Evidence-Based Medicine: Obesity, Obstructive Sleep Apnea and Tirzepatide

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Our patient . . .

A 46-year-old woman presents to her primary care provider to follow up management of obesity and obstructive sleep apnea. She has steadily gained weight over the last five years. She is 5’9”, now weights 240 lbs with a BMI of 35.

She has been working with a dietician to help manage her obesity. She also tries to walk two or three times per week.

She has a history of OSA confirmed by sleep study. She has done well with a positive airway pressure at night using a nasal CPAP mask.

Our patient . . .

PMH:

- OSA treated with PAP
- HTN
- No known CAD
- No known diabetes

Medications:

- Lisinopril 20 mg po daily
- Chlorthalidone 25 mg po daily
- Acetaminophen 1000 mg po tid prn knee pain

Our patient . . .

Social history: She is married and lives with her husband. She works at a local retail store. There is no hx of tobacco, alcohol or drug use. She has health insurance through her employer.

Family hx is significant for obesity and HTN but is otherwise negative.

Her vital signs and weight are stable today and her exam is otherwise without new findings.

Our patient . . .

She wants to discuss options for improving her OSA through additional weight loss.

She has also heard of a new weekly injectable medication for weight loss . . .

Obstructive Sleep Apnea—

"a disorder that is characterized by obstructive apneas, hypopneas, and/or respiratory effort-related arousals caused by repetitive collapse of the upper airway during sleep."

Kline L R, UpToDate 2025

Clinical Suspicion for Obstructive Sleep Apnea

- Loud or irregular snoring
- Daytime sleepiness
- Unrefreshing sleep regardless of sleep duration
- Increased fatigue when sedentary
- Nocturia
- Choking or gasping in sleep

New Engl J Medicine 2019; 380(15): 1442-1449

Clinical Suspicion for Obstructive Sleep Apnea

- Dry mouth on awakening
- Morning headaches
- BMI > 30
- Crowded oropharynx
- Neck circumference > 17 inches in men or > 15 inches in women

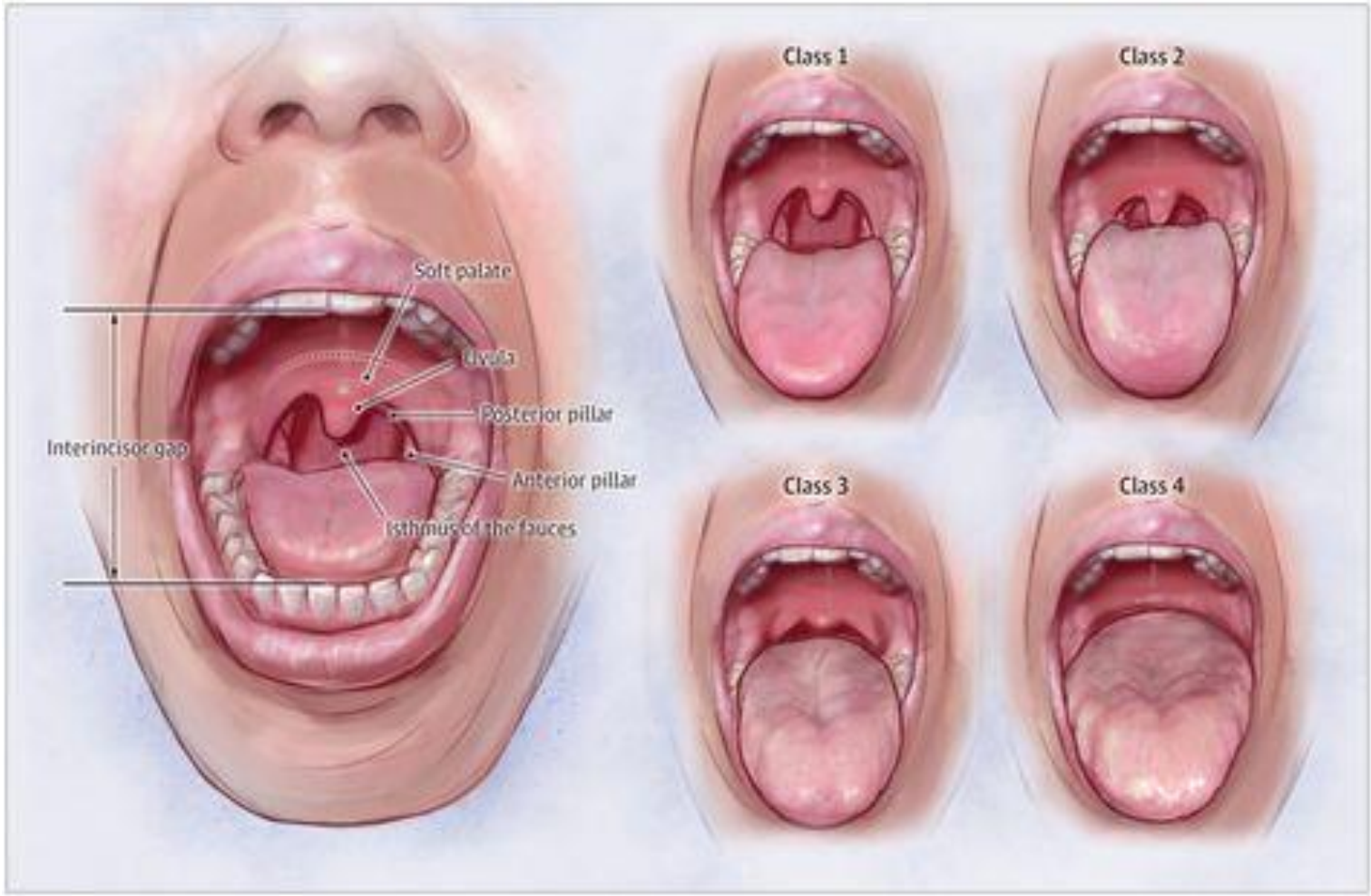
New Engl J Medicine 2019; 380(15): 1442-1449

Obesity and the Pathophysiology of OSA

A “crowded oropharynx—
The higher the Mallampati score, the higher the risk of OSA

Increased adipose tissue in the tongue and pharynx

Leads to increased collapsibility of the airway during sleep



New Engl J Medicine 2019; 380(15): 1442-1449

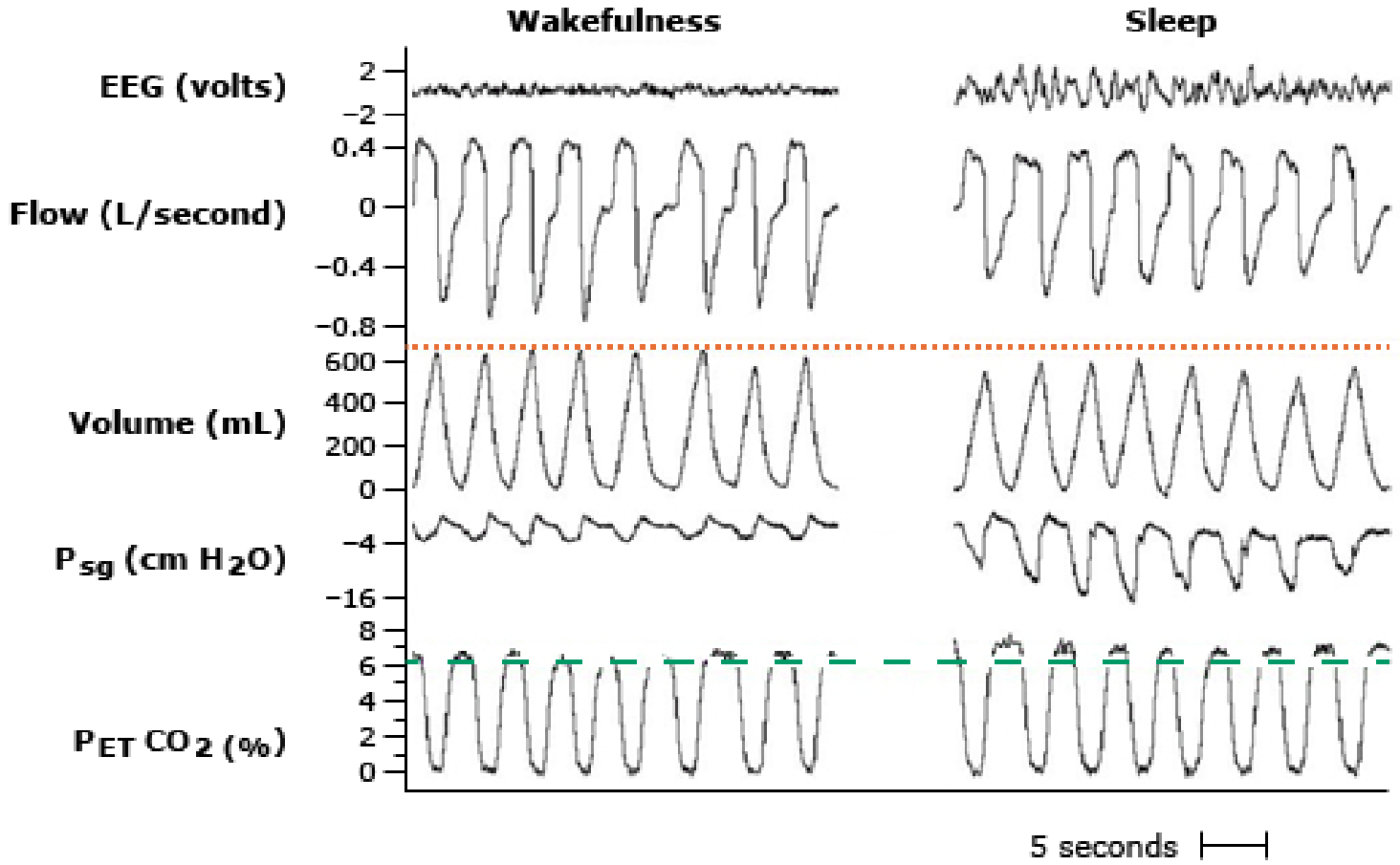
Effect of Sleep on Ventilation and Upper Airway Mechanics

During sleep compared to wakefulness:

Airflow ↓

Tidal volume ↓

End-tidal CO2 ↑

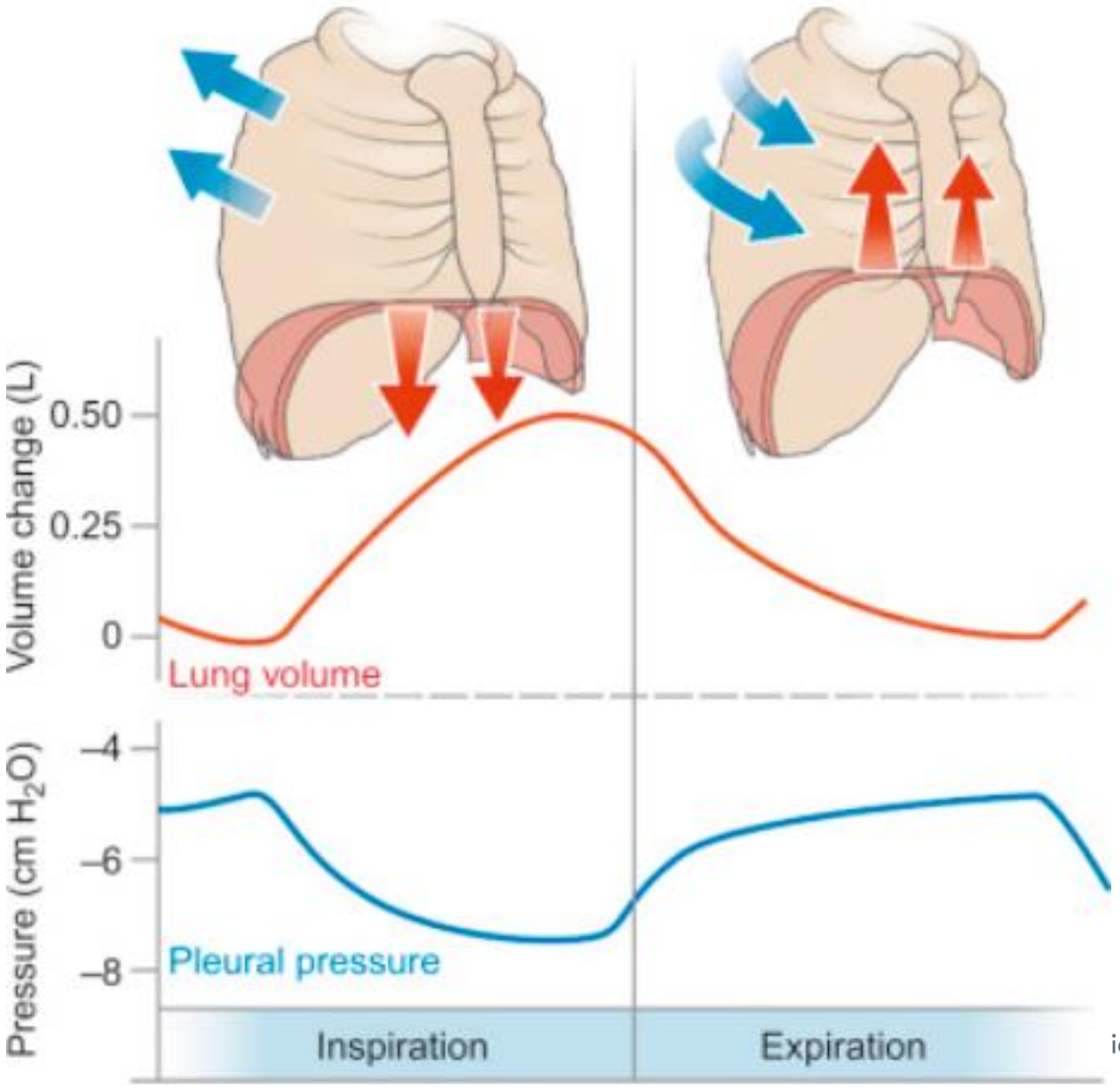


Badr M S UpToDate 2025

Obesity and Thoracic Cage Mechanics During Sleep:

Compared to wakefulness, **NREM sleep** is associated with a **greater contribution of the thoracic cage muscles to tidal volume**

Obesity introduces a **restrictive lung defect** which decreases tidal volume



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ic Medicine

Obesity and OSA

- Estimated that OSA is present in **> 40%** of patients with a BMI > 30
- Estimated that OSA is present in **> 60%** of patients with the metabolic syndrome

New Engl J Medicine 2019; 380(15): 1442-1449

Complications of OSA: Vascular

- HTN
- Stroke
- CAD
- Arrhythmias
- L-heart failure
- Pulmonary HTN
- R-heart failure

Kline L R, UpToDate 2025

Complications of OSA: Neuropsychiatric

- Drowsy driving
- Motor vehicle crashes
- Memory/cognitive deficits
- Depression
- Psychosis
- Sexual dysfunction

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Diagnosis of OSA

STOP BANG QUESTIONNAIRE

☐ Yes	☐ No	**Snoring?** Do you **snore loudly** (loud enough to be heard through closed doors, or your bed partner elbows you for snoring at night)?	**S**
☐ Yes	☐ No	**Tired?** Do you often feel **tired, fatigued, or sleepy** during the daytime (such as falling asleep during driving)?	**T**
☐ Yes	☐ No	**Observed?** Has anyone **observed** you **stop breathing** or **choking/gasping** during your sleep?	**O**
☐ Yes	☐ No	**Pressure?** Do you have or are you being treated for **high blood pressure**?	**P**
☐ Yes	☐ No	**Body mass index more than 35 kg/m^2?**	**B**
☐ Yes	☐ No	**Age older than 50 years old?**	**A**
☐ Yes	☐ No	**Neck size large (measured around Adam's apple)?** Is your shirt collar 16 inches or larger?	**N**
☐ Yes	☐ No	**Gender (biologic sex) = Male?**	**G**

Risk for OSA:

0 to 2 Yes = Low

3 to 4 Yes = Intermediate

5 to 8 Yes = High

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Epworth Sleepiness Scale (ESS): chance of dozing during eight ordinary situations during the day

- Sitting and reading
- Watching TV
- Sitting inactively in a public place
- Riding as a passenger in a car for one hour without a break
- Lying down to rest in the afternoon when circumstances permit
- Sitting and talking with someone
- Sitting quietly after lunch without alcohol
- Sitting in a car as a driver, while stopped for few minutes

0 = would never dose

1 = slight chance of dozing

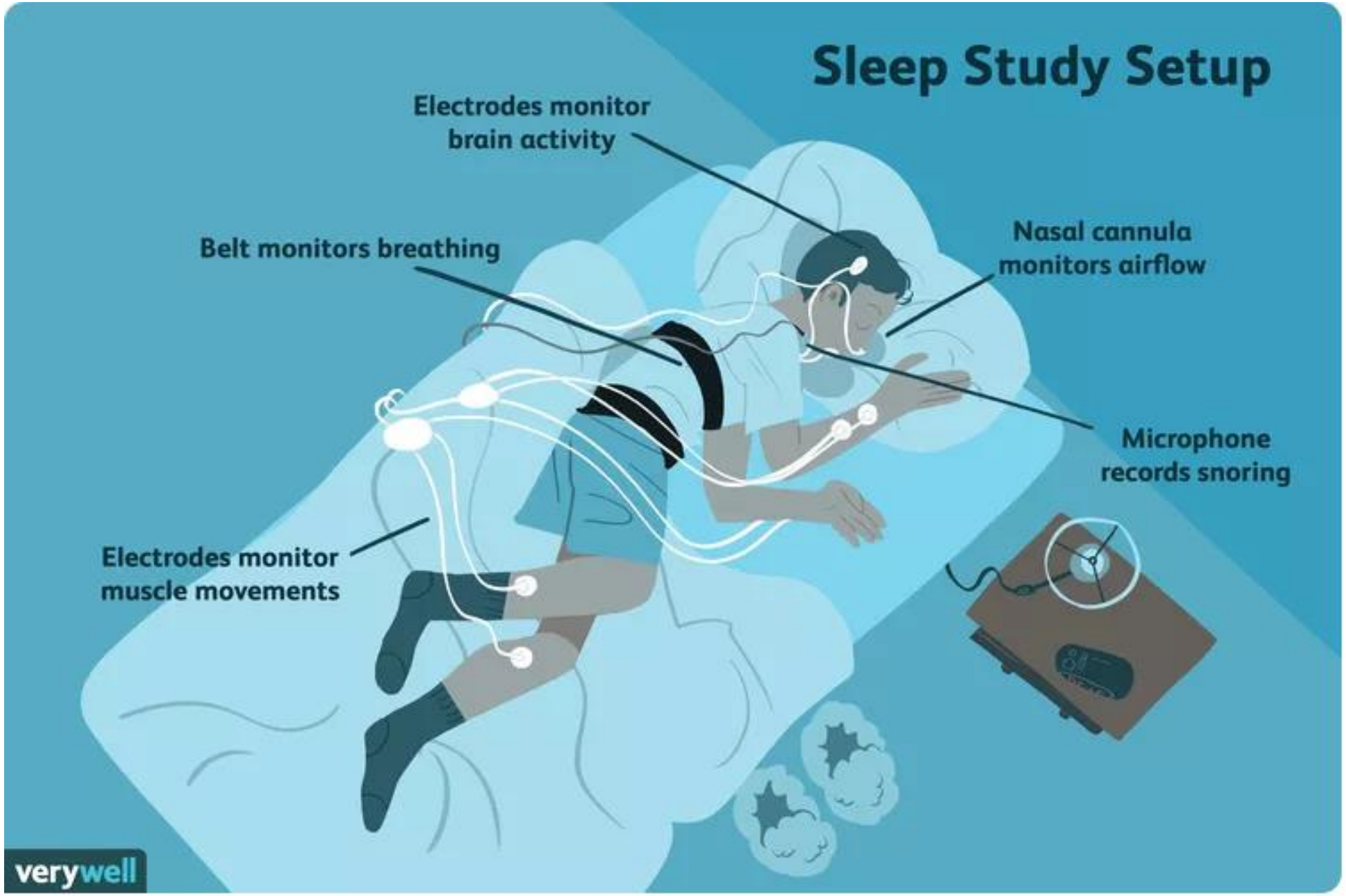
2 = moderate chance of dozing

3 = high chance of dozing

Score > 10 is consistent with excessive sleepiness

Freedman N, UpToDate 2025

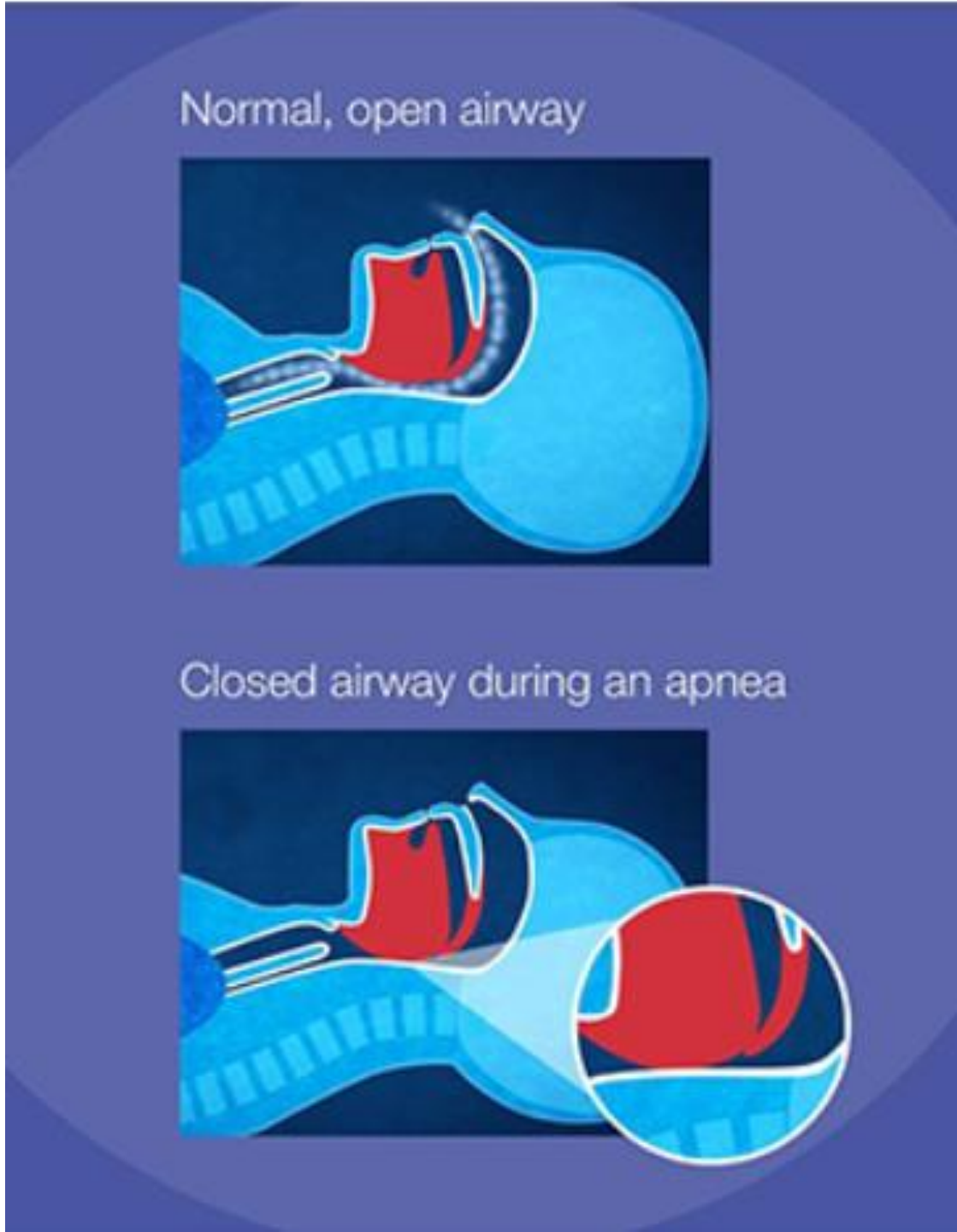
These and other clinical tools should NOT take the place of a careful history, physical examination, and **formal sleep study** . . .



https://www.verywellhealth.com

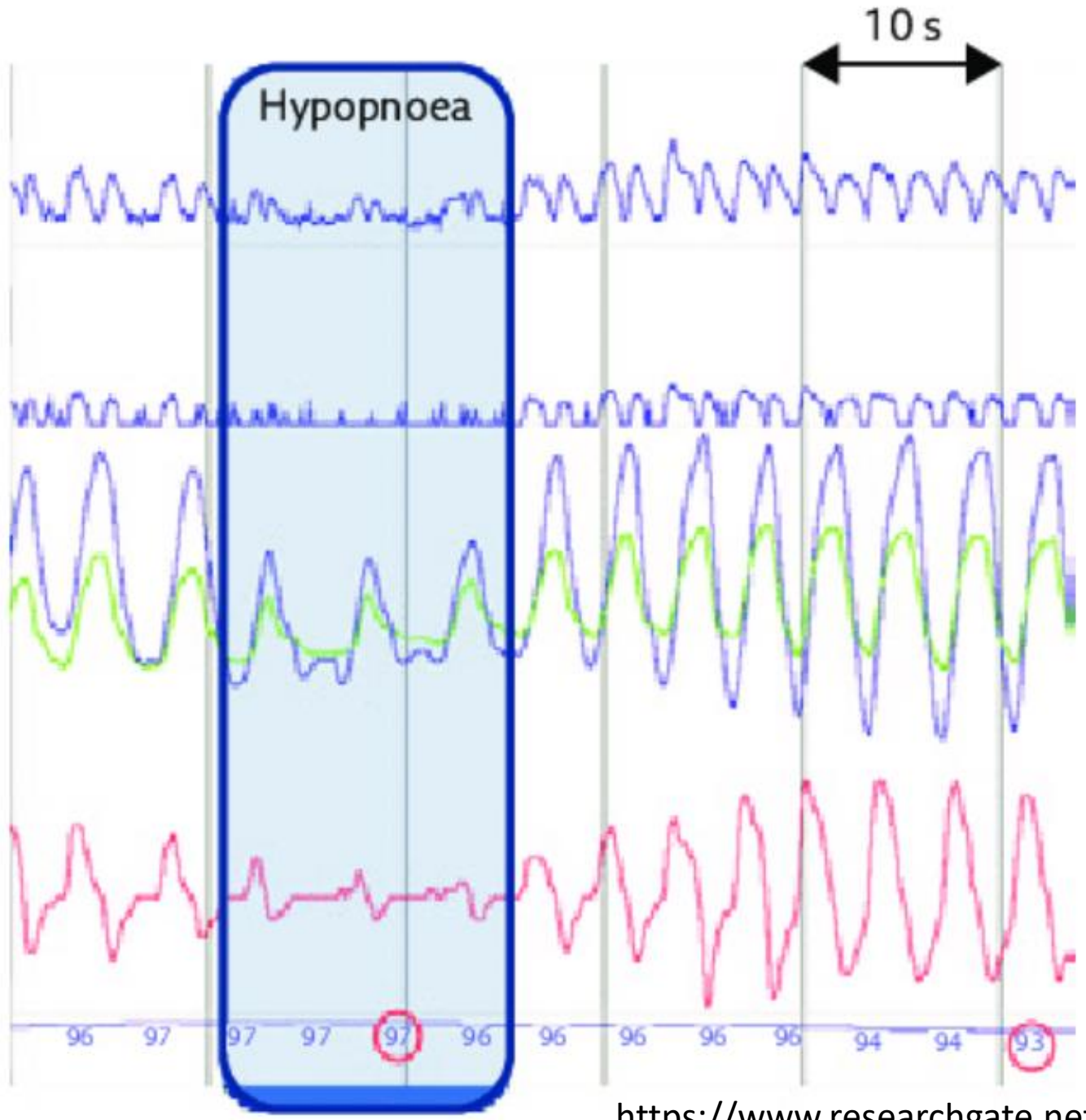
Apnea/Hypopnea Index (AHI)

Apnea Events



https://www.resmed.com/en-us/sleep-health

Apnea/Hypopnea Index (AHI)



Apnea-Hypopnea Index =

$$\frac{\text{Apneas + Hypopneas}}{\text{Total sleep time in hours}}$$

https://www.researchgate.net

Using Apnea-Hypopnea Index to Classify OSA

AHI (events per hour)	OSA Classification
< 5	Normal (No OSA)
5-15	Mild
15-30	Moderate
> 30	Severe

Management of OSA

Management of OSA

- Weight loss
  - Diet
  - Physical Activity
  - Bariatric surgery
  - Pharmacologic
- Lateral recumbent sleeping position
- Positive Airway Pressure (PAP)
- Oral Appliances
- AVOID
  - Alcohol
  - Sedatives
  - Barbiturates
  - Other antiepileptic medications (ex: gabapentin)
  - Tricyclic antidepressants
  - Antihistamines
  - Opiates

Malhotra A, Kundel V, UpToDate 2025

Positive Airway Pressure (PAP) for OSA: Indications

- Patients with AHI ≥ 15 events/hr

- Patients with
  - AHI ≥ 5 to 14 events/hour **with symptoms of OSA**

  AND/OR

  - AHI ≥ 5 to 14 events/hour **with comorbidities** such as hypertension

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Positive Airway Pressure (PAP) for OSA: Indications

Patients with AHI ≥ 5 to 14 events/hour without symptoms of OSA but who are "mission critical workers"

- Airline pilots
- Air traffic controllers
- Locomotive engineers
- Bus drivers
- Truck drivers

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Efficacy of Positive Airway Pressure (PAP) on OSA

Positive Airway Pressure (PAP) Improves Apnea-Hypopnea Index (AHI)

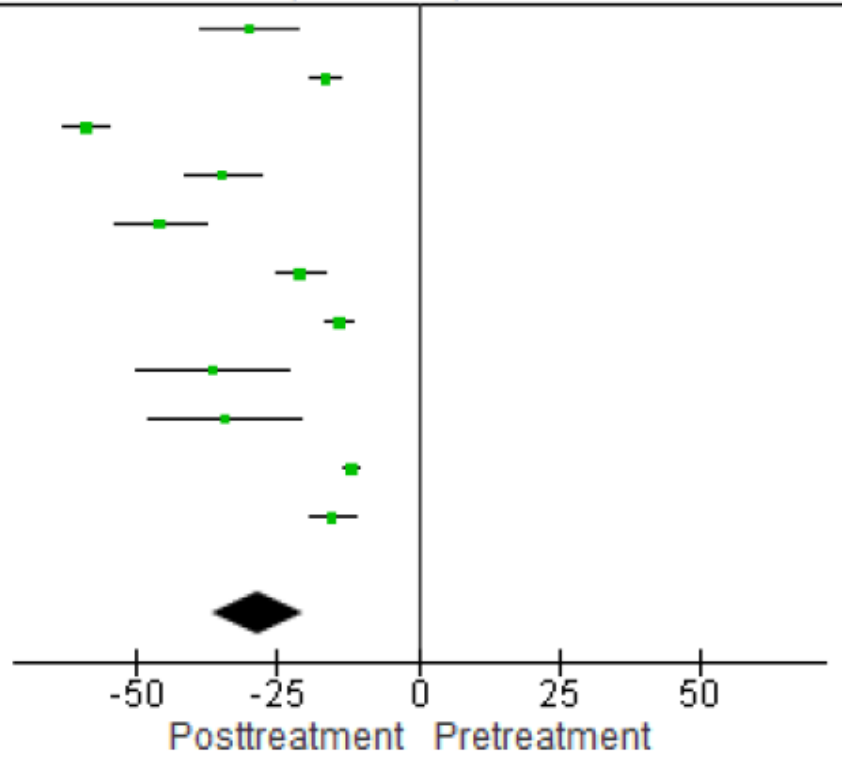
Meta-analysis 2019
11 RCTs

PAP led to a decrease in AHI of 29 events/hour

Figure S2. PAP Pre-treatment vs. Post-treatment (AHI, events/hr)

	Posttreatment			Pretreatment				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Amaro 2012	8	6	12	38	14	12	8.8%	-30.00 [-38.62, -21.38]
Barnes 2004	4.8	4.7	89	21.3	12.3	89	9.7%	-16.50 [-19.24, -13.76]
Becker 2003	3.4	3.1	16	62.5	8	16	9.5%	-59.10 [-63.30, -54.90]
Hoyos 2012	3.8	12.4	28	38.5	14.7	34	9.2%	-34.70 [-41.45, -27.95]
Ip 2006	1.7	1.8	14	47.7	15.3	14	8.9%	-46.00 [-54.07, -37.93]
Lam 2007	2.8	6.4	34	23.8	11.1	34	9.5%	-21.00 [-25.31, -16.69]
Montasterio 2001	6	8	66	20	6	66	9.7%	-14.00 [-16.41, -11.59]
Nguyen 2010	2.2	1.5	10	38.8	21.4	10	7.8%	-36.60 [-49.90, -23.30]
Phillips 2011	6.8	14.8	16	41.2	23.9	16	7.7%	-34.40 [-48.17, -20.63]
Weaver 2012	0.9	1.3	113	12.8	6.4	121	9.7%	-11.90 [-13.07, -10.73]
Woodson 2003	4.6	2.7	26	19.8	9.9	27	9.6%	-15.20 [-19.08, -11.32]
Total (95% CI)			**424**			**439**	**100.0%**	**-28.59 [-36.78, -20.40]**

Heterogeneity: $Tau^2 = 178.76$; $Chi^2 = 567.06$, df = 10 ($P < 0.00001$); $I^2 = 98\%$
Test for overall effect: $Z = 6.84$ ($P < 0.00001$)



J Clin Sleep Med. 2019;15(2):301–334.

Positive Airway Pressure (PAP) Improves 24-hr Systolic BP in Patients with Hypertension

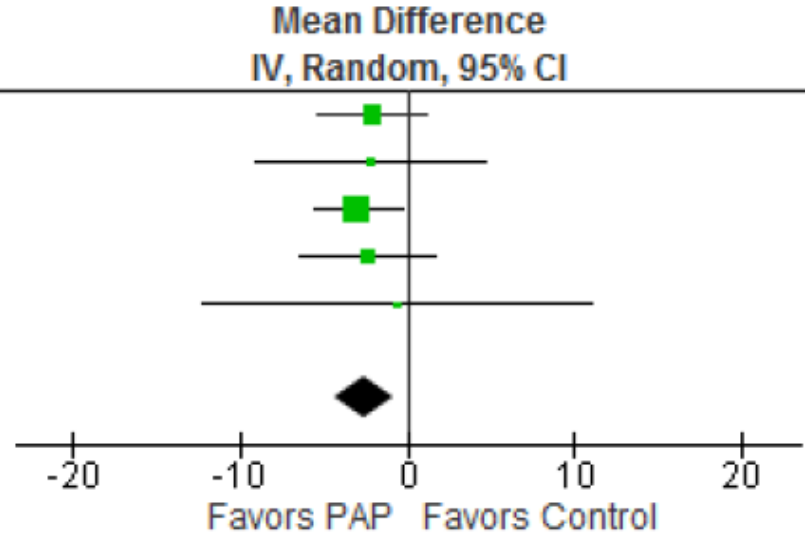
Meta-analysis 2019
5 RCTs

PAP led to a clinically significant decrease in systolic bp of 2.5 mm Hg over 24 hours

Figure S27. PAP vs. control conditions (change in 24-hr SBP) [Hypertensive patients]

	PAP			control conditions				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Barbe 2010	-6.3	15.3	178	-4.2	16.9	181	28.2%	-2.10 [-5.43, 1.23]
Campos-Rodriguez 2006	-1.6	12.8	34	0.6	16.1	34	6.6%	-2.20 [-9.11, 4.71]
Duran-Cantolla 2010	-3	13	169	0	12	171	44.3%	-3.00 [-5.66, -0.34]
Gottlieb 2014	-1.3	13.2	90	1.1	15.4	97	18.6%	-2.40 [-6.50, 1.70]
Robinson 2006	-3.3	16.2	16	-2.7	17.4	16	2.3%	-0.60 [-12.25, 11.05]
Total (95% CI)			**487**			**499**	**100.0%**	**-2.53 [-4.30, -0.76]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.30$, $df = 4$ ($P = 0.99$); $I^2 = 0\%$
Test for overall effect: $Z = 2.80$ ($P = 0.005$)



J Clin Sleep Med. 2019;15(2):301–334.

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Positive Airway Pressure (PAP) Improves 24-hr Diastolic BP in Patients with Hypertension

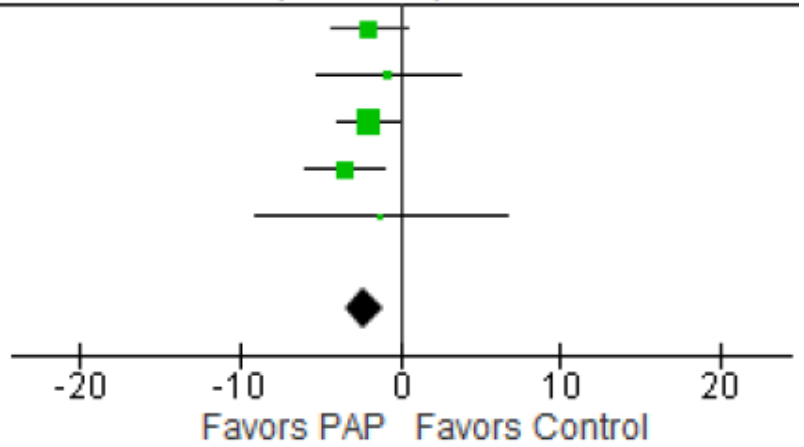
Meta-analysis 2019
5 RCTs

PAP led to a clinically significant decrease in diastolic bp of 2.2 mm Hg over 24 hours

Figure S28. PAP vs. control conditions (change in 24-hr DBP) [Hypertensive patients]

	PAP			control conditions				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Barbe 2010	-4.1	11.3	178	-2.2	11.6	181	25.5%	-1.90 [-4.27, 0.47]
Campos-Rodriguez 2006	-1.5	9.3	34	-0.8	9.8	34	6.9%	-0.70 [-5.24, 3.84]
Duran-Cantolla 2010	-2	8.5	169	0	9	171	41.3%	-2.00 [-3.86, -0.14]
Gottlieb 2014	-2.2	7.6	90	1.3	9.4	97	24.0%	-3.50 [-5.94, -1.06]
Robinson 2006	-1.1	11.4	16	0.1	11.4	16	2.3%	-1.20 [-9.10, 6.70]
Total (95% CI)			**487**			**499**	**100.0%**	**-2.23 [-3.42, -1.03]**

Heterogeneity: Tau² = 0.00; Chi² = 1.67, df = 4 (P = 0.80); I² = 0%
Test for overall effect: Z = 3.65 (P = 0.0003)



J Clin Sleep Med. 2019;15(2):301–334.

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Which appliance is best for PAP in the treatment of OSA?

PAP Appliances:
Oronasal Mask vs. Nasal Mask

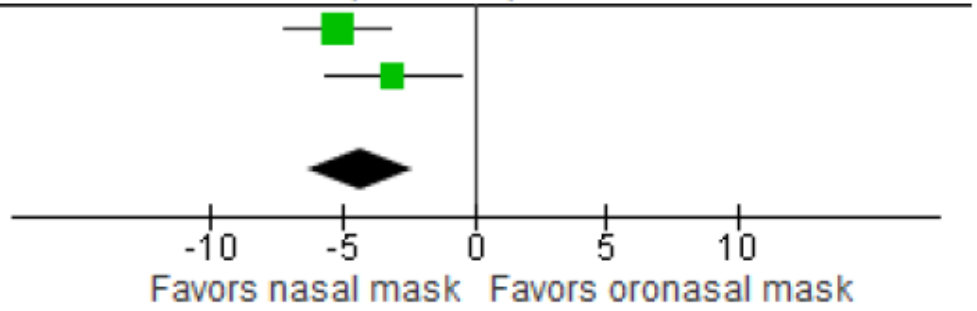
Difference in AHI between the two masks is not clinically significant, so choose the PAP appliance your patient can use most easily . . .

Figure S95. Oronasal mask vs. Nasal mask (AHI, events/hr) [RCTs]

	Nasal Mask			Oronasal Mask				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Ebben 2014	2.7	1.5	14	7.9	3.6	14	57.9%	-5.20 [-7.24, -3.16]
Rowland 2018	4	3.1	37	7.1	7.7	39	42.1%	-3.10 [-5.71, -0.49]
Total (95% CI)			**51**			**53**	**100.0%**	**-4.32 [-6.35, -2.28]**

Heterogeneity: $Tau^2 = 0.77$; $Chi^2 = 1.54$, df = 1 (P = 0.21); $I^2 = 35\%$

Test for overall effect: Z = 4.16 (P < 0.0001)



J Clin Sleep Med. 2019;15(2):301–334.

Additional management options---Oral Appliances for OSA

Cistulli P, UpToDate 2025

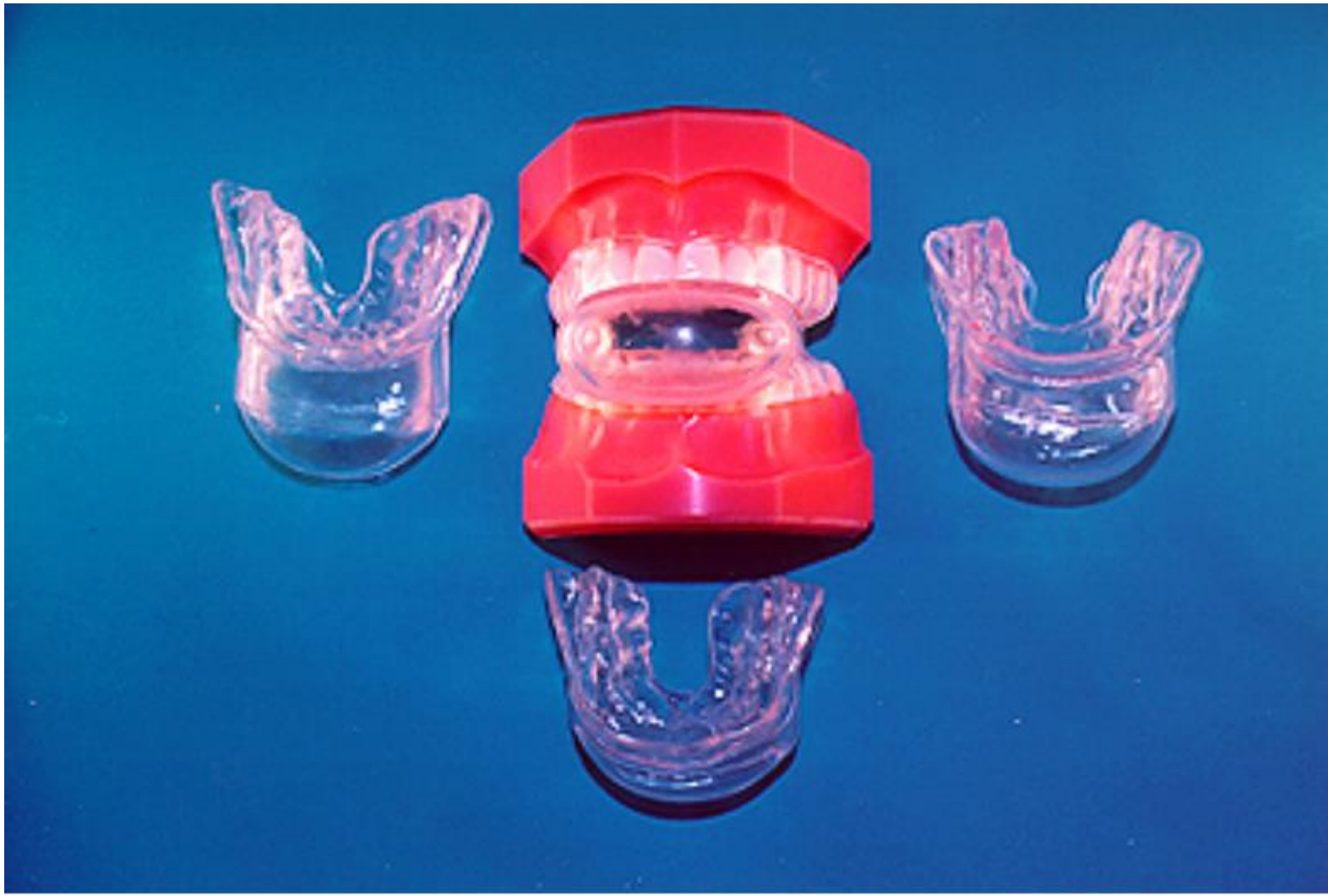
Oral Appliances for OSA: Mandibular Advancement Splint

- Manufactured from dental impressions
- Advances the mandible to maintain airway patency

Cistulli P, UpToDate 2025

Oral Appliances for OSA: Tongue Retaining Device

Pulls the tongue forward to maintain airway patency



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Oral appliances, primarily mandibular advancement splints, have been shown to lead to clinically meaningful improvements in AHI among patients with OSA.

However, PAP is superior to oral appliance treatment for OSA.

But understandably, patients often prefer an oral appliance to PAP treatment.

Cistulli P, UpToDate 2025

Indications for Oral Appliance for OSA

- Known diagnosis of OSA
- Additional OSA treatment other than behavior modification needed
- Patients who cannot tolerate or decline PAP treatment
- **Absence of contraindications to an oral appliance**

Cistulli P, UpToDate 2025

Contraindications for Oral Appliance for OSA

- Need for rapid intervention for severe symptomatic OSA
- Severe or prolonged oxygen desaturation during sleep
- Central sleep apnea
- Poor manual dexterity to place and remove appliance
- Dental conditions:
  - Temporomandibular joint disease
  - Periodontal disease
  - Inadequate dentition to hold device in place

Cistulli P, UpToDate 2025

Pharmacologic Treatment for OSA with Tirzepatide

Tirzepatide in Obesity: Pharmacology

- Brand name: Zepbound
- Synthetic peptide

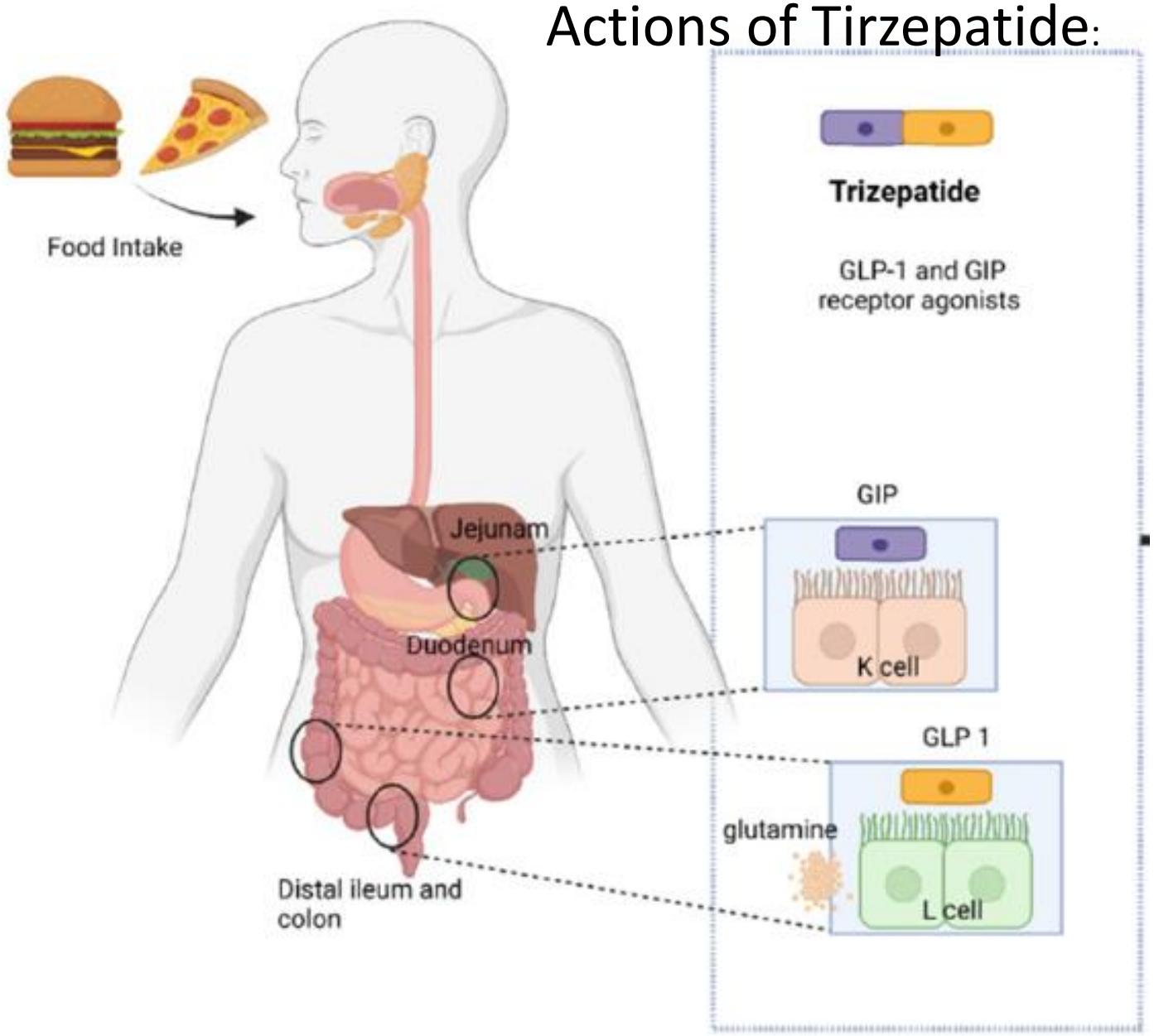
Only Zepbound is FDA approved for moderate to severe obstructive sleep apnea.

- Acts as a receptor <u>agonist</u> for <u>both:</u>
  - **Gastric inhibitory peptide (GIP)** (now called glucose-dependent insulinotropic polypeptide)

AND

  - **Glucagon-like peptide-1 (GLP-1)**

Actions of Tirzepatide:



Decreases appetite → Decreased food intake

Slows gastric emptying

Weight loss

Increases insulin synthesis and secretion

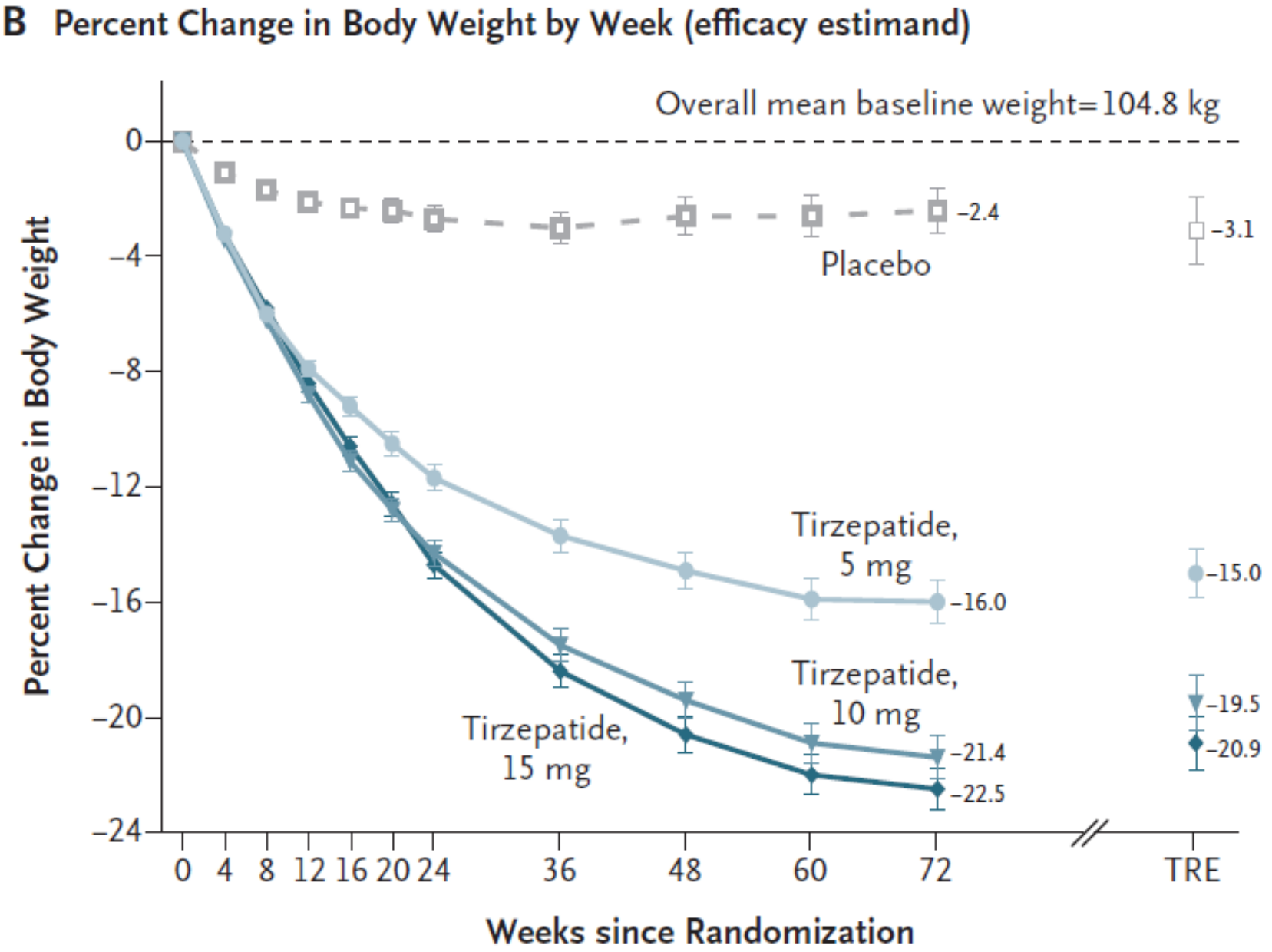
GLP-1 agonist:
- Increased lipolysis
- Increased cardioprotection

GIP agonist:
- Increased lipogenesis
- Decreased bone reabsorption

Increased beta cell survival

Molecules 2022, 27,4315. https://doi.org/10.3390/molecules27134315

Tirzepatide leads to about a 20% weight loss from baseline.



New Eng J Med 2022; 387(3):205-216

Tirzepatide for OSA and Obesity: SURMOUNT-OSA Trial

- Design: Two phase 3, double-blind, placebo-controlled trial
- Setting: Clinical centers in nine countries including the US
- Patients included
  - Adults
  - Moderate to severe sleep apnea: apnea-hypopnea index ≥ 15 events/hour
  - BMI > 30 kg/m2 (or > 27 kg/m2 in patients studied in Japan)
- Patients excluded
  - Type 1 diabetes
  - Type 2 diabetes
  - Change in body weight of > 5 kg in the prior three months before screening
  - Planned surgery for OSA or obesity
  - Diagnosis of central or mixed sleep apnea
  - Major craniofacial abnormalities

Malhotra A, et al., *New Engl J Med* 2024; 391(13): 1193-1205

Tirzepatide for OSA and Obesity: Interventions

Four-week screening period

Trial 1 = Patients **NOT receiving** Positive Airway Pressure (PAP) at baseline

RANDOMIZED

- Tirzepatide SQ weekly
- Placebo SQ weekly

Trial 2 = Patients **receiving** Positive Airway Pressure (PAP) at baseline

RANDOMIZED

- Tirzepatide SQ weekly
- Placebo SQ weekly

52-week trial
ALL participants:

- **Diet with deficit of 500 kcal/day**
- **Physical activity 150 minutes/week**

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Tirzepatide for OSA and Obesity: Interventions

- Tirzepatide titration
  - Initial dose 2.5 mg SQ weekly
  - Increased by 2.5 mg every four weeks
  - Target dose 10 or 15 mg SQ weekly by week 20

Tirzepatide for OSA and Obesity: Interventions

- Apnea-hypopnea index: measured by sleep laboratory polysomnography
  - –Week 20
  - –Week 52

- Definition of hypopnea:
  - –> 30% reduction in airflow for > 10 seconds AND
  - –Reduction in oxygen saturation $\geq$ 4%

Tirzepatide for OSA and Obesity : Interventions

Intention-to-treat analysis: Every randomized subject receiving at least one dose of tirzepatide or placebo was included in data analysis for the efficacy and safety endpoints.

Tirzepatide for OSA and Obesity: Outcomes

Tirzepatide for OSA and Obesity: Outcomes

- **Primary Endpoint**:

  Change in AHI from baseline (events/hr)

- **Secondary Endpoints**

  (controlled for type 1 errors (i.e., multiplicity))

  - % change in AHI
  - % of patients with AHI< 5 events/hr (i.e., when PAP no longer necessary)
  - % change in body weight
  - Change in systolic bp

Tirzepatide for OSA and Obesity: Safety Outcomes

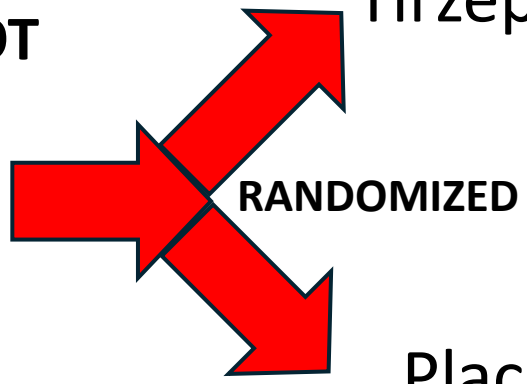
Any adverse events through the 52-week trial plus a four-week follow-up period.

Tirzepatide for OSA and Obesity: Main Results

Tirzepatide for OSA and Obesity: Main Results

Trial 1 = Patients **NOT receiving** Positive Airway Pressure (PAP) at baseline

(N=234)

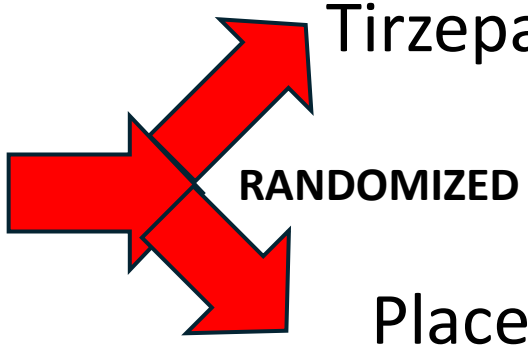


Tirzepatide SQ weekly **(N=114)**

Placebo SQ weekly **(N=120)**

Trial 2 = Patients **receiving** Positive Airway Pressure (PAP) at baseline

(N=235)



Tirzepatide SQ weekly **(N=120)**

Placebo SQ weekly **(N=115)**

52-week trial
ALL participants:

- **Diet with deficit of 500 kcal/day**
- **Physical activity 150 minutes/week**

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Tirzepatide for OSA and Obesity: Baseline Patient Characteristics

Tirzepatide for OSA and Obesity: Trial 1: Patients *not* receiving PAP at Baseline-- Patient Characteristics

Characteristic	**Tirzepatide (n=114)**	**Placebo (n =120)**
Mean age (years)	47.3	48.4
Female sex (%)	31.6	34.2
BMI (kg/m2)	39.7	38.6
Apnea-Hypopnea Index (AHI) events/hr	52.9	50.1

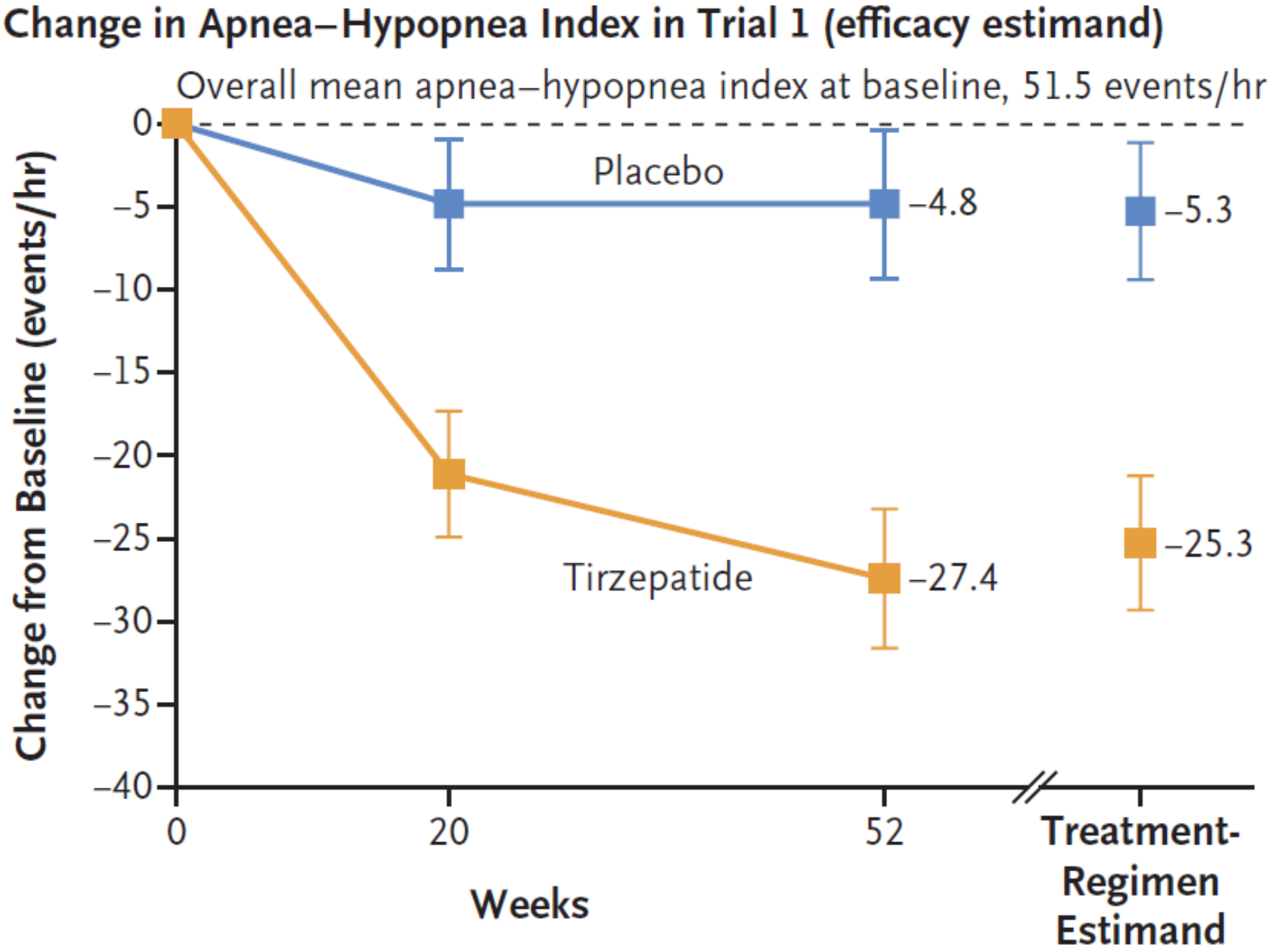
Tirzepatide for OSA and Obesity: Trial 2: Patients receiving PAP at Baseline-- Patient Characteristics

Characteristic	**Tirzepatide (n=120)**	**Placebo (n=115)**
Mean age (years)	50.8	52.7
Female sex (%)	27.5	27.8
BMI (kg/m2)	38.6	38.7
Apnea-Hypopnea Index (AHI) events/hr	46.1	53.1

Tirzepatide for OSA and Obesity: Primary Efficacy Endpoint

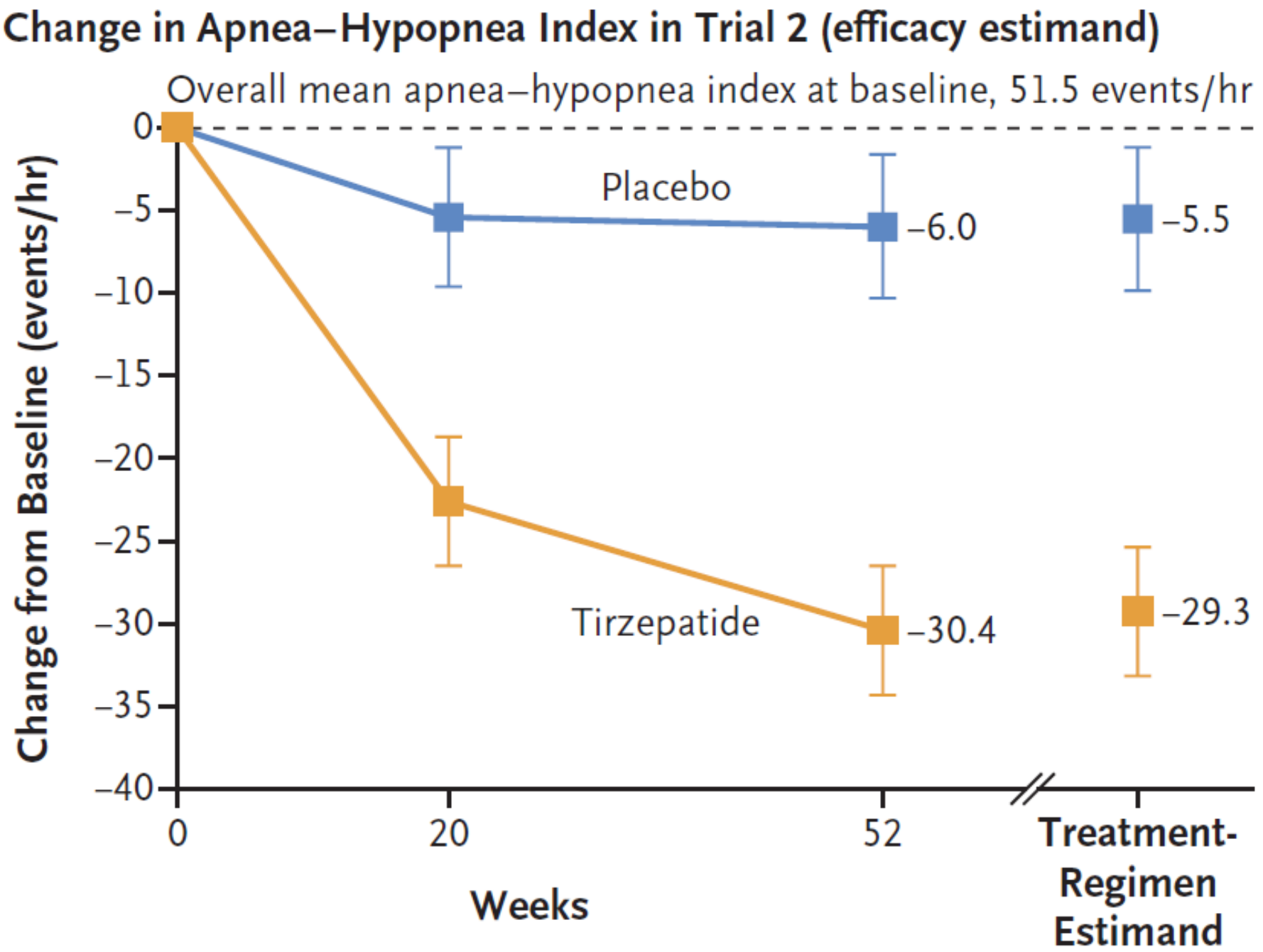
Trial 1: Patients NOT receiving PAP at baseline

Decrease of 20 events/hr in AHI with tirzepatide compared to placebo



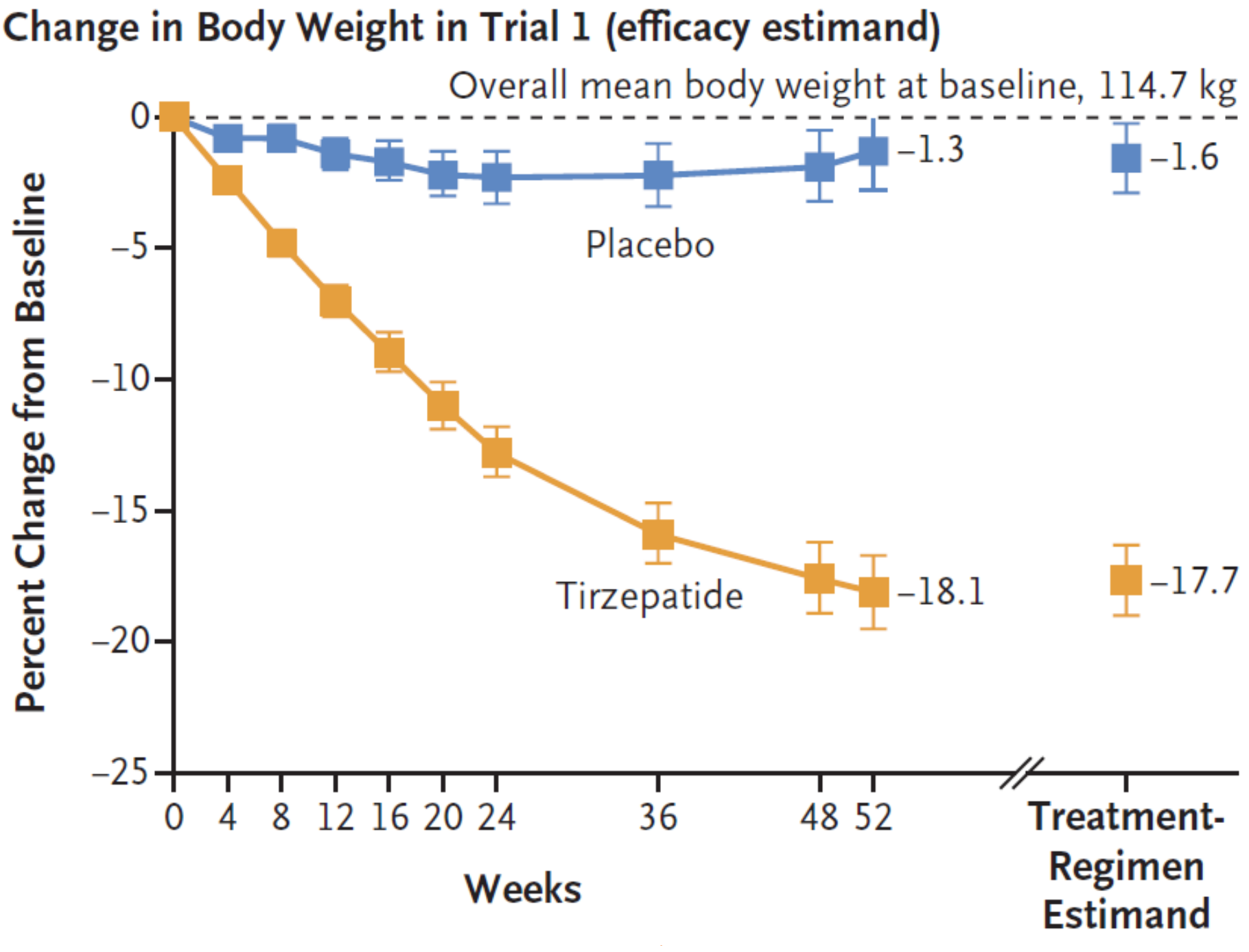
Trial 2:
Patients receiving PAP at baseline

Decrease of 24 events/hr in AHI with tirzepatide compared to placebo



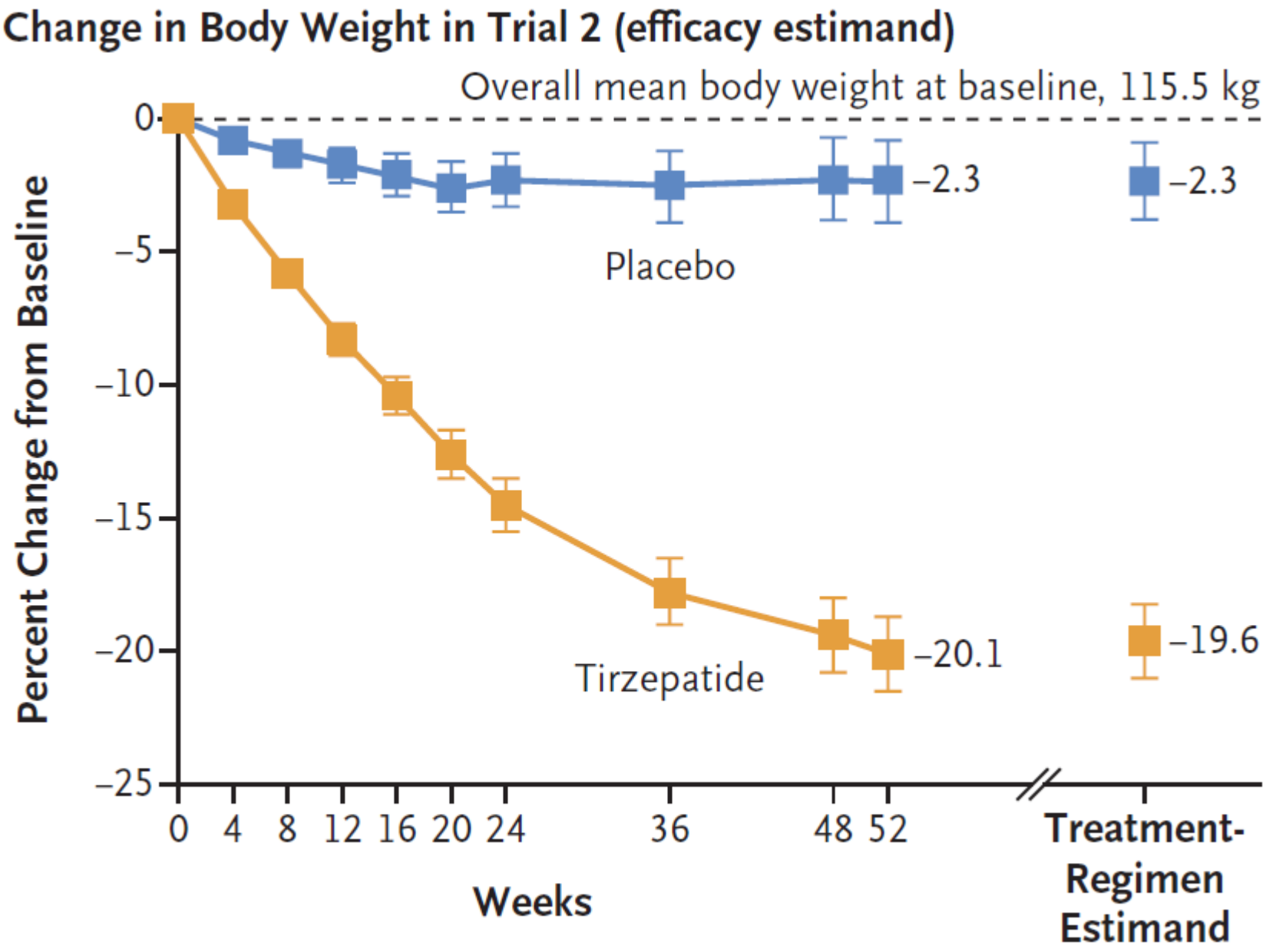
Trial 1: Patients NOT receiving PAP at baseline

18% drop from baseline weight with tirzepatide; 1.3% with placebo



Trial 2: Patients receiving PAP at baseline

20% drop from baseline weight with tirzepatide; 2.3% drop with placebo



Tirzepatide for OSA and Obesity: Trial 1: Patients *not* receiving PAP at Baseline-- Secondary Efficacy Endpoints

Endpoint	**Tirzepatide (n=114)**	**Placebo (n =120)**	**Estimated Treatment Difference or Relative Risk (95% CI)**
%Change in AHI	-50.7%	-3.0%	Difference: -47.7% (-65.8 to -29.6)
AHI < 5 or AHI 5 to 14 with ESS < 10 (ie. PAP no longer needed)	42.5%	15.9%	RR 2.9 (1.8 to 4.8)

Tirzepatide for OSA and Obesity: Trial 1: Patients *not* receiving PAP at Baseline-- Secondary Efficacy Endpoints

Endpoint	**Tirzepatide (n=114)**	**Placebo (n =120)**	**Estimated Treatment Difference or Relative Risk (95% CI)**
% Change in body weight	-17.1	-1.6	Difference -16.1 (-18.0 to -14.2)
Change in systolic bp (mm Hg)	-9.5	-1.8	Difference -7.6 (-10.5 to -4.8)

Tirzepatide for OSA and Obesity: Trial 2: Patients receiving PAP at Baseline-- Secondary Endpoints

Endpoint	Tirzepatide (n=120)	Placebo (n =115)	Estimated Treatment Difference or Relative Risk (95% CI)
%Change in AHI	-58.7%	-2.5%	Difference -56.2% (-73.7 to 38.7)
AHI < 5 or AHI 5 to14 with ESS < 10 (ie. PAP no longer needed)	50.2%	14.3%	RR 3.3 (2.0 to 5.4)

Tirzepatide for OSA and Obesity: Trial 2: Patients receiving PAP at Baseline-- Secondary Endpoints

Endpoint	Tirzepatide (n=120)	Placebo (n =115)	Estimated Treatment Difference or Relative Risk (95% CI)
% Change in body weight	-19.6	-2.3	Difference -17.3 (-19.3 to -15.3)
Change in systolic bp (mm Hg)	-7.6	-3.9	Difference -3.7 (-6.8 to -0.7)

Tirzepatide for OSA and Obesity: Adverse Events seen in > 5% of patients

	Trial 1		Trial 2	
Adverse Event (%)	**Tirzepatide (N= 114)**	**Placebo (N=120)**	**Tirzepatide (N=119)**	**Placebo (N= 114)**
≥ 1 adverse event	79.8	76.7	83.2	72.8
Death	0	0	0	0
Serious adverse event	7.9	5.8	5.9	10.5
Adverse event leading to stopping study drug or placebo	4.4	1.7	3.4	7.0

Tirzepatide for OSA and Obesity: Adverse Events seen in > 5% of patients

	Trial 1		Trial 2	
Adverse Event (%)	**Tirzepatide (N= 114)**	**Placebo (N=120)**	**Tirzepatide (N=119)**	**Placebo (N= 114)**
Diarrhea	26.3	12.5	21.8	8.8
Nausea	25.4	10.0	21.8	5.3
Vomiting	17.5	4.2	9.2	0.9
Constipation	15.8	2.5	15.1	4.4

Tirzepatide for OSA and Obesity: Adverse Events seen in > 5% of patients

	Trial 1		Trial 2	
Adverse Event (%)	**Tirzepatide (N= 114)**	**Placebo (N=120)**	**Tirzepatide (N=119)**	**Placebo (N= 114)**
Serious or severe GI event	3.5 2 pts diarrhea 1 pt GERD 1 pt nausea	0	3.4 3 pts diarrhea 2 pts nausea **1 pt acute pancreatitis**	0

Tirzepatide for OSA and Obesity : Main Conclusions

Tirzepatide for OSA and Obesity: Main Conclusions

- Among patients with obesity with moderate to severe OSA (i.e., AHI > 15 events/hr), treatment with tirzepatide titrated to a dose of 10 to 15 mg SQ weekly compared to placebo over 52 weeks led to:
  - A decrease in AHI of about 20 events/hour which is a about 50% decrease from baseline AHI
  - About an 16% decrease in body weight
  - About a 30% greater chance of no longer needing PAP
  - About a 3 to 7 mm Hg decrease in systolic bp

Tirzepatide for OSA and Obesity : Main Conclusions

- Among patients with obesity with moderate to severe OSA (i.e., AHI > 15 events/hr), treatment with tirzepatide titrated to a dose of 10 to 15 mg SQ weekly compared to placebo over 52 weeks led to:
  - Less than a 5% risk of an adverse event leading to stopping tirzepatide
  - Most common side effects of nausea, diarrhea, vomiting and constipation in about 15 to 25% of patients
  - Less than 4% risk of a severe gastrointestinal event such as severe diarrhea, vomiting, GERD or pancreatitis

Tirzepatide for OSA and Obesity: Study Strengths

- Multinational
- About 30% of patients were women
- Racially and ethnically diverse patients
- Clinically meaningful endpoints:
  - OSA-related
  - Cardiovascular

Tirzepatide for OSA and Obesity: Study Limitations

- Relative short study duration of one year
- Unable to assess longer-term cardiovascular outcomes
- Included patients with obesity but did not include patients who were overweight or normal weight
- Compliance with PAP was not tracked in Trial 2

Major Barrier to Tirzepatide = COST without insurance coverage

Cost/month	**$1,115 per month (4 pens of 15 mg/0.5 ml each) at Walmart *with Good Rx discount*** **$500 per month direct cash pay option through Eli Lilly**

Back to our patient . . .

A 46-year-old woman presents to her primary care provider to follow up management of obesity and obstructive sleep apnea. She has steadily gained weight over the last five years. She is 5’9”, now weights 240 lbs with a BMI of 35.

She has been working with a dietician to help manage her obesity. She also tries to walk two or three times per week.

She has a history of OSA confirmed by sleep study. She has done well with a positive airway pressure at night using a nasal CPAP mask.

Our patient . . .

She wants to discuss options for improving her OSA through additional weight loss.

She has also heard of a new weekly injectable medication for weight loss . . .

You advise her that in addition to her current diet, exercise regimen, and CPAP regimen, she is a candidate for tirzepatide. You discuss the benefits of a 20% weight loss which can lead to marked improvement in her OSA, a decrease in her blood pressure and a significant chance of no longer needing her home CPAP.

You discuss the common gastrointestinal side effects and counsel her to contact you for any other concerns. You confirm that her insurance will cover tirzepatide and start a dose of 2.5 mg SQ weekly with titration of to a target of 15 mg SQ daily.

Questions?

Thank you!

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