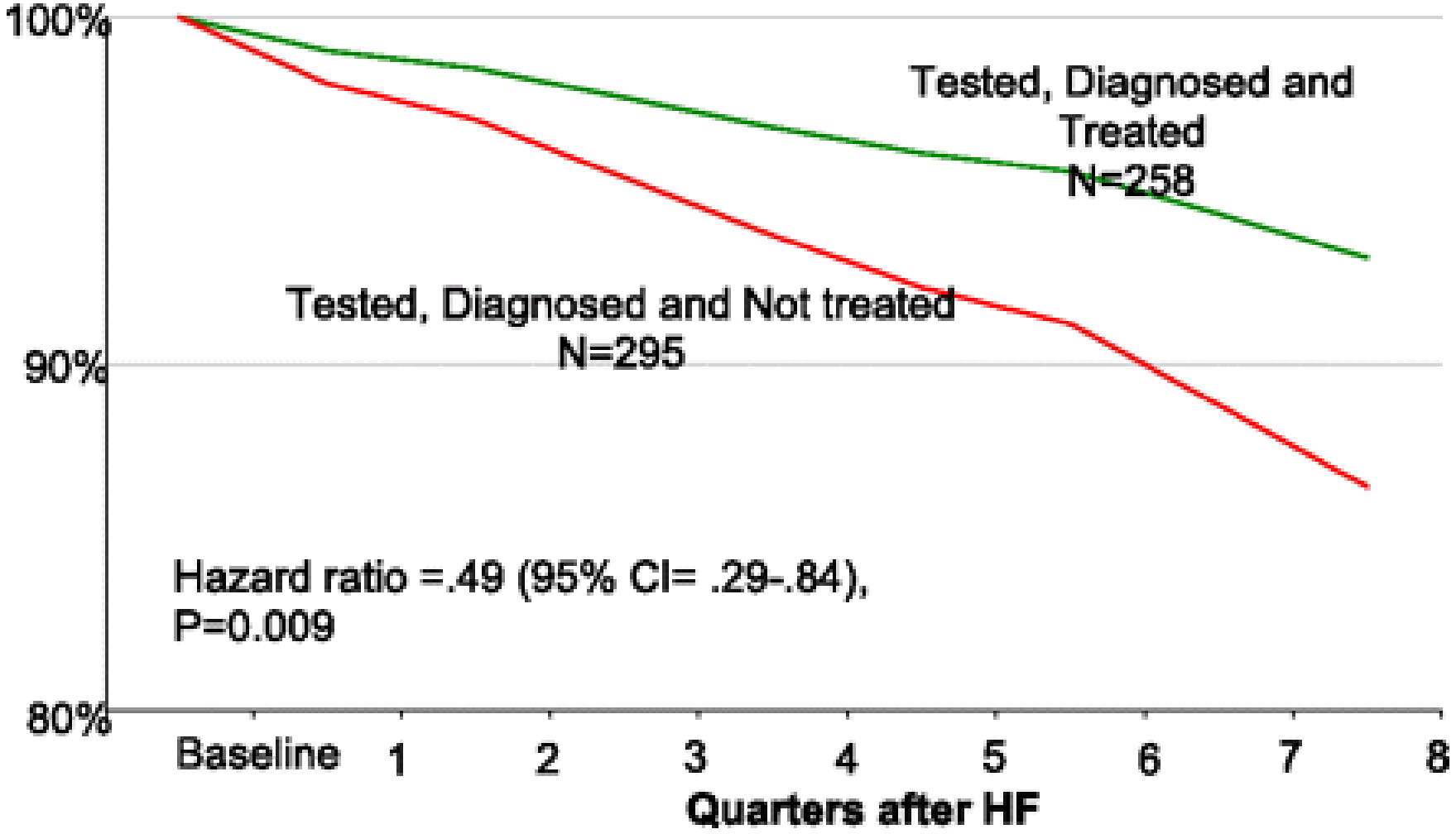
- Retrospective medicare cohort of >30K patients done by Javaheri et. al. in 2011
- Newly diagnosed heart failure
- Reviewed whether patients were tested, diagnosed, treated, and mortality

Javaheri et al. Am J Respir Crit Care Med 2011



Javaheri et al. Am J Respir Crit Care Med 2011


Percent of Cohort Alive
100%
90%
80%
70%
60%
Tested, Diagnosed, Treated,
N=258
Not Tested, Not Treated,
N=30,065
Hazard ratio = .33 (95% CI = .21-.51),
P <.0001
Baseline 1 2 3 4 5 6 7 8
Quarters after HF Onset

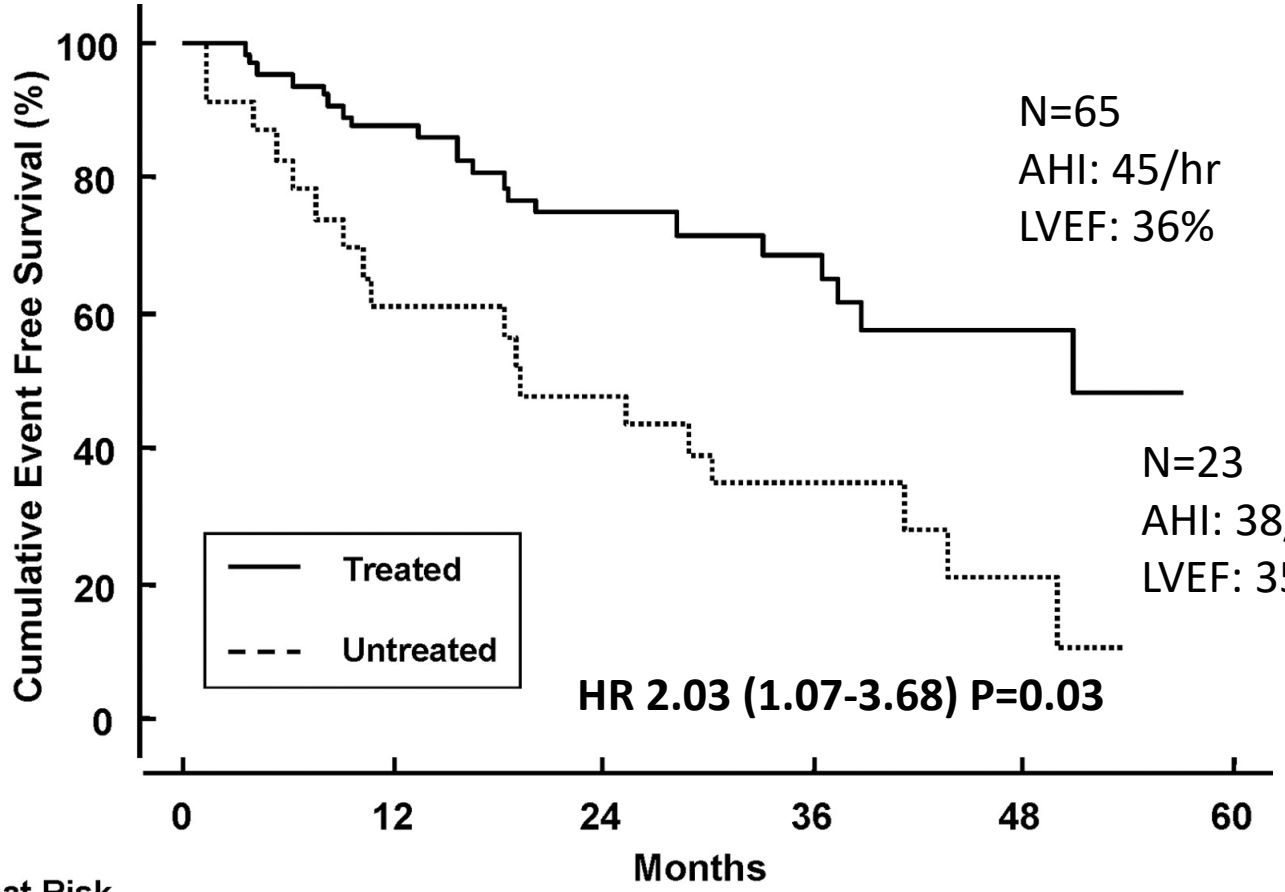

Percent of Cohort Alive
100%
90%
80%
Tested, Diagnosed and Treated
N=258
Tested, Diagnosed and Not treated
N=295
Hazard ratio =.49 (95% CI= .29-.84),
P=0.009
Baseline
1
2
3
4
5
6
7
8
Quarters after HF

Prognosis of systolic CHF and OSA

- Kasai T et al., Prospective cohort
- Systolic CHF (EF <50%)
- OSA (CSA patients were excluded)
- Looked at mortality associated with no treatment and inadequate usage of CPAP

Kasai T et al. Chest 2008;133:690-696

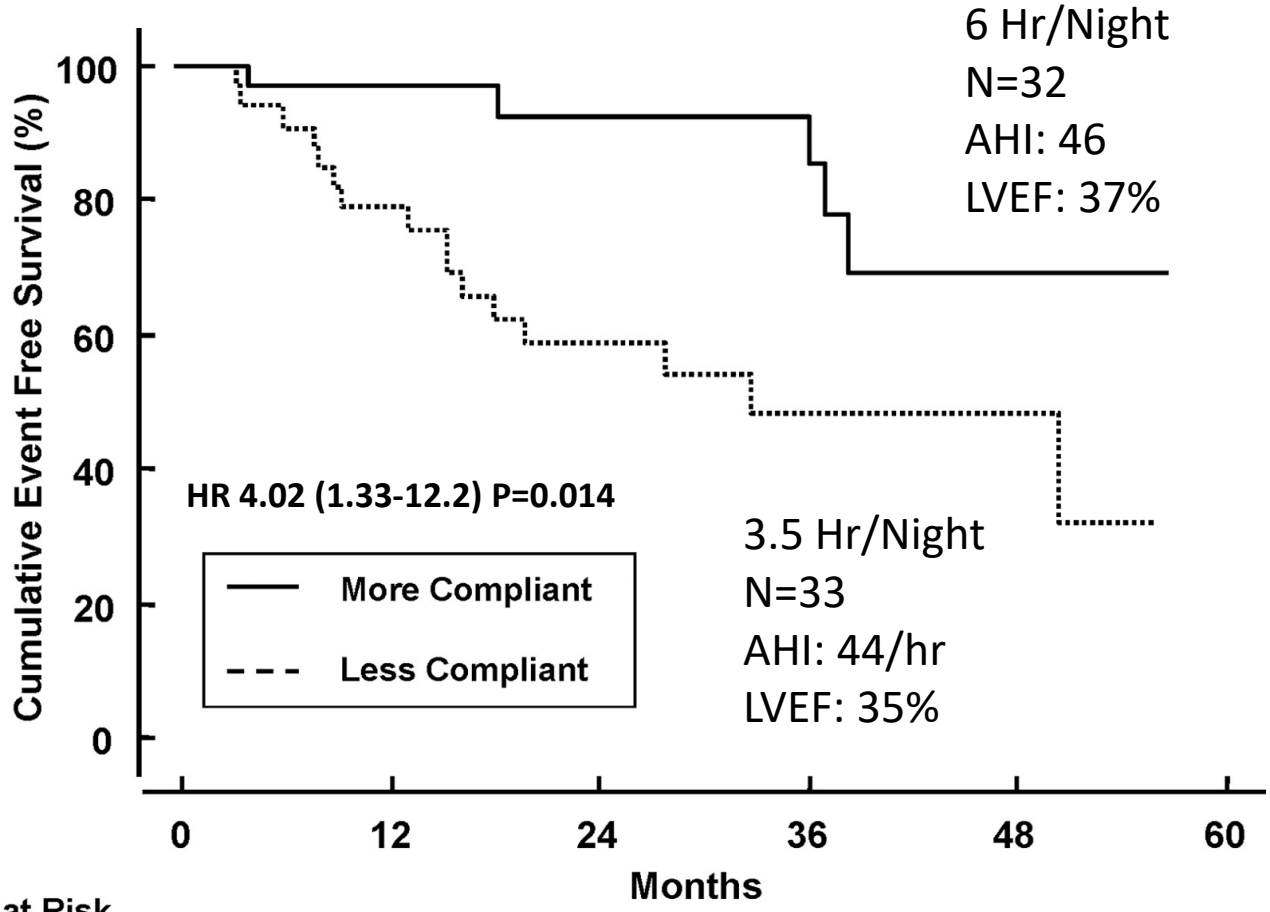
Cumulative event-free survival in CPAP-treated and untreated patients.



Numbers at Risk					
Treated	65	56	27	20	7
Untreated	23	14	11	6	2

Kasai T et al. Chest 2008;133:690-696

Cumulative event-free survival determined by compliance status.



Numbers at Risk					
More Compliant	32	30	14	12	4
Less Compliant	33	26	13	7	3

Kasai T et al. Chest 2008;133:690-696

Treatment of OSA in CHF

- Most patients respond to CPAP or BIPAP
- Some require additional supplemental oxygen
- In patients with CHF, central sleep apnea (CSA) is more prevalent and many times doesn't appear until treated with CPAP or BIPAP
- Weight loss (diet/exercise, medications i.e. GIP/GLP-1 receptor agonists, bariatric surgery)
- Mandibular advancement devices

Treatment of CSA in CHF

- Given treatment related development of CSA with positive pressure ventilation, patients with CHF should all have monitored sleep studies for titration (studies have shown increased mortality to CPAP nonresponders)
- Acetazolamide has been studied in small groups of patients and found to decrease episodes of CSA
- Appropriate CPAP can over time reduce CSA events
- Bipap with a set backup rate
- Adaptive servo-ventilation effective in reducing AHI but machines are expensive and increased mortality demonstrated in patients with reduced EF

Long and short term PAP compliance is a problem

- Patients really need to use for ≥ 4 hours nightly for significant benefit
- Given the fact that pts frequently do not have complaints of sleepiness, many do not feel the need to use it
- Use the above data to convince them otherwise
- Mandibular advancement devices can help some patients better tolerate PAP therapy and can be used for patients who cannot tolerate PAP

Mandibular Advancement vs CPAP

- No specific studies in CHF patients showing improved mortality
- Multiple studies show improvements in AHI with MAD
- Ou YH, et. al compared MAD to CPAP for blood pressure control
- 220 patients with mod to severe OSA and HTN
- Randomized to auto-CPAP (no titration done) vs MAD
- 4 hours/night: 72.9% MAD, 69.4% CPAP
- No statistically significant difference in 24 hr BP between the groups (MAD non inferior)

Ou YH, et.al.. Mandibular Advancement vs CPAP for Blood Pressure Reduction in Patients With Obstructive Sleep Apnea. J Am Coll Cardiol. 2024 May 7;83(18):1760-1772.

Weight loss

- Traditional (diet, exercise)
- Bariatric surgery
- Glucose dependent insulinotropic polypeptide receptor agonist/Glucagon-like peptide-1 receptor agonist (GIP/GLP-1) medication

Bariatric surgery

- Priyadarshini P, Singh VP, et. al. followed a prospective cohort of 27 patients with OSA and morbid obesity
- BMI average 48.4 preoperatively
- 51.3% with severe OSA preop
- Majority had sleeve gastrectomy with a small number having Roux-en-Y
- Mean BMI had dropped to 41.2
- Number of patients requiring CPAP dropped from 15 to 3 at average of 5.2 months
- Patients still requiring CPAP had drop in AHI on average from 31.8 to 20.2
- Average needed CPAP dropped from 11.3 cm/H20 to 6 cm/H20

Priyadarshini P, Singh VP, et. al. Impact of bariatric surgery on obstructive sleep apnoea-hypopnea syndrome in morbidly obese patients. J Minim Access Surg. 2017 Oct-Dec;13(4):291-295.

Bariatric surgery

- Al Oweidat K, et.al.. Bariatric surgery and obstructive sleep apnea, meta analysis
- 2310 patients across 32 studies
- Study inclusion criteria: OSA, any bariatric surgery, polysomnography post surgery
- Average BMI reduction of 11.9
- Average AHI decreased by 19.3
- OSA remission of 65%

Al Oweidat K, et.al.. Bariatric surgery and obstructive sleep apnea: a systematic review and meta-analysis. Sleep Breath. 2023 Dec;27(6):2283-2294.

Tirzepatide

- Glucose dependent insulinotropic polypeptide receptor agonist/Glucagon-like peptide-1 receptor agonist (GIP/GLP-1)
- Malhotra A, et. al, Moderate to severe OSA treatment with Tirzepatide
- 2 phase (phase 1 not on PAP at baseline, phase 2 on PAP at baseline)
- Double blind randomized controlled

Malhotra A, et.al.; SURMOUNT-OSA Investigators. Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity. N Engl J Med. 2024 Oct 3;391(13):1193-1205.

Tirzepatide cont.

- Phase 1 baseline mean AHI 51.5, BMI 39.1
- Phase 2 baseline mean AHI 49.5, BMI 38.7
- At 52 wks Phase 1 drop in weight with Tirzepatide -18.1 vs -1.3 placebo
- At 52 wks Phase 2 drop in weight with Tirzepatide -20.1% vs -2.3% placebo
- At 52 wks Phase 1 average drop in AHI with Tirzepatide -25.3 vs -5.3 placebo
- At 52 wks Phase 2 average drop in AHI with Tirzepatide -29.3 vs -5.5 with placebo

Malhotra A, et.al.; SURMOUNT-OSA Investigators. Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity. N Engl J Med. 2024 Oct 3;391(13):1193-1205.

Take Home Points

- Studies show sleep apnea is present in approx 50% of patients with CHF and central sleep apnea seen in about half of those patients
- Patients with CHF and concomitant sleep apnea are less likely to have sleepiness symptoms so they are infrequently referred for sleep studies
- Untreated sleep apnea increases mortality and worsens heart failure in patients with CHF
- Regular discussions of amount of use (at least 4 hours nightly) of PAP or mandibular advancement device and reasons why are important for compliance
- I would recommend referring **all** of your CHF patients for sleep studies (given the high prevelance and low number needed to treat to improve outcomes)

References

- **Bitter T, et. al. Sleep-disordered breathing in heart failure with normal left ventricular ejection fraction. Eur J Heart Fail. 2009 Jun;11(6):602-8.**
- **Javaheri S, et.al. Sleep apnea testing and outcomes in a large cohort of Medicare beneficiaries with newly diagnosed heart failure. Am J Respir Crit Care Med. 2011 Feb 15;183(4):539-46.**
- **Wang H et al. *J Am Coll Cardiol.* 2007; 49: 1632**
- **Kasai T et al. Chest 2008;133:690-696**
- **Ou YH, et.al.. Mandibular Advancement vs CPAP for Blood Pressure Reduction in Patients With Obstructive Sleep Apnea. J Am Coll Cardiol. 2024 May 7;83(18):1760-1772.**
- **Priyadarshini P, Singh VP, et. al. Impact of bariatric surgery on obstructive sleep apnoea-hypopnea syndrome in morbidly obese patients. J Minim Access Surg. 2017 Oct-Dec;13(4):291-295.**
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