The relationship of Obesity to OSA

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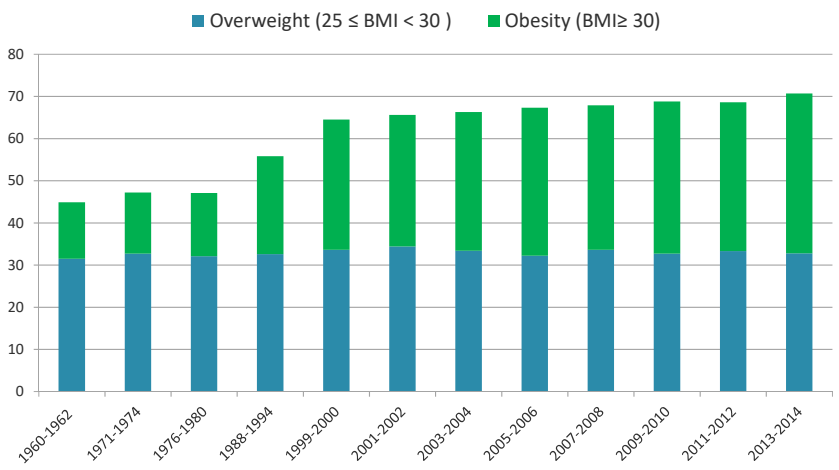
Overview

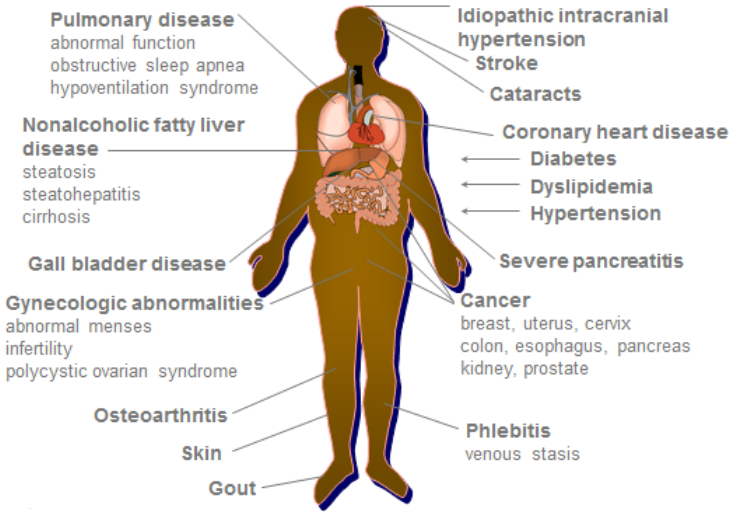
- Relationship between Obesity and OSA
- Effects of weight loss on OSA
  - Behavioral treatment
  - Pharmacological treatment
  - Surgery

Prevalence of Overweight and Obesity among US Adults



Fryar CD et al. NCHI Health Stats 2014
CDC. Health Statistics 2016

Medical Complications of Obesity

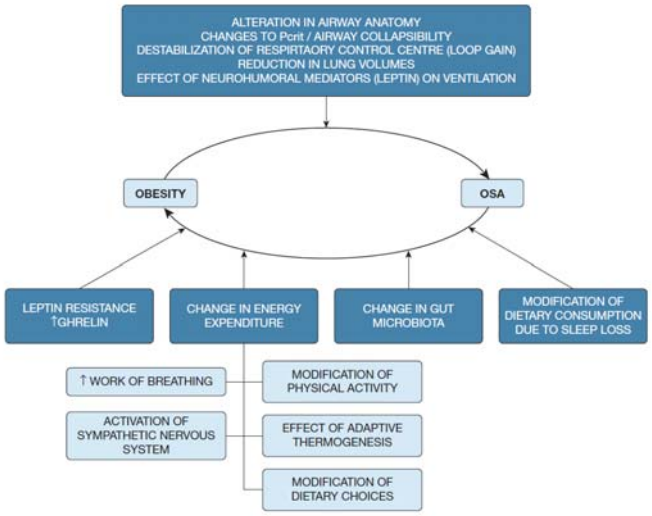


Obesity and OSA

- Two-thirds of patients with OSA have obesity[1]
- Obesity explains ~60% of the variance of AHI[2]
- One SD increase in BMI is associated with a 4-fold increase in AHI[3]
- 40% of weight-loss patients have AHI > 5[4,5]

[1]Guilleminault C. et al, Chest, 1998
[2]Joosten SA et al. CHEST 2017
[3] Young T. et al, NEJM, 1993
[4] Richman R. et al, IJO, 1994
[5] Vgontzas A. et al, Arch Intern Med, 1994

Bidirectional role of obesity and OSA



Joosten SA et al. CHEST 2017

Clinical Guideline for the Evaluation, Management and Long-term care of OSA in adults

Patients at high risk for OSA who should be evaluated for OSA symptoms:

obesity (BMI > 35), congestive heart failure, atrial fibrillation, treatment refractory hypertension, type 2 diabetes, nocturnal dysrhythmias, stroke, pulmonary hypertension, high-risk driving populations, preoperative for bariatric surgery

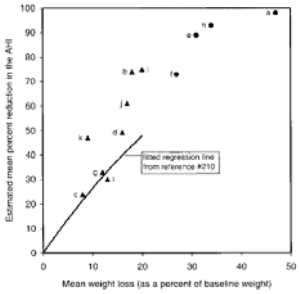
Treatment

- Behavioral treatment options include weight loss, ideally to a BMI of 25 kg/m^2"
  - " Successful dietary weight loss may improve the AHI in obese patients with OSA. **Weight loss should be recommended for all overweight OSA patients.** Weight loss should be combined with a primary treatment for OSA because of the low success rate of dietary programs and the low cure rate by dietary approach alone."

Epstein LJ et al for the Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2017

Weight Loss and OSA: early, uncontrolled studies

- Weight losses of 9% to 20% have been associated with reductions in AHI of 30% to 74%[1]
- A 1% change in weight is associated with a 3% change in AHI[2]
  - 10% ↓ in weight is associated with a 26% ↓ in AHI
  - 10% ↑ in weight is associated with a 32% ↑ in AHI
- In dietary *(triangles)* & surgical *(circles)* uncontrolled weight loss studies and an observational study *(regression line),* there is a clear relationship between weight loss and reduction in AHI[3]



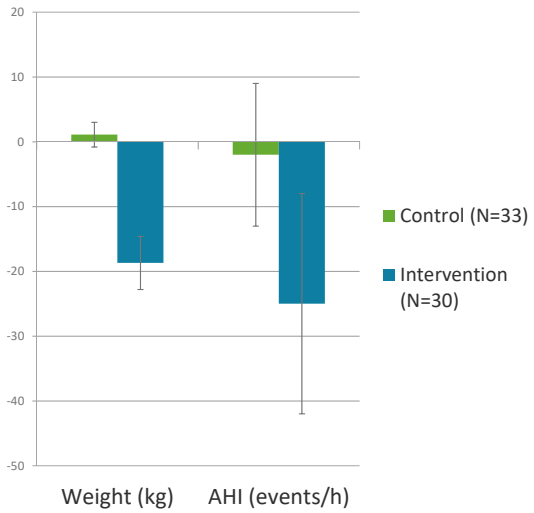
[1]Strobel RJ & Rosen RC., Sleep, 1996
[2]Peppard et al., JAMA, 2000 [3]Young et al. Am J Respir Crit Care Med 2002

Randomized trials of Weight loss and AHI

Treatment	Author/Year	Inclusion	% Men/Age (y)	Duration	Outcomes in Intervention Arm (Reductions)	
Medical	Foster[33]/2009	BMI > 25	41/61	1 y	Weight (kg)	108 to 91
		AHI > 5			BMI (kg/m²)	37 to 33
					AHI (eph)	23 to 18
	Johansson[34]/2009	BMI 30-40	100/49	1 y	Weight (kg)	113 to 95
		AHI > 15			BMI (kg/m²)	34 to 30
		CPAP prescribed			AHI (eph)	37 to 12
					No change in CPAP adherence	
	Tuomilehto[35,36]/2013, 2009	BMI 28-40	75/51	1 y	Weight (kg)	101 to 96
					BMI (kg/m²)	33 to 32
					AHI (eph)	10 to 9
	Kuna[37]/2013	BMI > 25	40/61	4 y	Weight (kg)	102 to 98
					BMI (kg/m²)	37 to 36
					AHI	23 to 16
Surgical	Dixon[69]/2012	BMI 35-55	58/49	2 y	Weight (kg)	135 to 107
		AHI > 20			BMI (kg/m²)	46 to 36
		CPAP prescribed			AHI (eph)	65 to 40
					No change in CPAP adherence	
	Aguiar[53]/2014	BMI 40-50	19/40	3 mo	Weight (kg)	119 to 90
					BMI (kg/m²)	48 to 37
					AHI (eph)	16 to 6
	Feigal-Guiller[52]/2015	BMI > 35	53/47	3 y	Weight (kg)	135 to 117
		AHI > 30			BMI (kg/m²)	49 to 42
		$Paco_2$ > 48 mm Hg			AHI (eph)	57 to 41
		NIV prescribed			No change in NIV adherence	

Joosten et al. CHEST 2017

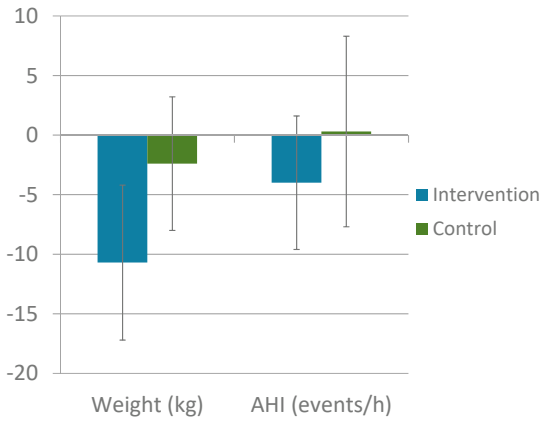
RCT: Effect of a VLCD on moderate-to-severe OSA in obese men: Changes in weight and AHI at 9 weeks



N=63	Combined
Mean age, y	49 ± 7.3
Mean weight, kg	112.5 ± 14.2
Mean BMI, kg/m²	34.6
Mean AHI, events/h	37± 15
Intervention: 7 weeks of liquid VLCD (2.3 MJ/dy), followed by 2 weeks of gradual introduction of normal foods to reach 6.3 mJ/d @ week 9 **Control:** usual diet	

Johansson et al., BMJ, 2009

RCT: Lifestyle intervention with weight reduction for mild OSA: Changes in weight & AHI at 1 yr.



[Data represent mean changes with standard deviation (SD)]

N=72 (73% male)	Control (n=37) 27M/10F	Intervention (n=35) 26M/9F
Mean age, y	50.9 ± 8.6	51.8 ± 9.0
Mean weight, kg	92.3 ± 11.3	101.2 ± 11.9
Mean BMI, kg/m²	31.4 ± 2.7	33.4 ± 2.8
Mean AHI, events/h	9.3 ± 3.0	10.0 ± 3.0

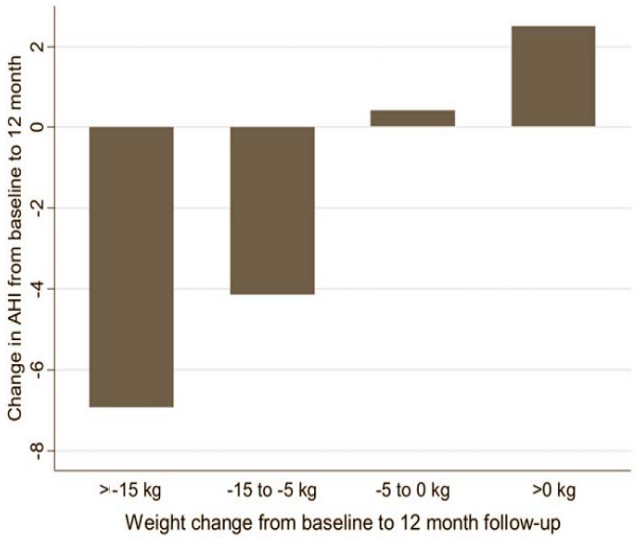
Intervention: 1-year supervised lifestyle intervention including initial 12-week VLCD (600-800 kcal/dy)

Control: Single general dietary and exercise counseling session

The odds ratio for having mild OSA at 1 y was 27% lower in the intervention group compared to control

Tuomilehto HP et al., Am J Respir Crit Care Med 2009

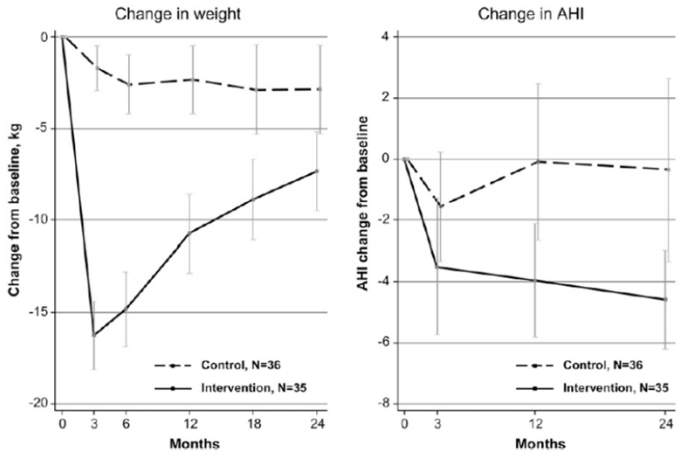
Changes in weight and AHI at 1 year



Tuomilehto HP et al., Am J Respir Crit Care Med 2009

2 year follow-up:
Changes in weight and AHI at 2 yr.

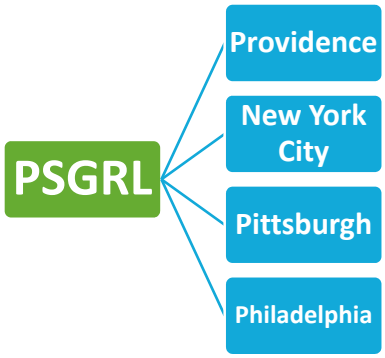
N= 71 (99% retention)
36 control/35 intervention



Vertical bars indicate 95% CIs.

Tuomilehto HP et al., Am J Clin Nutr, 2010

RCT: Effect of weight loss on OSA among obese patients with type 2 diabetes : Sleep AHEAD



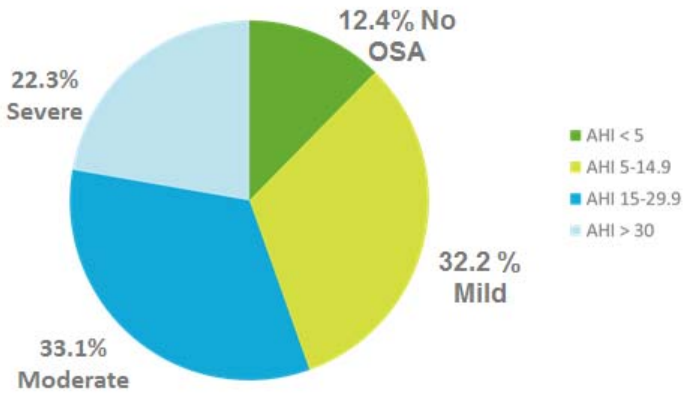
N=264	DSE (n=139)	ILI (n=125)
Mean age, y	61.2 ± 6.5	61.3 ± 6.4
Mean weight, kg	102.4 ± 18.3	102.0 ± 17.1
Mean BMI, kg/m²	36.7 ± 5.7	36.5 ± 5.7
Mean AHI, events/h	23.2 ± 16.5	23.5 ± 15.0

Intensive Lifestyle Intervention (ILI): 1-year supervised lifestyle intervention including using portion-controlled liquid meal replacements and entrees for the first 4 months

Diabetes Support and Education (DSE): 3 group sessions focused on diet, physical activity, and social support as they relate to effective diabetes management

Foster et al., Arch Intern Med, 2009

Undiagnosed, unscreened sleep disordered breathing in obese patients with Type 2 diabetes (N=202)



Only waist circumference was associated with an increase risk for OSA

- 1 cm increase in WC associated with 10% greater risk

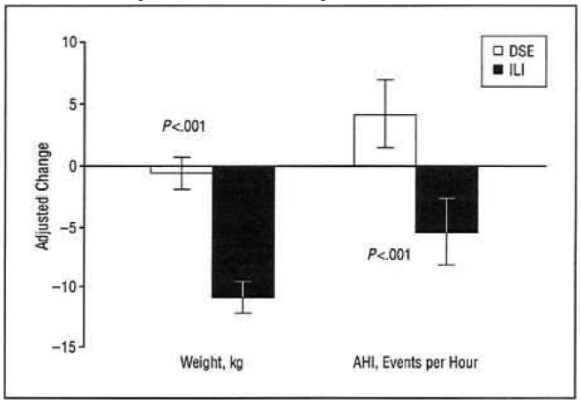
Foster et al., Diabetes Care, 2009

Sleep AHEAD subjects with OSA on treatment at follow-up visits

	Year 1	Year 2	Year 4	**Year 10**
Number of subjects completing FU	219 (83%)	210 (80%)	165 (63%)	**134 (50.8%)**
Number (%) receiving CPAP treatment	14 (6.4%)	19 (9.0%)	19 (11.5%)	**21 (15.7%)**

Kuna et al, Under Review

1 year: Changes in weight and AHI

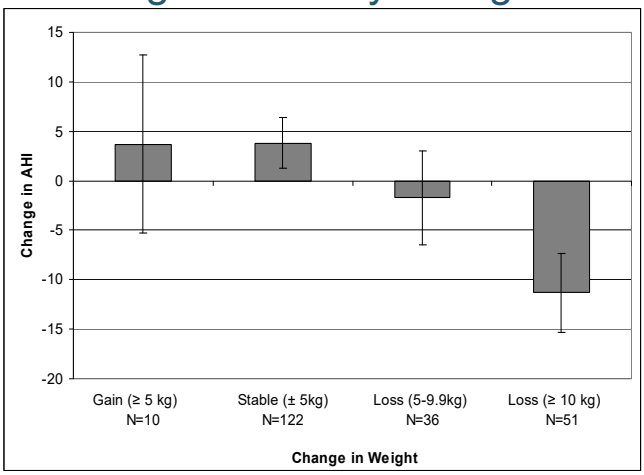


The between-group differences were significant for changes in weight (p <.0001) and AHI (p < .0001

- The only statistically significant multivariable predictor of change in AHI was **baseline AHI** (*b*=-.28, CI: -.40 to -.16; p<.0001).
- **Change in weight** was the only statistically significant predictor of change in AHI (*b*=.55, CI: .20 to .90; p=.003).

Foster et al., Arch Intern Med, 2009

1 year: Changes in AHI by changes in weight

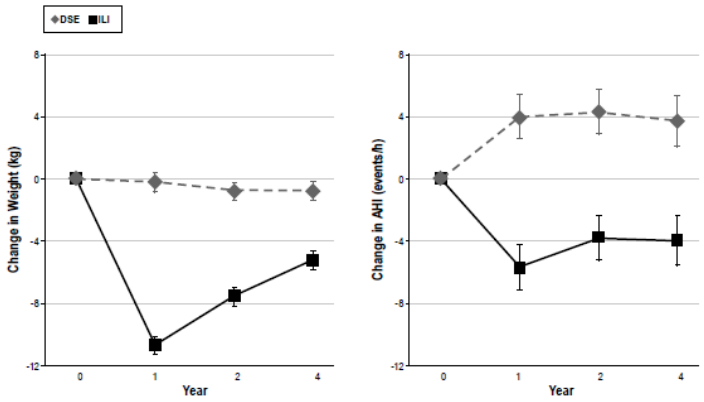


After controlling for multiple comparisons, participants who lost ≥ 10 kg had significantly greater reductions in AHI than all other groups (p < .01 for all).

Error bars represent 95% CIs.

Foster et al., Arch Intern Med, 2009

4 years: Sustained improvements of OSA by lifestyle changes



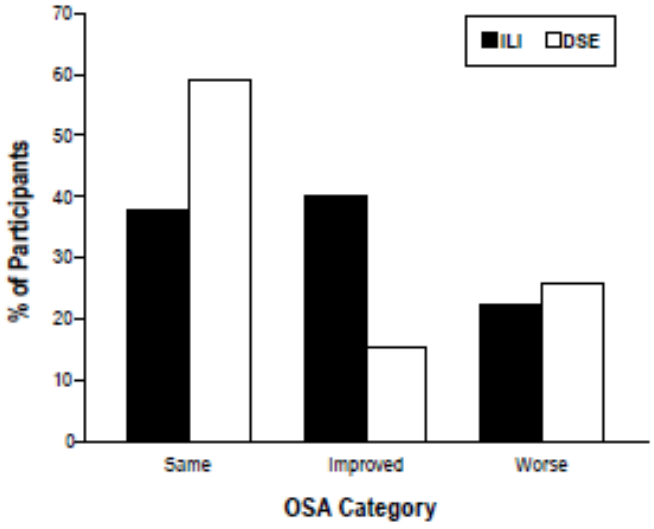
Data represents mean changes with standard error (SE)

Predictors of change in AHI:

- Baseline AHI
- Change in weight
- Intervention arm

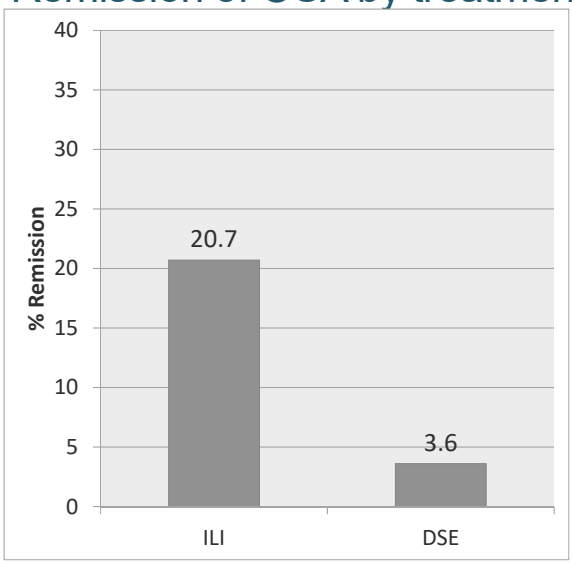
Kuna et al, Sleep 2013

4 years: Changes in OSA category



Kuna et al, Sleep 2013

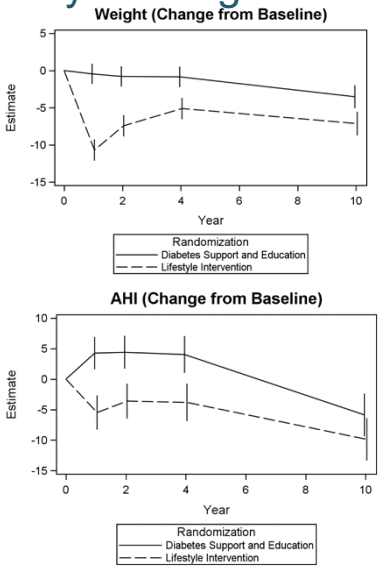
4 years: Remission of OSA by treatment group



Remission of OSA, AHI < 5 events/h

Kuna et al, Sleep 2013

10 years: Sustained improvements of OSA by lifestyle changes



The ILI group lost significantly more weight than the DSE group at 10 years ($p<0.001$)

No significant difference in AHI between groups **at** 10 years, but in a mixed effects model estimating change in AHI **over** 10 years, ILI had significantly greater reductions in AHI than DSE ($p=0.0001$)

Predictors of change in AHI:

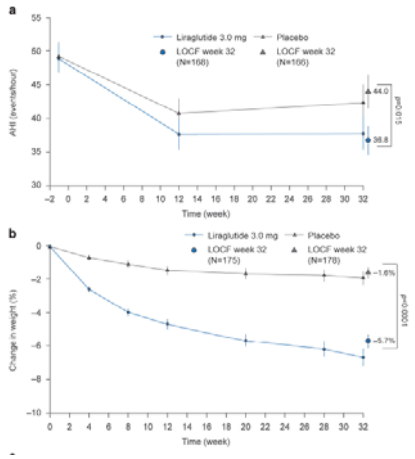
- Baseline AHI
- Change in weight
- Intervention arm

Data represents mean changes with standard error (SE)

Kuna et al, Preliminary

RCT: Effect of liraglutide 3.0mg in individuals with obesity and moderate-to-severe OSA over 32 weeks: the SCALE study

- **359 adults (age 48.5 y, 99.5% obese, mean AHI 49 events/h) were randomized to Liraglutide 3.0 mg or placebo. All participants received counseling on diet and PA every 2 weeks**



AHI: Liraglutide group had significantly greater improvements in AHI compared to placebo

- Most of the reduction in mean AHI occurred by week 12, with minimal changes thereafter

Weight: Liraglutide group had significantly greater weight loss compared to placebo

OSA: The majority of participants in both groups did not experience improvement/worsening of their baseline **OSA severity category** after 32 weeks

Blackman A et al. IJO 2016

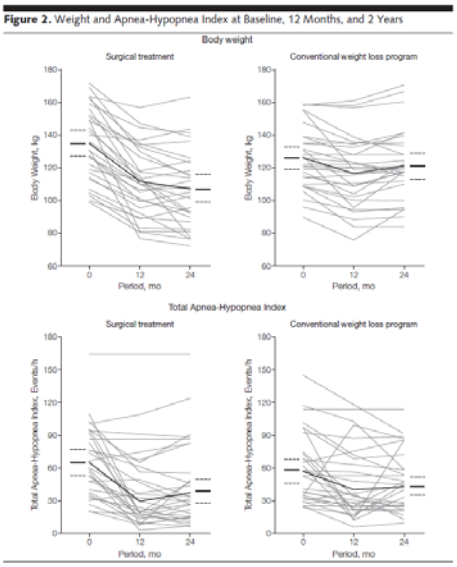
RCT: Surgical vs Conventional Therapy for Weight Loss Treatment of OSA

	Surgery (N=30)	Conventional (N=30)
Mean age, y	47.4 ± 8.8	50.0 ± 8.2
BMI, kg/m2	46.3 ± 6.0	43.8 ± 4.9
Mean AHI, events/h	65.0 ± 32.8	57.2 ± 30.3

- **Randomization:** 60 participants with obesity (BMI >35, <55), recently diagnosed with OSA (< 6 months), AHI of ≥ 20 events/hr., and prescribed CPAP, were randomized to 2 arms
  - Conventional weight loss
  - Bariatric surgery
- **Assessments**: baseline, 12 months, and 2 years
- **Endpoints:**
  - Primary: Change in AHI
  - Secondary: Change in weight, CPAP adherence, and functional status

Dixon JB et al. JAMA 2012

Change in AHI and weight



Weight: The surgery group lost significantly more weight than the conventional group, mean 27.8 kg vs 5. 1 kg

AHI: There were not significant differences in change in AHI between groups

- Surgery group decreased AHI by 25.5 events/hr, vs. 14.0 events/hr in the Conventional group

- The use of bariatric surgery compared to conventional weight loss therapy did not result in a statistically greater reduction in AHI despite major differences in weight

Dixon JB et al. JAMA 2012

Conclusions

Obesity is a potent, modifiable risk factor for OSA

OSA is present in a high proportion of obese adults with type 2 diabetes

Weight loss produces clinically significant improvements in AHI among various patient types and OSA severity levels

Change in AHI is related to initial AHI and weight loss, although other lifestyle factors likely play a role

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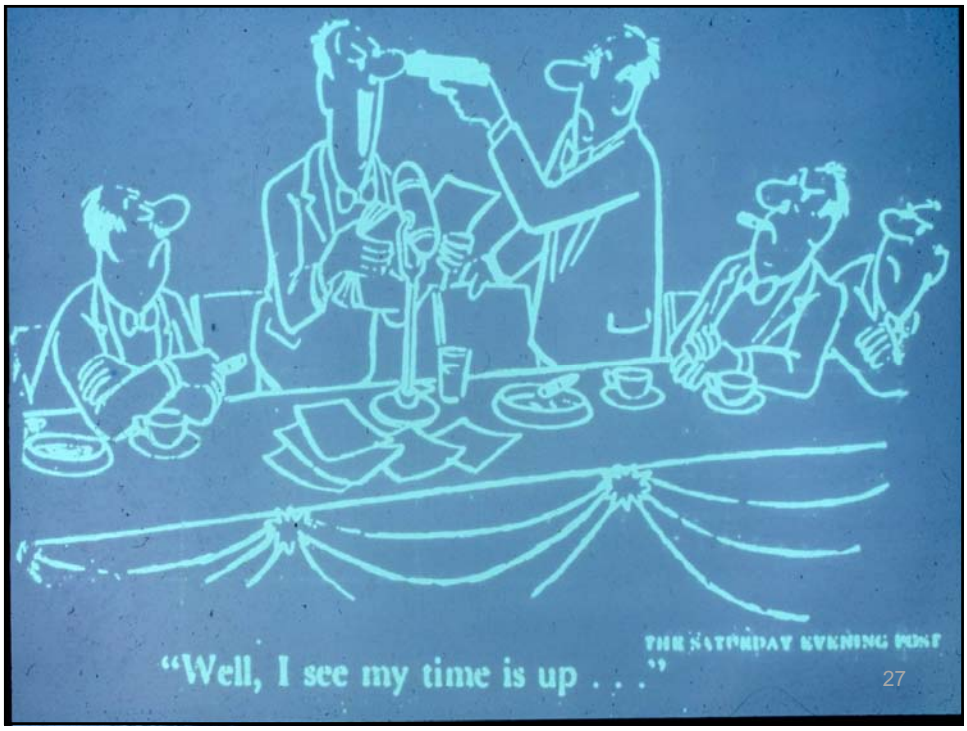

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Questions?

Appendix

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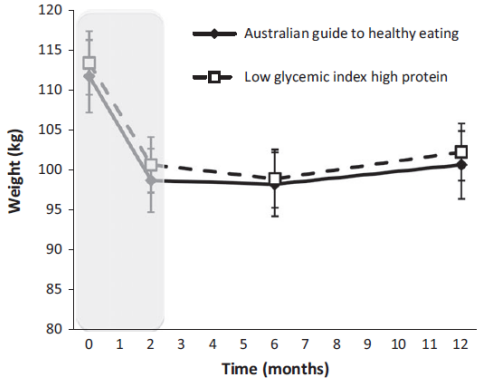
RCT: Maintenance diets after VLED

- **44 adults with OSA (age 49.4y, BMI 37.2, mean AHI 28.3 events/h) underwent an 8-week VLED, and at 2 months were randomized to one of two maintenance diets (Australian Guide to Healthy Eating which emphasized fiber, whole grains, and reduced sugar and fat, or Low Gylcemic Index-High Protein Diet) until 12 months**



No significant differences between groups

Weight:
- 2 mos. VLED: -12.9 kg
  - 12 mos. AGHE: -9.5 kg
  - 12 mos. LGHP: -10.1 kg

AHI:
- 2 mos. VLED: -12.9 kg
  - 12 mos. AGHE: -11.0 events/h
  - 12 mos. LGHP: -7.3 events/h

Cayanan EA et al. J Sleep Res. 2017

Sleep AHEAD publications

- Foster GD et al. Obstructive sleep apnea among obese patients with type 2 diabetes. Diabetes Care 32(6): 1017-1019, 2009.
- Foster GD et al. A randomized study on the effect of weight loss on obstructive sleep apnea among patients with type 2 diabetes: The Sleep AHEAD study. Arch. Int. Med. 169(17): 1621-1626, 2009.
- Rice TB et al. The relationship between obstructive sleep apnea and self-reported stroke or coronary heart disease in overweight and obese adults with type 2 diabetes mellitus. Sleep 35(9): 1293-1298, 2012.
- St-Onge MP et al. Associations of sleep disturbance and duration with metabolic risk factors in obese persons with type 2 diabetes: data from the Sleep AHEAD Study. Nature and Science of Sleep 4: 143-150, 2012

Sleep AHEAD publications

- Kuna ST et al. Sleep AHEAD Research Group: Long-term effect of weight loss on obstructive sleep apnea severity in obese patients with type 2 diabetes. Sleep 36(5): 641-649, 2013.
- Shechter A et al. Sleep architecture following a weight loss intervention in overweight and obese patients with obstructive sleep apnea and type 2 diabetes: Relationship to apnea-hypopnea index. J. Clin. Sleep Med. 10(11): 1205-1211, 2014.
- Kline CE et al. The effect of changes in cardiorespiratory fitness and weight on obstructive sleep apnea severity in overweight adults with type 2 diabetes. Sleep 2016;39(2): 317-325, 2016.
- Shechter A et al. Effects of a lifestyle intervention on REM sleep-related OSA severity in obese type 2 diabetes patients. Under Review