



Breathing Easy: Conquering Obstructive Sleep Apnea for Better Health

Screening and Management of OSA



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FACULTY



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AGENDA

5:00 Evaluating sleep health and identifying patients at-risk for OSA

5:00 Recognizing diverse presentations of OSA

20:00 Individualizing OSA management plans





EVALUATING SLEEP HEALTH AND IDENTIFYING PATIENTS AT-RISK FOR OSA

SLEEP EVALUATION

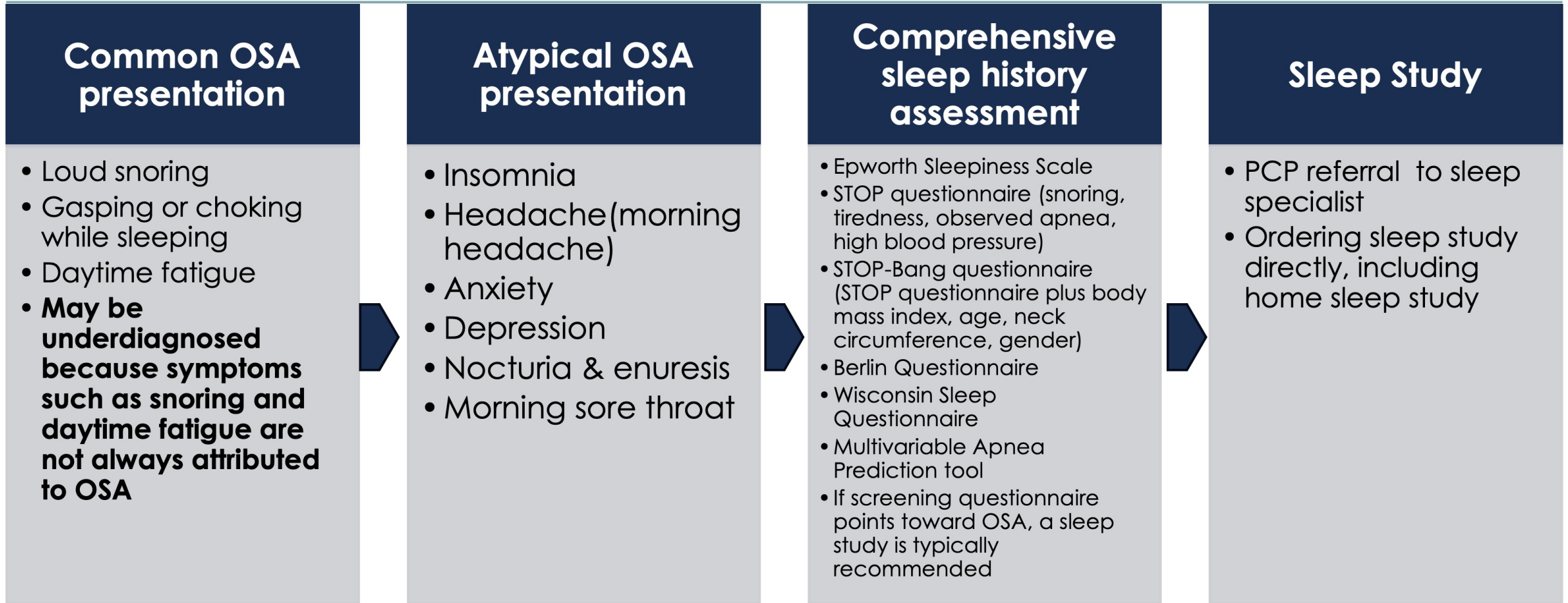
RISK FACTORS FOR OSA

OBESITY	GENDER	AGE	MEDICATION & ALCOHOL USE
Adipose deposition at the upper airway Increased risk of collapse	Males have increased adipose tissue deposition at the neck & longer airways	Aging leads to decreased genioglossus response to negative pressure and increased type I collagen, which delay the contractile-relaxant response	Opioids, benzodiazepine, baclofen, & alcohol can cause upper airway relaxation

Arredondo E, Udeani G, Panahi L, Taweeseedt PT, Surani S. Obstructive Sleep Apnea in Adults: What Primary Care Physicians Need to Know. *Cureus*. 2021 Sep 9;13(9):e17843; Jin J. Screening for Obstructive Sleep Apnea. *JAMA*. 2022;328(19):1988. doi:10.1001/jama. 2022.20142



SLEEP EVALUATION



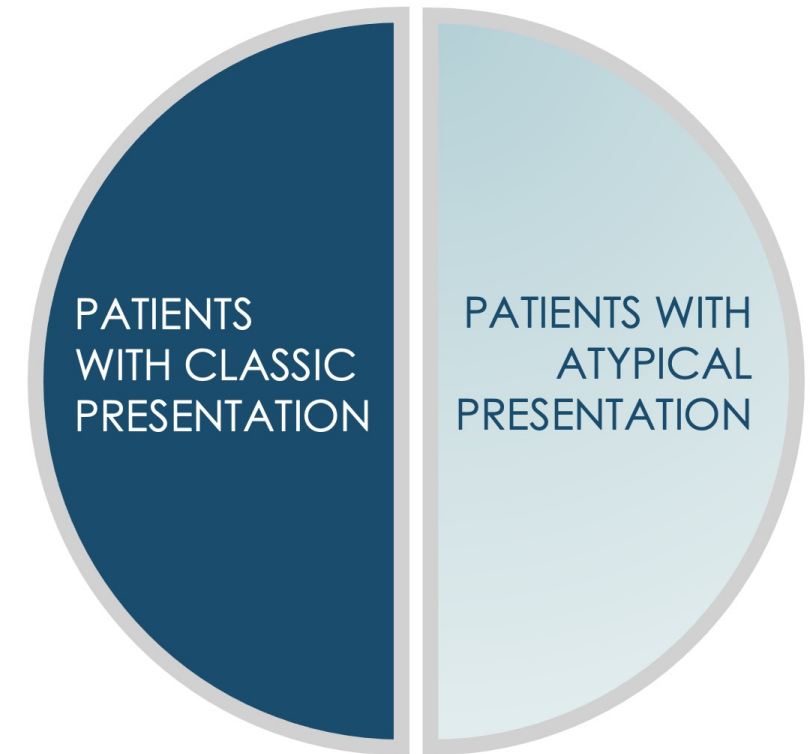
Arredondo E, Udeani G, Panahi L, Taweeseedt PT, Surani S. Obstructive Sleep Apnea in Adults: What Primary Care Physicians Need to Know. *Cureus*. 2021 Sep 9;13(9):e17843; Jin J. Screening for Obstructive Sleep Apnea. *JAMA*. 2022;328(19):1988. doi:10.1001/jama.2022.20142



RECOGNIZING DIVERSE PRESENTATIONS OF OSA

ATYPICAL OSA PRESENTATIONS

- A critical need exists around educating care providers on atypical clinical presentations of OSA
- Approximately half of patients may not present with “classic” OSA symptoms such as excessive daytime sleepiness
- Atypical symptoms may include insomnia, headache (morning headache), anxiety, depression, nocturia & enuresis, morning sore throat
- Atypical symptoms may be more common among women vs men



RECOGNIZING DIVERSE PRESENTATIONS OF OSA

Disturbed Sleeping: Insomnia-related symptoms

- Waking too early & trouble falling back to sleep
- Waking up too often
- Heavy perspiration
- Restless
- Sudden awakening gasping for breath

Excessive Daytime Sleepiness

- Falling asleep involuntarily during day
- Dozing off when driving
- Classic OSA symptoms (night breaking pauses and loud snoring)

Minimally Symptomatic:

- Lower probability of OSA symptoms
- More likely to experience comorbid hypertension, diabetes and cardiovascular disease

Men vs Women

Men are twice as likely to have OSA vs women.

Women often have atypical presentations of OSA including symptoms of depression, headache, anxiety, and fatigue.

Lee W, et al. Epidemiology of Obstructive Sleep Apnea: a Population-based Perspective. *Expert Rev Respir Med.* 2008;2(3):349-364; Ye L, Pien GW, Ratcliffe SJ, et al. The different clinical faces of obstructive sleep apnoea: a cluster analysis. *Eur Respir J.* 2014;44(6):1600-1607; Jin J. Screening for Obstructive Sleep Apnea. *JAMA.* 2022;328(19):1988. doi:10.1001/jama.2022.20142

RECOGNIZING DIVERSE PRESENTATIONS OF OSA

- Given the diverse presentations of OSA, especially among atypical and less symptomatic presentations, opportunity exists for HCPs to better recognize patients who may benefit from a comprehensive sleep history assessment
- Through recognition by care providers of diverse OSA presentations, the overall care model of OSA can be expanded to distribute work efforts across PCPs and sleep specialist

Lee W, et al. Epidemiology of Obstructive Sleep Apnea: a Population-based Perspective. *Expert Rev Respir Med.* 2008;2(3):349-364; Ye L, Pien GW, Ratcliffe SJ, et al. The different clinical faces of obstructive sleep apnoea: a cluster analysis. *Eur Respir J.* 2014;44(6):1600-1607; Jin J. Screening for Obstructive Sleep Apnea. *JAMA.* 2022;328(19):1988. doi:10.1001/jama.2022.20142



INDIVIDUAL OSA MANAGEMENT PLANS

INDIVIDUALIZING OSA MANAGEMENT PLANS: TREATMENT OPTIONS

TREATMENT OPTIONS FOR OSA



AHI, apnea-hypopnea index; CPAP, continuous positive airway pressure, MAD, mandibular adjustment device

Arredondo E, Udeani G, Panahi L, et al. Obstructive Sleep Apnea in Adults: What Primary Care Physicians Need to Know. *Cureus*. 2021; 3(9): e17843; Lee W, et al. Epidemiology of Obstructive Sleep Apnea: a Population-based Perspective. *Expert Rev Respir Med*. 2008;2(3):349-364; Papaetis GS. GLP-1 receptor agonists, SGLT-2 inhibitors, and obstructive sleep apnoea: can new allies face an old enemy? *Arch Med Sci Atheroscler Dis*. 2023 Feb 28;8:e19-e34; Xia F, Sawan M. Clinical and Research Solutions to Manage Obstructive Sleep Apnea: A Review. *Sensors (Basel)*. 2021 Mar 4;21(5):1784. Winfried Randerath, Jan de Lange, Jan Hedner, Jean Pierre T.F. Ho, Marie Marklund, Sofia Schiza, Jörg Steier, Johan Verbraecken *ERJ Open Research* 2022 8: 00126-2022; Tanriover, C., Uckol, D., Akyol, M. et al. Potential Use of SGLT-2 Inhibitors in Obstructive Sleep Apnea: A new treatment on the horizon. *Sleep Breath* 27, 77–89 (2023).

INDIVIDUALIZING OSA MANAGEMENT PLANS: TREATMENT OPTIONS

DEVICES		SURGERY	
CPAP	MAD	Uvulopalatopharyngoplasty	Hypoglossal nerve stimulation
Effectively maintain airway patency during sleep	Shift the position of the mandible forward and alter position of tongue and jaw	Widening of airway through removal of soft palate, uvula, and tonsils	Pacemaker-like device that provides neurostimulation of hypoglossal nerve
Benefits dose-dependent with hours of use	Option for patients who cannot tolerate CPAP treatment	Benefit to patients inconsistent	Benefit to patients inconsistent
More effective than control but long-term clinical outcomes unclear	Less efficacious compared to CPAP	Invasive procedure	Invasive procedure
Adherence can be challenging as long-term treatment	Long-term impact on teeth and jaw		
Does not address underlying pathophysiological mechanisms, especially for patients who are obese			

CPAP, continuous positive airway pressure, MAD, mandibular adjustment device

Arredondo E, Udeani G, Panahi L, et al. Obstructive Sleep Apnea in Adults: What Primary Care Physicians Need to Know. *Cureus*. 2021; 3(9): e17843; Lee W, et al. Epidemiology of Obstructive Sleep Apnea: a Population- based Perspective. *Expert Rev Respir Med*. 2008;2(3):349-364; Papaetis GS. GLP-1 receptor agonists, SGLT-2 inhibitors, and obstructive sleep apnoea: can new allies face an old enemy? *Arch Med Sci Atheroscler Dis*. 2023 Feb 28;8:e19-e34; Xia F, Sawan M. Clinical and Research Solutions to Manage Obstructive Sleep Apnea: A Review. *Sensors (Basel)*. 2021 Mar 4;21(5):1784. Winfried Randerath, Jan de Lange, Jan Hedner, Jean Pierre T.F. Ho, Marie Marklund, Sofia Schiza, Jörg Steier, Johan Verbraecken *ERJ Open Research* 2022 8: 00126-2022; Tanriover, C., Ucku, D., Akyol, M. et al. Potential Use of SGLT-2 Inhibitors in Obstructive Sleep Apnea: A new treatment on the horizon. *Sleep Breath* 27, 77–89 (2023)..



INDIVIDUALIZING OSA MANAGEMENT PLANS: TREATMENT OPTIONS

LIFESTYLE MODIFICATIONS, INCLUDING PHARMACOTHERAPY



Affecting structure/anatomy	Increasing arousal threshold	Increasing ventilatory stability	Improving airway muscle	Positional Therapy		Weight Loss	
Diuretics; Antihistamines, steroids; Vasoconstrictors	Benzodiazepines/Z-drugs; GABAergic drugs; Trazodone Inconsistent study results and more studies needed	Carbonic anhydrase inhibitors Xanthines Comorbid CVD targets Additional data needed	Serotonergic agonists Noradrenergic± antimuscarinic TASK-channel inhibitors Inconsistent study results and more studies needed	Use of positioning device to keep patient in non-supine position Limited evidence of benefit	Nutrition & Physical Activity Demonstrated benefit of intensive weight loss program for people with obesity and severe OSA Difficult to achieve and maintain weight loss	Bariatric surgery OSA remission can be obtained in the majority Invasive procedure & challenging compliance	Pharmacotherapy <ul style="list-style-type: none"> • Weight loss inducing drugs • Potential to reduce upper airway collapsibility and OSA severity • Anti-obesity pharmacotherapies can be evaluated following no improvement with other lifestyle modifications <ul style="list-style-type: none"> • GLP1-RAs • GIP/GLIP1-RAs • SGLT-2 inhibitors • Lipase inhibitor Side-effects, contraindications, & rebound weight gain if treatment ceased

Arredondo E, Udeani G, Panahi L, et al. Obstructive Sleep Apnea in Adults: What Primary Care Physicians Need to Know. *Cureus*. 2021; 3(9): e17843; Hamilton GS, Edwards BA. The potential impact of GLP-1 agonists on obstructive sleep apnoea. *Respirology*. 2023; 28(9): 824–825; Lee W, et al. Epidemiology of Obstructive Sleep Apnea: a Population- based Perspective. *Expert Rev Respir Med*. 2008;2(3):349-364; Papaetis GS. GLP-1 receptor agonists, SGLT-2 inhibitors, and obstructive sleep apnoea: can new allies face an old enemy? *Arch Med Sci Atheroscler Dis*. 2023 Feb 28;8:e19-e34; Xia F, Sawan M. Clinical and Research Solutions to Manage Obstructive Sleep Apnea: A Review. *Sensors (Basel)*. 2021 Mar 4;21(5):1784. Winfried Randerath, Jan de Lange, Jan Hedner, Jean Pierre T.F. Ho, Marie Marklund, Sofia Schiza, Jörg Steier, Johan Verbraecken *ERJ Open Research* 2022 8: 00126-2022; Tanriover, C., Ucku, D., Akyol, M. et al. Potential Use of SGLT-2 Inhibitors in Obstructive Sleep Apnea: A new treatment on the horizon. *Sleep Breath* 27, 77–89 (2023).



WEIGHT LOSS IN OSA: PHARMACOTHERAPY

Effect of weight loss pharmacotherapies on OSA

 Results available
 Ongoing study

Liraglutide (GLP-1 agonist), plus diet and exercise	Phentermine (appetite suppressant) plus topiramate (seizure and migraine treatment)	Sibutramine (appetite suppressant)	Naltrexone (opioid receptor agonist) plus bupropion (dopamine reuptake inhibitor)	Tirzepatide (GIP/GLP-1 RA): SURMOUNT-OSA
Among people with obesity and moderate or severe OSA, significant improvements in OSA outcomes vs diet and exercise alone	Among people with obesity and moderate to severe OSA, significant improvements in OSA outcomes vs placebo	Among people with obesity and OSA, improvements in OSA outcomes in single-arm trial	Among people with sleep apnea, no significant difference in OSA outcomes vs placebo	Approved in the T2D (US and EU) and obesity (US), is being globally trialed for its ability to reduce severity of OSA <ul style="list-style-type: none"> • Randomized, double-blind, Ph 3 placebo-controlled trial among people with obesity and OSA • Results expected in 2024

GIP, glucose-dependent insulintropic polypeptide; GLP-1, glucagon-like peptide 1 receptor; OSA, obstructive sleep apnea

Blackman, A, Foster, GD, Rosenberg, R. International Journal of Obesity (2016) 40, 1310–1319; ClinicalTrials.gov/NCT05412004. Accessed December 21, 2023; Pi-Sunyer, X, Apovian, CM, McElroy, SL. International Journal of Obesity (2019). 43:2085-2094; Steffen, KJ, Kolotkin, RL. Comb Prod Ther (2012) 2:3; Winslow, DH, Bowden, CH, KiKonato KP. SLEEP, Vol. 35, No. 11, 2012; Yee, BJ, Phillips, CL, Banerjee, D. Int J Obes (2007) 31, 161-168.



PHARMACOLOGIC MANAGEMENT OF OBESITY

1st and 2nd Generation Anti-obesity Medications (AOMs)

	Generic (Brand)	Duration of use	MOA	Effect	How taken	Weight loss
1 st generation	Phentermine (Adipex)	Short Term (≤12 weeks)	Sympathomimetic amine	↓ appetite	PO, up to TID	~3-7%
	Orlistat (Alli, Xenical)	Chronic Obesity Management	Gastrointestinal lipase inhibitor	↓ fat absorption	PO, up to TID	~3-4%
	Phentermine/Topiramate-ER (Qsymia)	Chronic Obesity Management	Sympathomimetic amine + anticonvulsant, carbonic anhydrase inhibitor, gabaminergic	↓ appetite	PO, once daily	~5-11%
	Naltrexone-ER/Bupropion-ER (Contrave)	Chronic Obesity Management	Opioid receptor antagonist + dopamine-norepinephrine reuptake inhibitor	↓ appetite	PO, twice daily	~3-6%
2 nd generation	Liraglutide (Saxenda)	Chronic Obesity Management	GLP-1 RA	↓ appetite	SQ, once daily	~5-7%
	Semaglutide (Wegovy)	Chronic Obesity Management	GLP-1 RA	↓ appetite	SQ, once weekly	~10-16%
	Tirzepatide (Zepbound)	Chronic Obesity Management	Dual GIP/GLP-1 RA	↓ appetite	SQ, once weekly	~15-21%

GLP-1, glucagon-like peptide-1; PO, oral; SQ, subcutaneous injection.

Blonde L, et al. *Endocr Pract.* 2022; Grunvald E, et al. *Gastroenterology.* 2022; FDA Prescribing Information; Jastreboff AM, et al. *N Engl J Med.* 2022; Enright C, et al. *J Endocr Soc.* 2023. Wadden T, et al. *Nat Med.* 2023.

GLP-1 RA AND GIP/GLP-1 RA MEDICATIONS FOR LOWERING GLUCOSE

IMPROVEMENT OF HbA1c BY:

Augment glucose dependent

Insulin secretion and glucagon suppression

Decelerate gastric emptying

Curb post-meal glycemic increments

Reduce appetite, energy intake, and body weight

AND

APPROVED FOR:

Reducing risk of MACE in adults with T2D with established CVD* or multiple cardiovascular risk factors†

Chronic weight management‡

Davies MJ et al. *Diabetes Care*. 2022;45(11):2753-2786.

*dulaglutide, liraglutide, and subcutaneous semaglutide; †dulaglutide; ‡subcutaneous liraglutide titrated to 3.0 mg once daily; subcutaneous semaglutide titrated to 2.4 mg once weekly GIP, glucose-dependent insulinotropic polypeptide; GLP-1 RA, glucagon-like peptide 1 receptor agonist

WEIGHT LOSS WITH TIRZEPATIDE VS PLACEBO IN SURMOUNT TRIALS

PEOPLE WITH OBESITY

SURMOUNT-1

TZP 5 mg baseline - wk 72	TZP 10 mg baseline - wk 72	TZP 15 mg baseline - wk 72	Placebo baseline - wk 72
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SURMOUNT-2

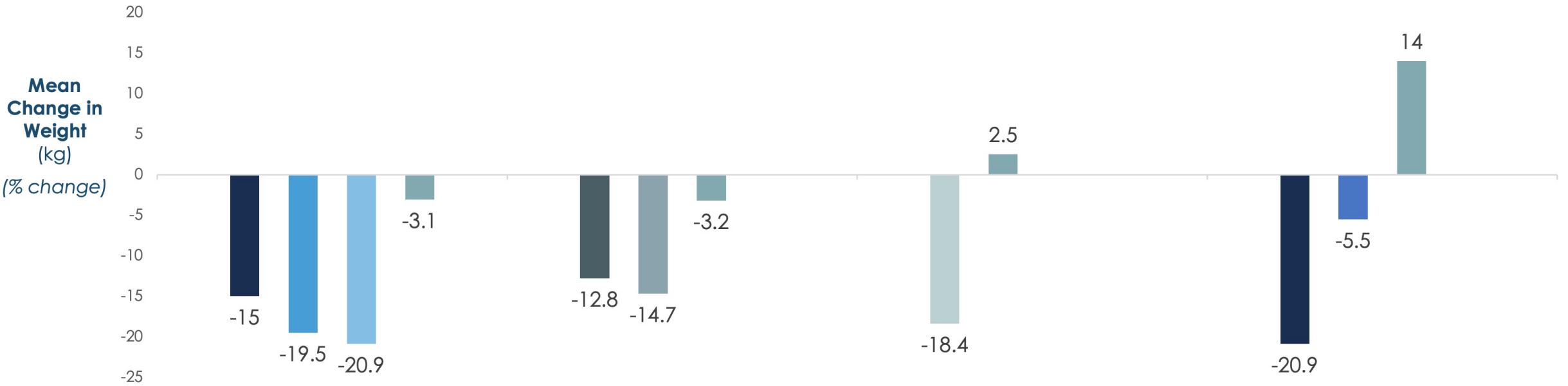
TZP 10 mg baseline - wk 72	TZP 15 mg baseline - wk 72	Placebo baseline - wk 72
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SURMOUNT-3

TZP 10 or 15 mg baseline - wk 72	Placebo baseline - wk 72
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SURMOUNT-4

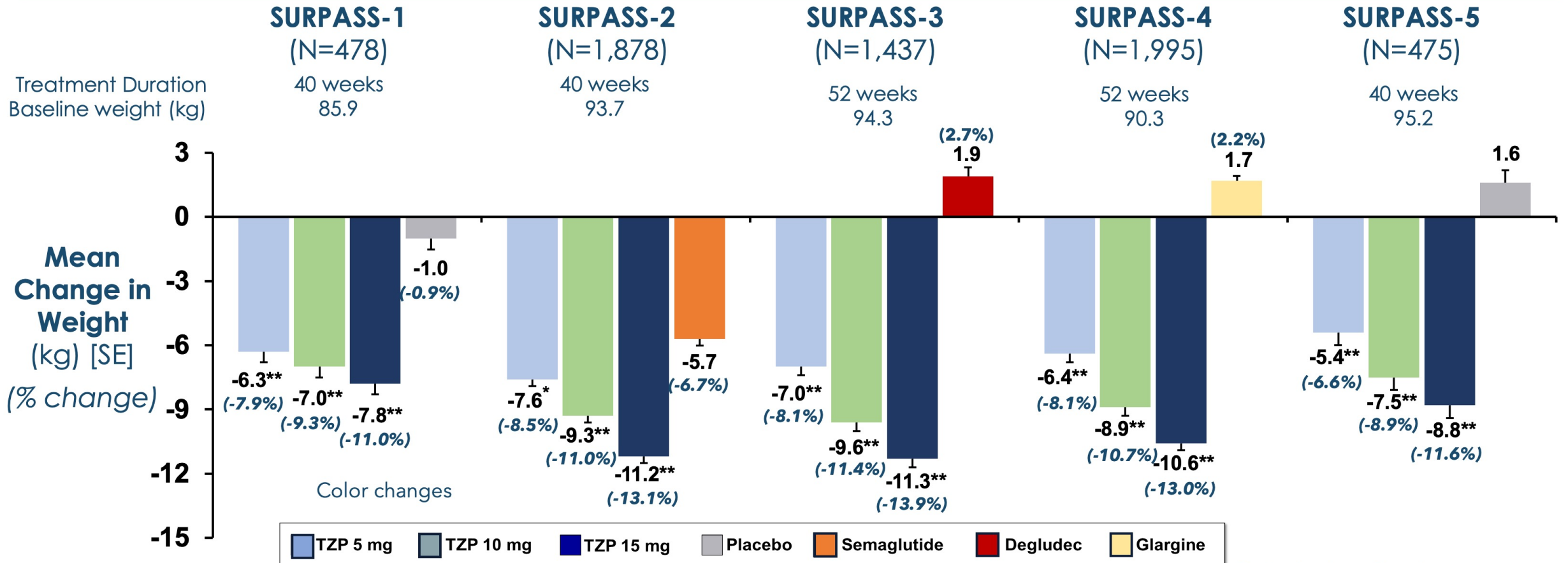
TZP 10 or 15 mg baseline - wk 36	TZP 10 or 15 mg wk 36 - 88	Placebo wk 36 - 88
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Aronne LJ, Sattar N, Horn DB, et al. Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial. *JAMA*. 2024;331(1):38-48; Garvey WT, Frias JP, Jastreboff AM, et al; SURMOUNT-2 investigators. Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial. *Lancet*. 2023 Aug 19;402(10402):613-626; Jastreboff AM, Aronne LJ, Ahmad NN, et al; SURMOUNT-1 Investigators. Tirzepatide Once Weekly for the Treatment of Obesity. *N Engl J Med*. 2022 Jul 21;387(3):205-216; Wadden, T.A., Chao, A.M., Machineni, S. et al. Tirzepatide after intensive lifestyle intervention in adults with overweight or obesity: the SURMOUNT-3 phase 3 trial. *Nat Med* 29, 2909-2918 (2023).



WEIGHT LOSS WITH TIRZEPATIDE VS COMPARATORS IN SURPASS TRIALS



Rosenstock J, et al. *Lancet*. 2021; Frías JP, et al. *N Engl J Med*. 2021; Ludvik B, et al. *Lancet*. 2021; Del Prato S, et al. *Lancet*. 2021; Dahl D, et al. *JAMA*. 2022.

Treatment-regimen estimand
 Superiority vs placebo or active comparator: *P<0.05;
 **P<0.001



MOST COMMON SIDE EFFECTS OF SEMAGLUTIDE AND TIRZEPATIDE



Abdominal pain



Constipation



Dyspepsia



Vomiting



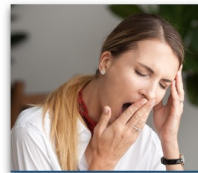
Diarrhea



Nausea



Headache



Fatigue



Abdominal bloating



Belching



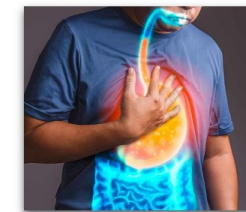
Hypoglycemia in people with T2D



Gas and flatulence



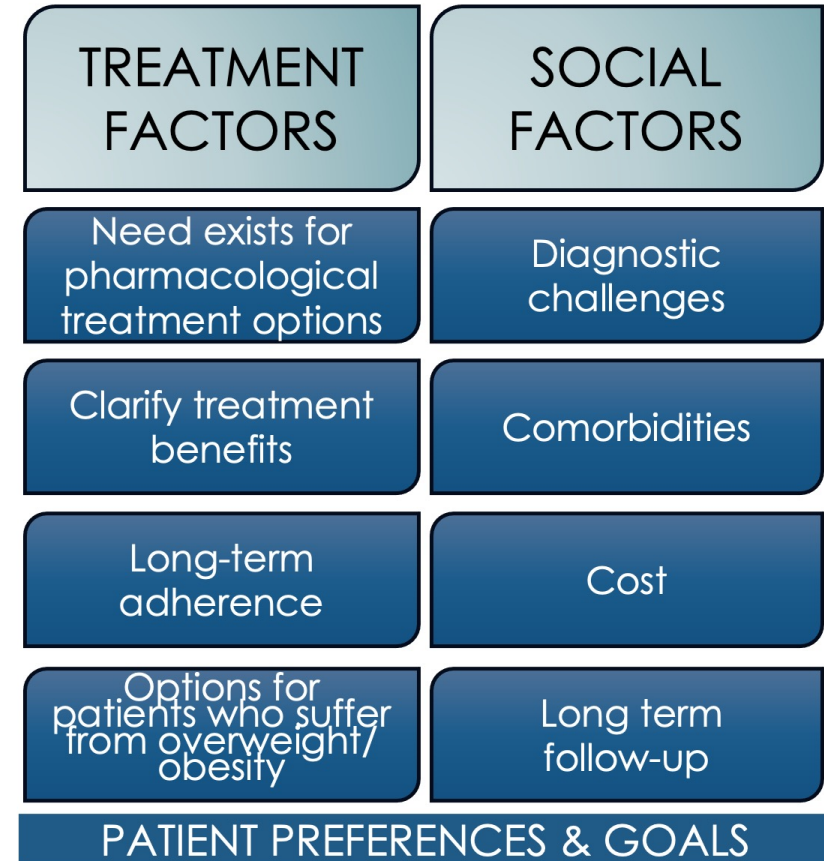
Gastroenteritis



GERD

INDIVIDUALIZING OSA MANAGEMENT PLANS: PERSONALIZATION OF TREATMENT

- Personalization of OSA treatment
- Accounting for treatment and social factors, as well as patient preferences and goals
- A Ph 3 study (SURMOUNT-OSA) is currently underway evaluating the effect and safety of GIP/GLP-1 RA in people with OSA and obesity



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CLINICAL QUEST – DIGITAL COIN PIECE 2



<https://mli.link/coin2-fqb>

