A Review of Clinical Studies and Emerging Data

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ZEALAND PHARMA MEDICAL AFFAIRS TRAINING PROGRAM

MODULE 2

1

Your Speaker

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Vice President, Clinical Affairs, The Obesity Society

15 years owned and operated NP Obesity Treatment Clinic in Flagstaff, AZ

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Learning Objectives

- Describe the efficacy, safety, and indications of FDA-approved medications for obesity
- Discuss the results of obesity and related complications with outcomes trials of FDA-approved medications for obesity
- Compare and contrast the dosing and route of administration of available medications to treat obesity
- Outline medications for obesity that are in the pipeline

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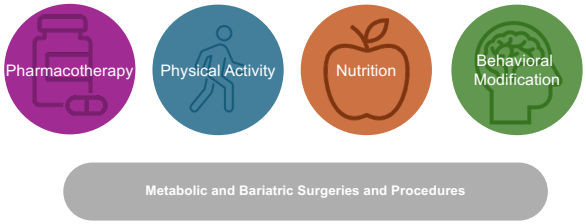
Components of an Effective Obesity Management Program



Metabolic and Bariatric Surgeries and Procedures

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Considerations for Pharmacotherapy

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General Considerations in Pharmacologic Initiation

Pharmacologic interventions may be helpful as adjunct therapy with lifestyle interventions for patients with BMI ≥30 kg/m^2 or ≥27 kg/m^2 with ≥1 obesity-related complication(s).

- Different patients respond to different medications
  - If one option does not work, clinicians should consider others
- Consider discontinuing medication in patients who do not respond with weight reduction of at least 5% at 12 weeks after maximum dose[a]
- Pharmacological therapy may be prescribed indefinitely if the patient responds without any significant side effects

[a]Liraglutide label suggests only 4% weight loss at 12 weeks after maximum dose.
Apovian CM, et al. *J Clin Endocrinol Metab* 2015;100(2):342-362.

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Therapeutic Goals

- Weight reduction of 5%-10% of body weight
- >25% weight reduction now possible with some medications
- Different health conditions require varying amounts of weight reduction to see improvement

Reduces obesity-associated complications within 6 months

Improves patient health and quality of life

Reduces CVD risk factors, prevents/delays T2D, and improves osteoarthritis

Reduces sleep apnea, depression and improves physical functioning

CVD, cardiovascular disease.

Jensen MD, et al. *Circulation*. 2014;129:S102-S138. Garvey WT, et al. *Endocr Pract*. 2016;22(suppl 3):1-203. Yanovski SZ, et al. *JAMA*. 2014;311:74-86. Apovian CM, et al. *J Clin Endocrinol Metab*. 2015;100(2):342-362.

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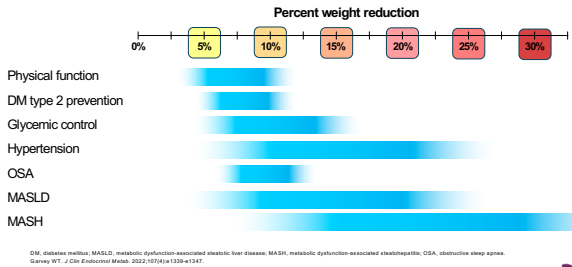
Weight Reduction Targets and Obesity Complications



DM, diabetes mellitus; MASLD, metabolic dysfunction-associated steatotic liver disease; MASH, metabolic dysfunction-associated steatohepatitis; OSA, obstructive sleep apnea.

Garvey WT. *J Clin Endocrinol Metab*. 2022;107(4):e1339-e1347.

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FDA-Approved Medications

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FDA-Approved Short-Term Obesity Medications

Medication	Mechanism of Action
Benzphetamine	Sympathomimetic
Diethylpropion	Sympathomimetic
Phendimetrazine	Sympathomimetic
Phentermine[a]	Sympathomimetic

[a]Phentermine is often prescribed off-label for long-term use, but clinicians should be aware of their state laws.

FDA, US Food and Drug Administration.
Bray GA, et al. Circulation. 2012;125(13):1695-1703.

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FDA-Approved Long-Term Obesity Medications

Medication	Mechanism of Action
Liraglutide (subcutaneous injection)	GLP-1 receptor agonist
Naltrexone/bupropion ER (oral)	Opioid receptor antagonist; dopamine and noradrenaline reuptake inhibitor
Orlistat (oral)	Pancreatic lipase inhibitor—impairs gastrointestinal energy absorption, causing excretion of approximately 30% of ingested triglycerides in stool
Phentermine/topiramate ER (oral)	Noradrenergic + GABA-receptor activator, kainite/AMPA glutamate receptor inhibitor causing appetite suppression
Semaglutide (subcutaneous injection, oral)	GLP-1 receptor agonist
Tirzepatide (subcutaneous injection)	GIP and GLP-1 dual receptor agonist
Setmelanotide	Melanocortin 4 receptor agonist

AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; ER, extended release; GABA, gamma-aminobutyric acid; GIP, gastric inhibitory protein; GLP, glucagon-like peptide.
DailyMed. Accessed January 19, 2026. https://dailymed.nlm.nih.gov/dailymed/index.cfm

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Long-term Obesity Medications Indications Overview

Drug	Brand name(s)	Indication(s)			
		Patient age:	Patient characteristics:	To/For:	In conjunction with:
Orlistat	Xenical	12+	with an initial BMI of ≥30 kg/m², or ≥27 kg/m² with other risk factors	Obesity management, including weight reduction and weight maintenance	reduced-calorie diet
	Alli	18+	with overweight	Weight reduction	reduced-calorie diet
Phentermine-topiramate	Qsymia	12+ 18+	with obesity with overweight in the presence of at least one weight-related comorbid condition	Reduce excess body weight and maintain weight reduction long term	reduced-calorie diet, increased physical activity
Naltrexone-bupropion	Contrave	18+	with obesity or overweight in the presence of at least one weight-related comorbid condition	Reduce excess body weight and maintain weight reduction long term	reduced-calorie diet, increased physical activity

12+ = age 12+ 18+ = age 18+ = reduced-calorie diet = increased physical activity
XENICAL Prescribing Information. https://gskpro.com/content/dam/global/hcpportal/en_US/Downloads/PDF/Xenical_Full_Prescribing_Information.pdf. ALLI Approval Letter. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2007/021887s000_APPROV.pdf. QSYMIA (PI). www.rxqsymia.com/patient/includes/media/pdf/qsymia-prescribing-information.pdf. CONTRAVE (PI). https://www.contrave.com/PI/Contrave-label-current.pdf

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Long-term Obesity Medications Indications Overview (cont)

Drug	Brand name(s)	Indication(s)			
		Patient age:	Patient characteristics:	To/For:	In conjunction with:
Liraglutide	Saxenda	≥12	with obesity or with overweight and at least one comorbid condition with body weight greater than 60 kg and obesity.	To reduce excess body weight and maintain weight reduction long term	
	Victoza	≥10	with type 2 diabetes	Improve glycemic control	
		≥18	with type 2 diabetes and established CVD	Reduce the risk of MACE	
Tirzepatide	Zepbound	≥18	with obesity or with overweight and at least one comorbid condition	Reduce excess body weight and maintain weight reduction long term	
			with obesity	Moderate to severe obstructive sleep apnea	
	Mounjaro	≥10	with type 2 diabetes	Improve glycemic control	

SAXENDA Prescribing Information. https://www.novo-pi.com/saxenda.pdf. Victoza Prescribing Information. https://www.novo-pi.com/victoza.pdf. Zepbound Prescribing Information. https://pi.lilly.com/us/zepbound-uspi.pdf. Mounjaro Prescribing Information. https://pi.lilly.com/us/mounjaro-uspi.pdf.

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Long-term Obesity Medications Indications Overview (cont)

Drug	Brand name(s)	Indication(s)			
		Patient age:	Patient characteristics:	To/For:	In conjunction with:
Semaglutide	Wegovy (injection)	≥18	with obesity	Reduce excess body weight and maintain weight reduction long term	
			with overweight and at least one comorbid condition		
			with CV disease and obesity or overweight	Reduce the risk of MACE	
			with MASH with moderate to advanced liver fibrosis	Treat MASH	
	Wegovy (oral)	≥18	with obesity or overweight and at least one comorbid condition	Reduce excess body weight and maintain weight reduction long term	
			with established CV disease and either obesity or overweight	Reduce the risk of MACE	
	Ozempic	≥18	with type 2 diabetes	Glycemic control	
			with type 2 diabetes and established CV disease	Reduce the risk of MACE	
			With type 2 diabetes and chronic kidney disease	Reduce the risk of sustained eGFR decline	

Wegovy Prescribing Information. https://www.novo-pi.com/wegovy.pdf. Ozempic Prescribing Information. https://www.novo-pi.com/ozempic.pdf.

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Efficacy

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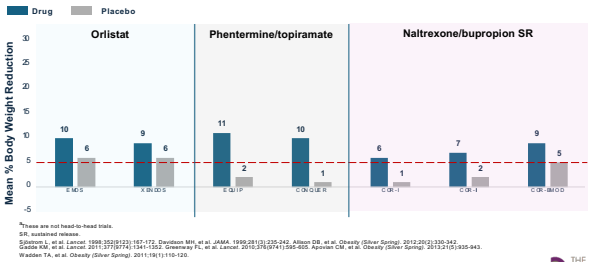
Average Percent Weight Reduction (Drug vs Placebo) From Randomized, Controlled Trials[a] (T2D Excluded)



[a]These are not head-to-head trials.
SR, sustained release.

Sjostrom L, et al. Lancet. 1998;352(9123):167-172. Davidson MH, et al. JAMA. 1999;281(3):235-242. Allison DB, et al. Obesity (Silver Spring). 2012;20(2):330-342.
Gadde KM, et al. Lancet. 2011;377(9774):1341-1352. Greenway FL, et al. Lancet. 2010;376(9741):595-605. Apovian CM, et al. Obesity (Silver Spring). 2013;21(5):935-943.
Wadden TA, et al. Obesity (Silver Spring). 2011;19(1):110-120.

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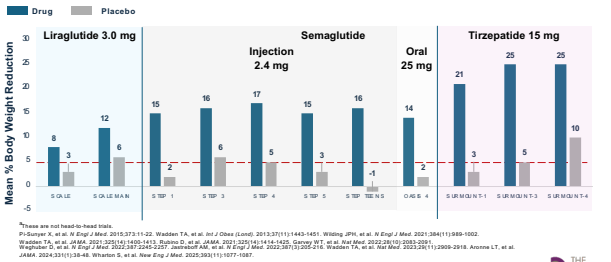
Average Percent Weight Reduction (Drug vs Placebo) From Randomized, Controlled Trials[a] (T2D Excluded) (cont)



[a]These are not head-to-head trials.

Pi-Sunyer X, et al. *N Engl J Med*. 2015;373:11-22. Wadden TA, et al. *Int J Obes (Lond)*. 2013;37(11):1443-1451. Wilding JPH, et al. *N Engl J Med*. 2021;384(11):989-1002.
Wadden TA, et al. *JAMA*. 2021;325(14):1403-1413. Rubino D, et al. *JAMA*. 2021;325(14):1414-1425. Garvey WT, et al. *Nat Med*. 2022;28(10):2083-2091.
Weghuber D, et al. *N Engl J Med*. 2022;387:2245-2257. Jastreboff AM, et al. *N Engl J Med*. 2022;387(5):205-216. Wadden TA, et al. *Nat Med*. 2023;29(11):2909-2918. Aronne LT, et al. *JAMA*. 2024;331(1):38-48. Wharton S, et al. *New Engl J Med*. 2025;393(11):1077-1087.

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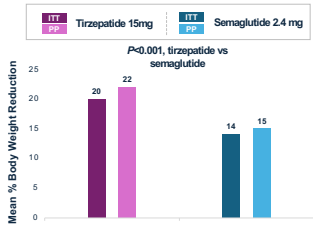
Average Percent Weight Reduction: Tirzepatide vs Semaglutide Head-to-Head Trial (SURMOUNT-5)



Aronne LJ et al. *N Engl J Med*. 2025;393(1):26-36.

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Additional Outcomes Summary

	BP Change, SBP/DPB mmHg		HR Change BPM		LDL Change %		HDL Change %		TG Change %	
	Therapy	Placebo	Therapy	Placebo	Therapy	Placebo	Therapy	Placebo	Therapy	Placebo
Orlistat	-1.01/-1.19	0.58/0.46	NR	NR	-4.0	5.0	9.3	12.8	1.34	2.9
Phentermine/ topiramate (Equip)	-2.9/-1.5	0.9/0.4	1.0	-0.8	-8.4	-5.5	3.5	0	-5.2	9.1
Naltrexone/ bupropion (COR-I)	-0.1/0.0	-1.9/-0.9	1.0	-0.2	-2.0	-0.5	8.0	0.8	-11.6	1.7

All data from maximum doses.
BPM, beats per minute; NR, not reported; SC, subcutaneous.
XENICAL (PI). https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020765s026lbl.pdf . QSYMIA (PI). https://www.rxsaxenda.com/pdf/saxenda-label-current.pdf
CONTRAVE (PI) https://www.contrave.com/pdf/contrave-label-current.pdf

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Additional Outcomes Summary (cont)

	BP Change, SBP/DPB mmHg		HR Change BPM		LDL Change %		HDL Change %		TG Change %	
	Therapy	Placebo	Therapy	Placebo	Therapy	Placebo	Therapy	Placebo	Therapy	Placebo
Liraglutide	-4.2/-2.6	-1.5/-1.9	2.5	0.1	-3.0	-1.0	2.3	0.07	-13.3	-5.5
Semaglutide (SC)	-5.7/-4.4	-1.6/-0.8	NR	NR	-6.1	-2.7	9.6	8.15	-19.0	3.7
Semaglutide (oral)	-8.4/-3.0	-0.8/-1.0	4.1	-0.4	-1.2	1.5	5.2	1.3	-26.9	-4.3
Tirzepatide	-7.2/-4.8	-1.0/-0.8	NR	NR	-5.8	-1.7	8.0	-0.7	-24.8	-5.6

All available results, $P < .05$. All data from maximum doses.
BPM, beats per minute; NR, not reported; SC, subcutaneous.
1. Pi-Sunyer et al. *N Engl J Med*. 2015;373(1):11-22. 2. Garvey WT et al. *Nat Med*. 2022;28(10):2083-2091. 3. Knop KF et al. *Lancet*. 2023;402(10403):705-719. 4. Jastreboff AM et al. *N Engl J Med*. 2022;387(3):205-216.

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Safety and Tolerability

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Participant Poll

- What are the three most common adverse events for obesity medications?
  - Nausea
  - Constipation
  - Headache
  - Dizziness
  - Dyspepsia
  - Insomnia
  - Paresthesia
  - Fecal Urgency

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Orlistat Safety and Tolerability

Adverse Event	Year 1		Year 2	
	Placebo (n = 1466)	Orlistat 120 mg tid (n = 1913)	Placebo (n = 524)	Orlistat 120 mg tid (n = 613)
Oily spotting[a]	1.3%	26.6%	0.2%	4.4%
Flatus with discharge	1.4%	23.9%	0.2%	2.1%
Fecal urgency	6.7%	22.1%	1.7%	2.8%
Fatty/oily stool[a]	2.9%	20.0%	0.6%	5.5%
Oily evacuation[a]	0.8%	11.9%	0.2%	2.3%
Increased defecation	4.1%	10.8%	0.8%	2.6%
Fecal incontinence	0.9%	7.7%	0.2%	1.8%

[a]Oily discharge may be clear or have a coloration such as orange or brown
Adapted from: Xenical [package insert]. Montgomery, AL: H2-Pharma, LLC.

Contraindications/Warnings and Precautions:
- Contraindicated for those with chronic malabsorption syndrome or cholestasis
- Do not use in pregnancy or when breastfeeding
- Drug interactions

Clinical Considerations:
- May interfere with absorption of fat-soluble vitamins/medications/OCPs, especially if experiencing diarrhea
- Need vitamins A/D/E/K/beta-carotene >2 hours separated from medication and levothyroxine ≥4 hours from medication

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Phentermine/Topiramate Safety and Tolerability

Adverse Event	Placebo (n = 1561)	PHEN/TPM 3.75/23 mg (n = 240)	PHEN/TPM 7.5/46 mg (n = 498)	PHEN/TPM 15/92 mg (n = 1580)
Paresthesia	2%	4%	14%	20%
Dry mouth	3%	7%	14%	19%
Constipation	6%	8%	15%	16%
Dysgeusia	1%	1%	7%	9%
Insomnia	5%	5%	6%	9%
Dizziness	3%	3%	7%	9%

BP, blood pressure; HR, heart rate; PHEN, phentermine; TPM, topiramate.
Modified from: Qsymia [package insert]. Campbell, CA: Vivus, Inc.

Contraindications/Warnings and Precautions:
- Monitor for reduced sweating/increased body temperature
- Pregnancy test (baseline & monthly) due to birth defect risk
- Worsening depression/suicidal thoughts
- Increased BP and HR
- Do not use in pregnancy, glaucoma, hyperthyroidism

Clinical Considerations:
- Must be discontinued gradually to avoid increased seizure risk
- Monitor kidney function
- Taper doses if necessary to discontinue

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Naltrexone/Bupropion Safety and Tolerability

Adverse Event[a]	Placebo (n = 1515)	Naltrexone/bupropion 32/360 mg (n = 2545)
Nausea	6.7%	32.5%
Constipation	7.2%	19.2%
Headache	10.4%	17.6%
Vomiting	2.9%	10.7%
Dizziness	3.4%	9.9%
Insomnia	5.9%	9.2%
Dry mouth	2.3%	8.1%
Diarrhea	5.2%	7.1%

Contraindications/Warnings and Precautions:
- Contraindications: uncontrolled hypertension, seizure disorders, anorexia or bulimia, opioid use, monoamine oxidase inhibitors
- Do not use in pregnancy

Clinical Considerations:
- Avoid taking with high-fat meal to minimize seizure risk
- Monitor for increased suicidal ideation
- Monitor BP and HR

Modified from: Contrave [package insert]. Brentwood, TN: Currax Pharmaceuticals LLC.

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Participant Poll

- What is the most common adverse event that causes patients to discontinue a NuSH medication?
  - GI-related AEs
  - Injection-site reactions
  - Paresthesia
  - Headache

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Incretin-Based Therapies Safety and Tolerability

Liraglutide

Adverse Event[a]	Placebo (n = 1,941)	Liraglutide 3.0 mg (n = 3,384)
Nausea	13.8%	39.3%
Diarrhea	9.9%	20.9%
Constipation	8.5%	19.4%
Vomiting	3.9%	15.7%
Injection site reaction[b]	10.5%	13.9%
Headache	12.6 %	13.6%
Hypoglycemia in T2D[c]	6.6%	12.6%
Dyspepsia	2.7%	9.6%
Fatigue	4.6%	7.5%
Dizziness	5.0%	6.9%
Abdominal pain	3.1%	5.4%
Increased Lipase	2.2%	5.3%
Upper abdominal pain	2.7%	5.1%

Semaglutide (SC)

Adverse Event[a]	Placebo (n = 1,261)	Semaglutide 2.4 mg (n = 2,116)
Nausea	16%	44%
Diarrhea	16%	30%
Vomiting	6%	24%
Constipation	11%	24%
Abdominal pain[b]	10%	20%
Headache	10%	14%
Fatigue[c]	5%	11%
Dyspepsia	3%	9%
Dizziness	4%	8%
Abdominal distension	5%	7%
Eructation	<1%	7%
Hypoglycemia in T2D[d]	2%	6%
Flatulence	4%	6%
Gastroenteritis	4%	6%
GERD	3%	5%

Oral formulation AEs were similar in type and percentage to injection.

Tirzepatide

Adverse Event[a]	Placebo (n = 958)	Tirzepatide 10 mg (n = 948)	Tirzepatide 15 mg (n = 941)
Nausea	8%	29%	28%
Diarrhea[b]	8%	21%	23%
Vomiting	2%	11%	13%
Constipation[c]	5%	14%	11%
Abdominal pain[d]	5%	9%	10%
Dyspepsia	4%	9%	10%
Injection site reactions[e]	2%	8%	8%
Fatigue[f]	3%	6%	7%
Hypersensitivity reactions	3%	5%	5%
Eructation	1%	5%	5%
Hair loss	1%	4%	5%

SAXENDA Prescribing Information. [illegible] Wegovy Prescribing Information. [illegible] Zepbound Prescribing Information. [illegible]

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Incretin-Based Therapies Clinical Considerations

Contraindications/Warnings and Precautions:

- Contraindication: personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2
- Warnings and precautions: risk of thyroid C-cell tumors; GI adverse reactions; AKI, gallbladder disease, and pancreatitis
- Do not use in pregnancy or when breastfeeding

Clinical Considerations:

- Monitor for signs and symptoms of pancreatitis, cholelithiasis
- Monitor for depression and suicidal thoughts
- Must stay hydrated to avoid AKI
- May slow absorption of other medications

SAXENDA Prescribing Information. https://www.novo-pi.com/saxenda.pdf. Wegovy Prescribing Information. https://www.novo-pi.com/wegovy.pdf. Zepbound Prescribing Information. https://uspl.lilly.com/zepbound/zepbound.pdf

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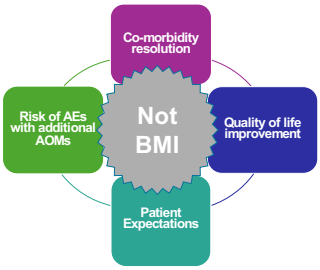
Therapeutic Endpoint for AOM titration



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Lifestyle in Obesity Trials

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New Clinical Trial Guidance in 2025

Updated draft guidance from the FDA revises earlier language that indicated that weight management medications and devices should be used *adjunct* with intensive lifestyle modification interventions

2007:

"The use of a weight-management product should be contemplated only after a sufficient trial of lifestyle modification has failed."

…now reads…

2025:

"At least one phase 3 trial should incorporate a standard-of-care diet and physical activity program (i.e., a program that strikes appropriate balance between effectiveness and simplicity that could be implemented in a primary care setting)."

FDA. 2025. Accessed May 17, 2025. https://www.fda.gov/media/71252/download

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Pharmacotherapy Trials

- Pivotal trials all included lifestyle intervention per FDA requirements:
  - "Regular" lifestyle counseling sessions with a dietitian/qualified healthcare professional with a focus on healthful, balanced meals
  - 500-kcal deficit per day
  - ≥150 minutes of physical activity per week
  - Used in DPP and Look AHEAD
- What happens if paired with intensive lifestyle (behavioral) interventions?
  - First 8 weeks: 1000 to 1200 kcal/day meal replacements (eg, liquid shakes, meal bars)
  - Then 1200 to 1800 kcal/day of conventional food for the remainder of the 68 weeks
  - 100 minutes of weekly physical activity, increased gradually to 200 minutes/week

DPP, diabetes prevention program.

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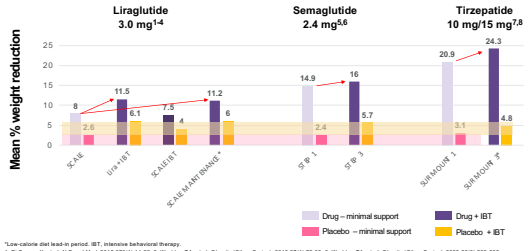
Examining the Added Effect of Intensive Behavioral Therapy (IBT) in Clinical Trials



*Low-calorie diet lead-in period. IBT, intensive behavioral therapy.

1. Pi-Sunyer X, et al. *N Engl J Med*. 2015;373(1):11-22. 2. Wadden TA, et al. *Obesity (Silver Spring)*. 2019;27(1):75-86. 3. Wadden TA, et al. *Obesity (Silver Spring)*. 2020;28(3):529-536. 4. Wadden TA, et al. *Int J Obesity (Lond)*. 2013;37(11):1443-1451. 5. Wilding JPH, et al. *N Engl J Med*. 2021;384(11):989-1002. 6. Wadden TA, et al. *JAMA*. 2021;325(14):1403-1413. 7. Jastreboff AM, et al. *N Engl J Med*. 2022;387(3):205-216. 8. Wadden TA, et al. *Nat Med*. 2023;29(11):2909-2918.

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Additional Indications

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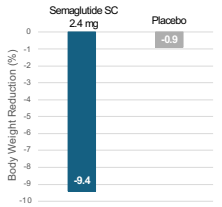
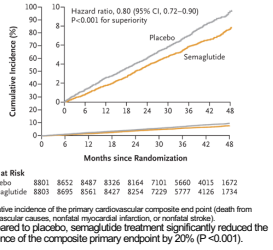
MACE Outcomes: Semaglutide





Cumulative incidence of the primary cardiovascular composite end point (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke).
Compared to placebo, semaglutide treatment significantly reduced the incidence of the composite primary endpoint by 20% (P <0.001).

SC, subcutaneous.
Lincoff AM et al. *N Engl J Med*. 2023;389(24):2221-2232.

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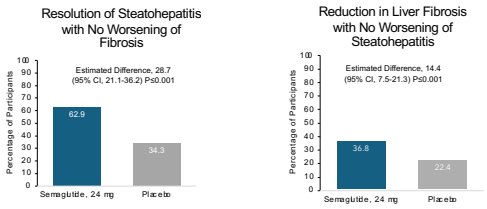
MASH Outcomes: Semaglutide
ESSENCE Study



MASH, metabolic-associated steatohepatitis.
1. Sanyal AJ et al. *N Engl J Med*. Jun 5 2025;392(21):2089-2099.

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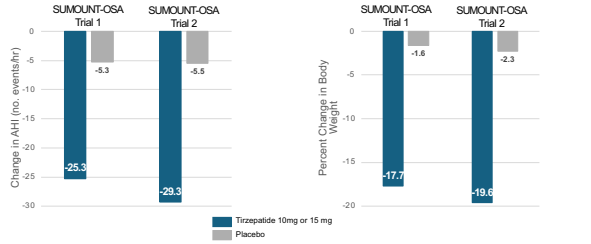
Obstructive Sleep Apnea Outcomes: Tirzepatide

SURMOUNT-OSA Study



AHI, apnea-hypopnea index; OSA, obstructive sleep apnea.
Malhotra, AA, et al. *N Engl J Med*. 2024;391(13):1193-1205.

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New Information – Not On Label

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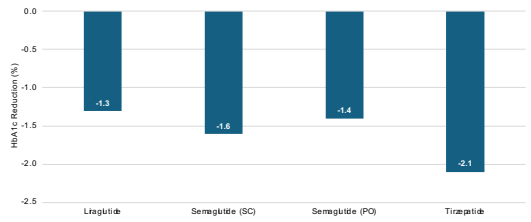
HbA1c Reduction in Patients with T2D



SC, subcutaneous.
1. Davies MJ et al. *JAMA*. 2015;314(7):687. 2. Davies MJ et al. *Lancet*. 2021;397(10278):971-984. 3. Aroda VR et al. *Diabetes Care*. 2019;42(9):1724-1732. 4. Garvey WT et al. *Lancet*. 2022;402(10402):613-626.

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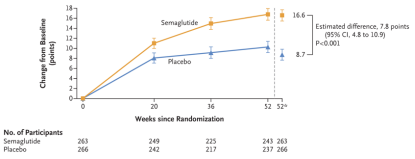
HFpEF Outcomes: Semaglutide
STEP-HFpEF Study



Observed (i.e., as-measured) mean changes from baseline in the KCCQ-CSS.

Semaglutide treatment resulted in significantly greater improvement compared to placebo (*P*<0.001).

KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire clinical summary score.

1. Kosiborod MN et al. *N Engl J Med*. 2023;389(12):1069-1084.

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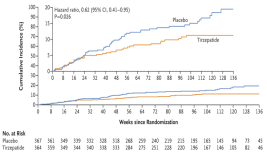
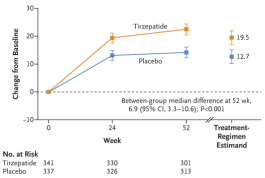
HFpEF Outcomes: Tirzepatide
Summit Study



Composite of cardiovascular death or worsening HF event.

Tirzepatide reduced the risk of a primary endpoint event by 38% (*P*<0.026).



Observed mean changes from baseline in KCCQ-CSS responses

Tirzepatide treatment resulted in a significant (*P* <0.001) improvement in the KCCQ-CSS at 52 weeks

1. Packer M et al. *N Engl J Med*. 2025;392(5):427-437.
KCCQ-CSS, Kansas City Cardiomyopathy Questionnaire clinical summary score.

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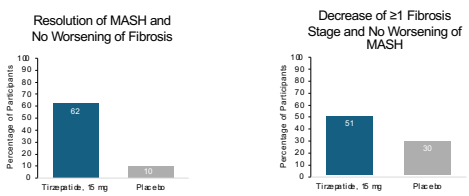
MASH Outcomes: Tirzepatide
SYNERGY-MASH Study



At all three doses, tirzepatide treatment resulted in significantly (*P* <0.001 for all comparisons) more patients achieving resolution of MASH without worsening fibrosis and improvement in fibrosis.

MASH, metabolic-associated steatohepatitis.

1. Loomba R et al. *N Engl J Med*. Jul 25 2024;391(4):299-310.

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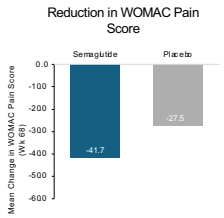
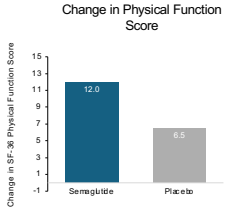
Osteoarthritis Outcomes: Semaglutide
STEP-9 Study





SF-36, Short Form Health Survey; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
Bliddal H, et al. *N Eng J Med*. 2024;391:1573-1583.

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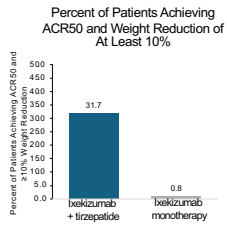
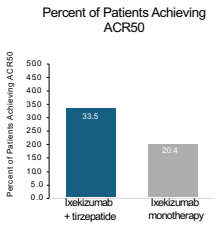
Psoriatic Arthritis: Tirzepatide
TOGETHER-PsA Study[a]





Phase 3b study topline results.
Eli Lilly and Company. Accessed Feb 13, 2026. https://investor.lilly.com/news-releases/news-release-details/lillys-taltz-ixekizumab-and-zepbound-tirzepatide-used-together

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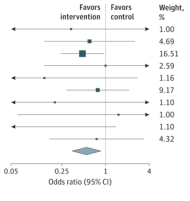
Dementia: GLP-1 Receptor Agonists
Meta-analysis and Systematic Review

Study	Intervention event	Total	Control event	Total	ARR (95% CI)	Odds ratio (95% CI)	Weight, %
Pfeffer et al,[39] 2015	0	3034	1	3034	0.03 (-0.06 to 0.12)	0.33 (0.01 to 8.18)	1.00
Marso et al,[31] 2016	3	1648	5	1649	0.12 (-0.21 to 0.46)	0.60 (0.14 to 2.51)	4.69
Marso et al,[40] 2016	12	4668	25	4672	0.28 (0.02 to 0.53)	0.48 (0.24 to 0.95)	16.51
Holman et al,[41] 2017	2	7356	2	7396	0.00 (-0.05 to 0.05)	1.01 (0.14 to 7.14)	2.59
Hernandez et al,[47] 2018	0	4731	3	4732	0.06 (-0.02 to 0.15)	0.14 (0.01 to 2.77)	1.16
Gerstein et al,[42] 2019	7	4949	9	4952	0.04 (-0.12 to 0.20)	0.78 (0.29 to 2.09)	9.17
Husain et al,[43] 2019	0	1591	2	1592	0.13 (-0.09 to 0.34)	0.20 (0.01 to 4.17)	1.10
Gerstein et al,[44] 2021	1	2717	0	1359	-0.02 (-0.15 to 0.12)	1.50 (0.06 to 36.88)	1.00
Frias et al,[45] 2022	0	304	2	102	2.26 (-0.74 to 5.27)	0.07 (0.00 to 1.39)	1.10
Lincoff et al,[46] 2023	3	8803	4	8801	0.01 (-0.05 to 0.07)	0.75 (0.17 to 3.35)	4.32
RE model for subgroup: Q = 4.72; *df* = 9; *P* = .86; I^2 = 0%					0.07 (0.02 to 0.1)	0.55 (0.35 to 0.86)	



Medications included in studies: liraglutide, semaglutide, albiglutide, dulaglutide, efpeglenatide.
Seminar A, et al. JAMA Neurol. 2025;85(5):450-460.

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Investigational Medications

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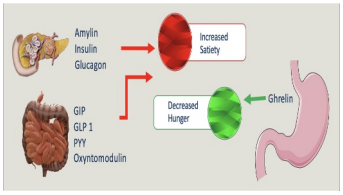
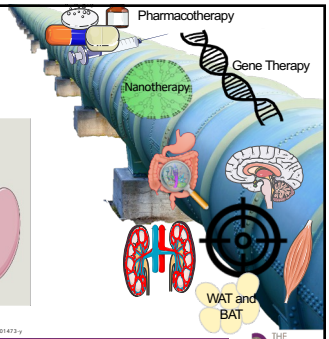
In The Pipeline

- 50 + companies are developing obesity therapies
- 80 + therapies in trials





Melson, E., Ashraf, U., Papamargaritis, D. et al. *Int J Obes.* 2024:https://doi.org/10.1038/s41366-024-01473-y

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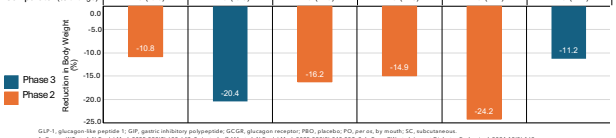
Reduction in Body Weight
Investigational Medications

	Cagrilintide	Semaglutide/ cagrilintide	Maridebart/ cafraglutide	Survodutide	Retatrutide	Orforglipron
MoA	Amylin	GLP-1 +Amylin	GLP-1 +GIP	GLP-1 +GCGR	GLP-1+GIP +GCGR	GLP-1
Route	SC	SC	SC	SC	SC	PO
Timepoint (w)	26	68	52	46	48	72
Comparator (% change)	PBO (-3.0)	PBO (-3.0)	PBO (-2.5)	PBO (-2.0)	PBO (-2.1)	PBO (-2.1)



GLP-1, glucagon-like peptide 1; GIP, gastric inhibitory polypeptide; GCGR, glucagon receptor; PBO, placebo; PO, *per os*, by mouth; SC, subcutaneous.

1. Garvey WT et al. *N Engl J Med.* 2025;393(7):635-647. 2. Jastreboff AM et al. *N Engl J Med.* 2025;393(9):843-857. 3. le Roux CW et al. *Lancet Diabetes Endocrinol.* 2024;12(3):162-173. 4. Jastreboff AM et al. *N Engl J Med.* 2023;389(6):514-526. 5. Wharton S et al. *N Engl J Med.* 2025;(NEJMoa2511774).

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Additional Outcomes Summary

	BP Change, SBP/DPB mmHg		HR Change BPM		LDL Change %		HDL Change %		TG Change %	
	Therapy	Placebo	Therapy	Placebo	Therapy	Placebo	Therapy	Placebo	Therapy	Placebo
Cagrilinitide	-2.8/0.5	NR	-2.0	NR	-1.0	0	0	0	-0.3	0.1
Semaglutide + cagrilinitide	-9.9/-5.0	-3.2/-1.9	NR	NR	-5.9	-0.7	11.3	1.3	-25.8	-4.3
Maridebart cafraglutide	-10.4/-5.7	-3.1/-1.1	4.5	0.2	-7.7	0.8	6.0	-0.1	-24.7	1.3
Survodutide	-5.6/-5.4	-2.5/-1.8	NR	NR	-8.3	-0.4	2.9	0.1	-46.9	-1.6
Retatrutide	-9.4/-2.5	-3.4/-1.7	9.2	0.8	-16.4	-3.6	-8.4	0.4	-34.0	-3.1
Orforglipron	-5.7/-2.4	-1.4/-1.4	4.3-5.3	0.38	-4.8	-1.3	NR	NR	-14.8	-3.8

All data from maximum doses except survodutide, which is 2.4 mg data. Data from 24 weeks.
BPM, beats per minute; NR, not reported; PBO, placebo; PO, per os; by mouth; SC, subcutaneous.
5. Lau DCW et al. Lancet. 2021;398(10317):2160-2172. 6. Garvey WT et al. N Engl J Med. 2025;393(7):635-647. 7. Jastreboff AM et al. N Engl J Med. 2025;393(9):843-857. 8. le Roux et al. Lancet Diabetes Endocrinol. 2024;12(3):162-172. 9. Jastreboff AM et al. N Engl J Med. 2023;389(6):514-526. 10. Wharton S et al. N Engl J Med. 2025;(NEJMoa2511774).

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Summary

Approved obesity medications in combination with lifestyle modification reduce body weight and improve markers of cardiometabolic health to varying degrees.

For clinicians, therapeutic goals are to reduce obesity-associated complications and improve patient overall health and quality of life.

For some obesity medications, indications are expanding as they demonstrate improvements in related conditions.

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ZEALAND PHARMA MEDICAL AFFAIRS TRAINING PROGRAM

Thank you!

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