Pharmacology and Obesity Management:
Discussion of Medications and Use

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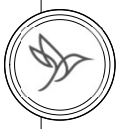

Wendy L. Wright
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Owner – Wright & Associates Family Healthcare
Amherst, NH
Owner – Partners in Healthcare Education, LLC
Faculty – Fitzgerald Health Education Associates
Lawrence, MA

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Disclosures

- Speaker Bureau:
  - Sanofi-Pasteur, Merck, Pfizer, Seqirus, Moderna: Vaccines
  - AbbVie and Pfizer: Migraines
  - AstraZeneca: Asthma and COPD
- Consultant:
  - Sanofi-Pasteur, Merck, Pfizer, Moderna, and Seqirus: Vaccines
  - Idorsia: Insomnia
  - Shield Therapeutics: Iron Deficiency Anemia
- No real or potential conflict of interest to disclose.
- No experimental or investigational use of drugs or devices will be presented.
- Off-label use will be identified as such if discussed.
- All relevant financial relationships have been mitigated.

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Objectives

- At the end of this presentation, the participant will be able to:

1. Discuss the statistics regarding obesity.
2. Identify the various pharmacologic agents to treat overweight and obesity.
3. Compare pharmacologic strategies for weight stabilization or loss in the overweight or obese individual.

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Tips

- References
  - Listed throughout and at the end of the presentation

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Obesity, if Multifactorial

- Genetic
- Environmental
- Immune
- Endocrine
- Medical
- Neurobehavioral

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Definition of Obesity

"Obesity is defined as a chronic, progressive, relapsing, and treatable multi-factorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial health consequences."[1]

Obesity Medicine Association, 2021 Definition of Obesity

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Today…

- 108 million Americans with hypertension
- 78 million adults in the United States qualify for a statin.
- 108 million Americans living with obesity; yet it is often not treated in the same way.

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Screening and Diagnosis

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Practical Diagnosis

- Weight
  - Easily understood by all
- Height
  - Allows you to calculate the BMI
- Look at medication list
- BMI

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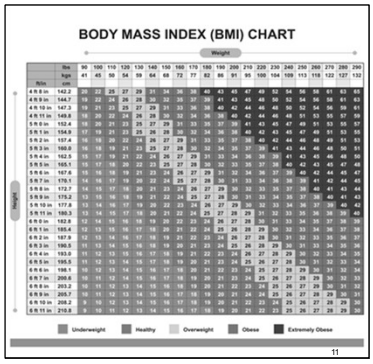
Body Mass Index Chart



https://www.shutterstock.com/image-vector/body-mass-index-bmi-chart-1610175649

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BMI (kg/m²)	Classification	Disease Risk* (Waste Circumference)		
		Men Women	≤40" (102 cm) ≤35" (89 cm)	>40" (102 cm) >35" (89 cm)
<25.0–29.9	Overweight	Increased		High
30.0–34.9	Class 1 Obesity	High		Very high
35.0–39.9	Class 2 Obesity	Very high		Very high
>40	Class 3 Obesity	Extremely high		Extremely

Image source: Powell-Wiley, T.M., Poirier, P., Burke, L.E., Després, J.P., Gordon-Larsen, P., Lavie, C.J., Lear, S.A., Ndumele, C.E., Neeland, I.J., Sanders, P., St-Onge, M.P.; American Heart Association Council on Lifestyle and Cardiometabolic Health; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Epidemiology and Prevention; and Stroke Council. (2021). Obesity and Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation*, 143(21):e984-e1010. https://www.ahajournals.org/doi/full/10.1161/CIR.0000000000000973

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2025: New ICD 10 Codes

- **Class 1 Obesity**: Body Mass Index (BMI) ≥ 30.0 to less than 35.0
- **Class 2 Obesity**: BMI ≥ 35.0 to less than 40.0
- **Class 3 Obesity**: BMI ≥ 40.0

The specific codes for these classifications include:

- **E66.811**: Obesity Class 1
- **E66.812**: Obesity Class 2
- **E66.813**: Obesity Class 3

https://obesitymedicine.org/blog/new-icd-10-codes-for-obesity-treatment-advancements-in-accurate-diagnosis-and-care/ Accessed 01-02-2025

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Practical Diagnosis

- Waist
  - Obtained by taking a measurement between the iliac crest and the bottom of the rib cage after mild exhalation
  - Waist circumference of >102 cm (>40 inches) in men or 89 cm (>35 inches) in women is an essential component of the metabolic syndrome diagnosis.

Fahed, G., Aoun, L., Bou Zerdan, M., Allam, S., Bou Zerdan, M., Bouferraa, Y., & Assi, H. I. (2022). Metabolic syndrome: Updates on pathophysiology and management in 2021. *International Journal of Molecular Sciences, 23*(2), 786. https://doi.org/10.3390/ijms23020786

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Waist Circumference

- As the individual gets older, it becomes much more predictive of morbidity and mortality than the BMI.
  - When waist circumference is 36 inches (91 cm): 3× more likely to develop diabetes
  - 40 inches (101.6 cm): 12× more likely

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Slide 13

WW0 https://obesitymedicine.org/blog/new-icd-10-codes-for-obesity-tre

Accessed 01-02-2025
Wendy Wright, 2025-01-05T13:23:57.443

WW0 0 New slide
Wendy Wright, 2025-01-05T13:24:04.702

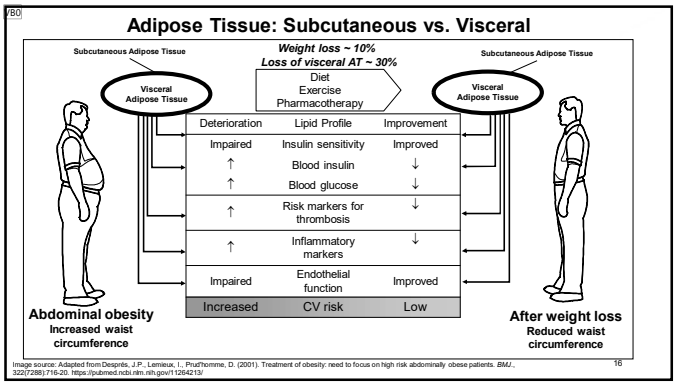
Slide 14

LD0 Hi Wendy, just pointing out that this source is 24 years old.
Larlene Dunsmuir, 2025-02-12T21:25:44.224

LD0 0 Here is a current study that might help:
Kenneth Lo, Yu-Qing Huang, Geng Shen, Jia-Yi Huang, Lin Liu, Yu-Ling Yu, Chao-Lei Chen, Ying Qing Feng, Effects of waist to height ratio, waist circumference, body mass index on the risk of chronic diseases, all-cause, cardiovascular and cancer mortality, Postgraduate Medical Journal, Volume 97, Issue 1147, May 2021, Pages 306–311, https://doi.org/10.1136/postgradmedj-2020-137542
Larlene Dunsmuir, 2025-02-13T20:46:07.621

JR0 1 Replaced with
Fahed, G., Aoun, L., Bou Zerdan, M., Allam, S., Bou Zerdan, M., Bouferraa, Y., & Assi, H. I. (2022). Metabolic syndrome: Updates on pathophysiology and management in 2021. International Journal of Molecular Sciences, 23(2), 786. https://doi.org/10.3390/ijms23020786

From Wendy's Obesity 2024 presentation
Jill Racicot, 2025-02-25T07:22:09.936


BD
Adipose Tissue: Subcutaneous vs. Visceral
Subcutaneous Adipose Tissue
Visceral Adipose Tissue
Weight loss ~ 10%
Loss of visceral AT ~ 30%
Diet
Exercise
Pharmacotherapy
Subcutaneous Adipose Tissue
Visceral Adipose Tissue
Deterioration
Lipid Profile
Improvement
Impaired
Insulin sensitivity
Improved
↑
Blood insulin
↓
↑
Blood glucose
↓
↑
Risk markers for thrombosis
↓
↑
Inflammatory markers
↓
Impaired
Endothelial function
Improved
Increased
CV risk
Low
Abdominal obesity
Increased waist circumference
After weight loss
Reduced waist circumference
Image source: Adapted from Després, J.P., Lemieux, I., Prud'homme, D. (2001). Treatment of obesity: need to focus on high risk abdominally obese patients. BMJ., 322(7288):716-20. https://pubmed.ncbi.nlm.nih.gov/11264213/
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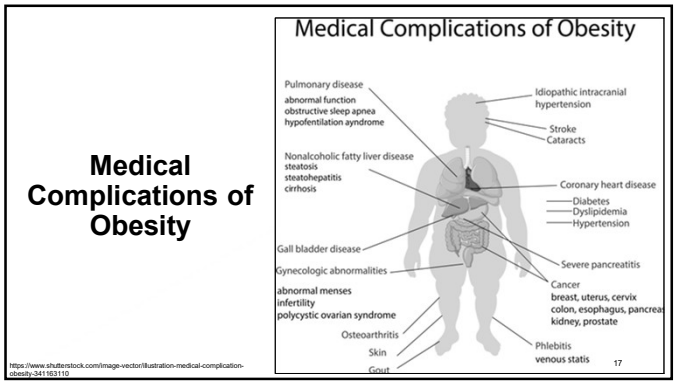
Medical Complications of Obesity
Medical Complications of Obesity
Pulmonary disease
abnormal function
obstructive sleep apnea
hypofentilation ayndrome
Idiopathic intracranial hypertension
Stroke
Cataracts
Nonalcoholic fatty liver disease
steatosis
steatohepatitis
cirrhosis
Coronary heart disease
Diabetes
Dyslipidemia
Hypertension
Gall bladder disease
Severe pancreatitis
Kynecologic abnormalities
Cancer
breast, uterus, cervix
colon, esophagus, pancrea
kidney, prostate
abnormal menses
infertility
polycystic ovarian syndrome
Osteoarthritis
Skin
Gout
Phlebitis
venous statis
https://www.shutterstock.com/image-vector/illustration-medical-complication-obesity-341163110
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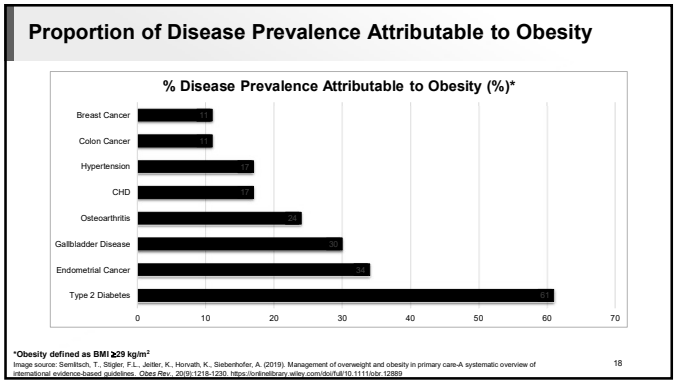
Proportion of Disease Prevalence Attributable to Obesity
% Disease Prevalence Attributable to Obesity (%)*
Breast Cancer
11
Colon Cancer
11
Hypertension
17
CHD
17
Osteoarthritis
24
Gallbladder Disease
30
Endometrial Cancer
34
Type 2 Diabetes
61
0
10
20
30
40
50
60
70
*Obesity defined as BMI ≥29 kg/m²
Image source: Semlitsch, T., Stigler, F.L., Jeitler, K., Horvath, K., Siebenhofer, A. (2019). Management of overweight and obesity in primary care-A systematic overview of international evidence-based guidelines. Obes Rev. 20(9):1218-1230. https://onlinelibrary.wiley.com/doi/full/10.1111/obr.12889
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Slide 16

VB0 I cleaned up this graphic a bit.
Valerie Bruder, 2025-02-06T03:58:04.230

Obesity is associated with 60 comorbidities, most of which are improved or reduced with weight loss.

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DO

Relationship Between BMI and Cardiovascular Mortality

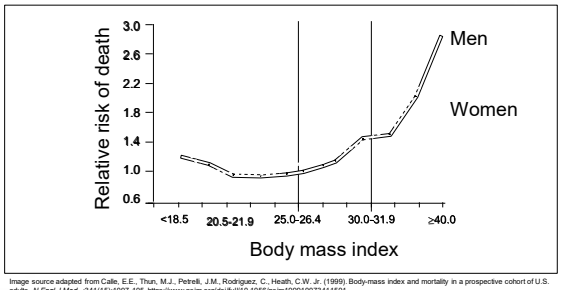

Image source adapted from Calle, E.E., Thun, M.J., Petrelli, J.M., Rodriguez, C., Heath, C.W. Jr. (1999). Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med.*, 341(15):1097-105. https://www.nejm.org/doi/full/10.1056/nejm199910073411501

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New Goals of Weight Loss

"The initial goal of weight loss therapy for overweight patients is to decrease body weight by about 10%. Moderate weights loss (of this magnitude) can significantly decrease the severity of obesity-associated risk factors."

~NIH/NHLBI

Wing, R.R. et al. (2011) Look AHEAD Research Group. (2011).
Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes.
Diabetes Care, 34(7):1481-6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3120182/

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Slide 20

LD0 Here is a current article to consider:

Wei S. et al. (2025). The combined impact of BMI and ABSI on all-cause mortality among American adults with diabetes. Diabetology & Metabolic Syndrome 17(1):48. doi: 10.1186/s13098-025-01614-x. PMID: 39920852; PMCID: PMC11806875.
https://pmc.ncbi.nlm.nih.gov/articles/PMC11806875/
Larlene Dunsmuir, 2025-02-14T23:42:16.974

JR0 0 Previously approved in Wendy's 2024 Obesity program
Jill Racicot, 2025-02-25T07:25:05.048

D0

Change in Weight and CHD Risk Factor Clustering: Framingham Offspring Study

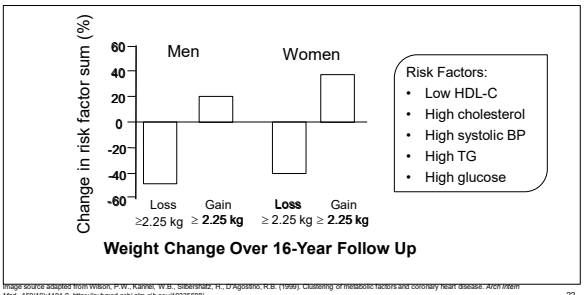

Image source adapted from Wilson, P.W., Kannel, W.B., Silbershatz, H., D'Agostino, R.B. (1999). Clustering of metabolic factors and coronary heart disease. *Arch Intern Med.*, 159(10):1104-9. https://pubmed.ncbi.nlm.nih.gov/10335688/

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Intentional Weight Loss and Reduction in Mortality

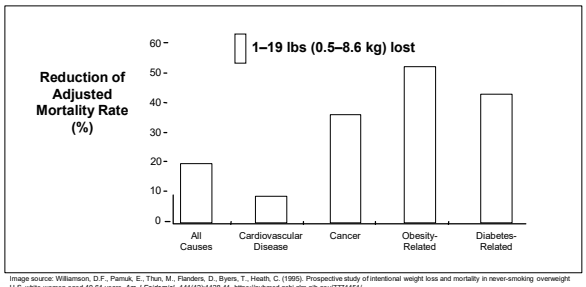

Image source: Williamson, D.F., Pamuk, E., Thun, M., Flanders, D., Byers, T., Heath, C. (1995). Prospective study of intentional weight loss and mortality in never-smoking overweight U.S. white women aged 40-64 years. *Am J Epidemiol.*, 141(12):1128-41. https://pubmed.ncbi.nlm.nih.gov/7771451/

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Case Study – BL

- 52-year-old female; struggled with obesity since teenager
  - Increase in weight with each pregnancy
  - Increase in weight with menopause
- PMH: Asthma, MDD, hyperlipidemia, obesity, history of breast cancer 1-year ago

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Slide 22

LD0 Not sure if you could find something more current but this source is more than 25 years old.
Larlene Dunsmuir, 2025-02-14T23:49:08.346

JR0 0 Previously approved in Wendy's 2024 Obesity program
Jill Racicot, 2025-02-25T07:25:34.579

Slide 23

LD0 Source is 30 years old.
Larlene Dunsmuir, 2025-02-14T23:49:30.001

JR0 0 Previously approved in Wendy's 2024 Obesity program
Jill Racicot, 2025-02-25T07:25:54.344

Case Study – BL

- Medications
  - Fluticasone/salmeterol 250 mg/50 mg 1-puff BID
  - Albuterol 2 puffs every 4–6 hours PRN
  - Tamoxifen 20 mg once daily
  - Citalopram 20 mg 1-pill daily
  - Multivitamin daily

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Selected medications that can cause weight gain

- Psychotropic medications
  - Tricyclic antidepressants
  - Monoamine oxidase inhibitors
  - Specific SSRIs
  - Atypical antipsychotics
  - Lithium
  - Specific anticonvulsants
- β-adrenergic receptor blockers

SSRI=Selective serotonin reuptake inhibitor

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Selected medications that can cause weight gain

- Diabetes medications
  - Insulin
  - Sulfonylureas
  - Thiazolidinediones
- Highly active antiretroviral therapy
- Tamoxifen
- Steroid hormones
  - Glucocorticoids
  - Progestational steroids

SSRI=Selective serotonin reuptake inhibitor

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Case Study – BL

- What role, if any, do you think her medication may be playing in her obesity?
  - Are there better medication options for her?

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NHLBI Guidelines: A Guide to Selecting Treatment for Obesity in Adults

	BMI (kg/m^2) Category				
Treatment	**Overweight 25–26.9**	**Overweight 27–29.9**	**Obesity (Class 1) 30–34.9**	**Obesity (Class 2) 35–39.9**	**Extreme Obesity (Class 3) ≥40**
Diet, physical activity, and behavior therapy	✔ (With comorbidities)	✔ (With comorbidities)	✔	✔	✔
Pharmacotherapy		✔ (With comorbidities)	✔	✔	✔
Surgery			✔ (With comorbidities)	✔ (With comorbidities)	✔ (With comorbidities)

BMI=Body mass index; NHLBI=National Heart, Lung, and Blood Institute, division of National Institute of Health (NIH).
Image source: Table adapted from NHLBI. (2000). The Practical Guide: Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. NIH Publication 00-4084. https://www.nhlbi.nih.gov/files/docs/guidelines/prctgd_c.pdf

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The Modalities of Obesity Treatment

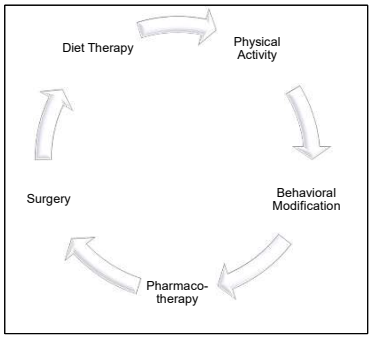

Image source: Table adapted from NHLBI. (2000). The Practical Guide: Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. NIH Publication 00-4084. https://www.nhlbi.nih.gov/files/docs/guidelines/prctgd_c.pdf

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Slide 29

LD0 Is this helpful for a more recent source?
https://www.ncbi.nlm.nih.gov/books/NBK588750/
Larlene Dunsmuir, 2025-02-14T23:55:33.284

LD0 0 If so, it might be useful on the next slide as well.
Larlene Dunsmuir, 2025-02-14T23:56:16.282

JR0 1 Previously approved in Wendy's 2024 Obesity program
Jill Racicot, 2025-02-25T07:26:13.670

Medications

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Other Major Messages from 2013 Obesity Guidelines

- Who needs to lose weight?
  - BMI ≥30 kg/m^2 or BMI ≥25 kg/m^2 with a risk factor (e.g., elevated waist circumference)
- You don't need to get your patients to an ideal weight.
  - Modest weight loss has major health benefits.
- There is no magic diet for weight loss.
  - It's about a calorie deficit.
  - Choose the diet composition based on the patient's health status and preference.

Comier, M.-A. (2022). A review of current guidelines for the treatment of obesity. *The American Journal of Managed Care*, *28*(suppl 15), S288-S296. https://www.ajmc.com/view/review-of-current-guidelines-for-the-treatment-of-obesity

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Other Major Messages from 2013 Obesity Guidelines

- Everyone who needs to lose weight should have access to a comprehensive lifestyle intervention program with 14 sessions in 6 months and follow-up for a year.
  - If your patient doesn't have access to a comprehensive program in a medical or community setting, a commercial program with an evidence-base to recommend is acceptable.

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Slide 33

LD0 What do you think of using this here instead?
https://www.ajmc.com/view/review-of-current-guidelines-for-the-tr
Larlene Dunsmuir, 2025-02-15T00:03:21.130

JR0 0 Updated on previous slide
Jill Racicot, 2025-02-25T07:29:35.471

History of Medications Utilized for the Treatment of Obesity

Date	Medication	Problems
1890s	Thyroid	Hyperthyroid
1930s	Dinitrophenol	Cataracts and neuropathy
1930s	Amphetamines	Addiction
1960s	Digitalis and diuretics	Death
1970s	Aminorex	Pulm HTN
1996–7	(Dex)fenfluramine and phentermine	Valvular disease

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Why use pharmacotherapy?

- Rationale
  - Patients can lose an average of 4–20% more with medication than diet and exercise alone.

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Pharmacotherapeutic Options

Drug	Class	Short/Long Term	Schedule	Efficacy 2
Phentermine	Sympathomimetic amine anorectic	Short term	IV	3.6 kg (7.9 lb); 2–24 wk
Diethylproprion	Sympathomimetic amine anorectic	Short term	IV	3.0 kg (6.6 lb); 6–52 wk
Orlistat	Lipase inhibitor	Long term	n/a	2.9–3.4 kg (6.5–7.5 lb), 2.9–3.4%; 1 y
Alli	Lipase inhibitor	Long term	n/a	2.9–3.4 kg (6.5–7.5 lb), 2.9–3.4%; 1 y
Phentermine/ Topiramate	Sympathomimetic amine anorectic/ Antiepileptic analogue	Long term	IV	6.6 kg (14.5 lb) (recommended dose), 6.6% 8.6 kg (18.9 lb) (high dose), 8.6%; 1 y
Naltexone/ Buproprion	Opioid antagonist / Antidepressant	Long term	n/a	4.8%; 1y

Am J Manag Care. 2022;28(suppl 15):S288-S296. doi:10.37765/ajmc.2022.89292
2 Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: an endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2015;100(2):342-362. doi:10.1210/jc.2014-3415. doi:10.1210/jc.2015-1782

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Pharmacotherapeutic Options

Drug	Class	Short/Long Term	Schedule	Efficacy 2
Liraglutide	GLP 1 receptor agonist	Long term	n/a	5.8 kg; 1 y
Semaglutide	GLP 1 receptor agonist	Long term	n/a	16-17kg, 68 weeks
Tirzepatide	GIP/GLP 1 receptor agonist	Long term	n/a	48 pounds, 72 weeks

Am J Manag Care. 2022;28(suppl 15):S288-S296. doi:10.37765/ajmc.2022.89292
2 Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: an endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2015;100(2):342-362. doi:10.1210/jc.2014-3415. doi:10.1210/jc.2015-1782

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Older Pharmacotherapies[17–19]

Agent	Mechanism	Approval	Comments
Phentermine	Central noradrenergic	Short-term use DEA Schedule IV	Rare cases of pulmonary HTN and valvular heart disease have been reported.
Diethylproprion	Central noradrenergic	Short-term use DEA Schedule IV	Rare cases of pulmonary HTN have been reported.
Orlistat	Peripheral pancreate lipase inhibitor	Long-term use Not scheduled	Monitor renal function in patients at risk of renal impairment.

Drug Enforcement Agency (DEA)

Sources: https://www.empr.com/drug/diethylpropion/ ; https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/085128s065lbl.pdf ; https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/085128s065lbl.pdf

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Phentermine

- Approved 16 years of age and older
- Short-term use
- 7.5 mg, 8 mg, 15 mg, or 37.5 mg
- Monitor – Blood pressure, heart rate
- Avoid use – CAD, cerebrovascular disease, pregnancy

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Long term use of Phentermine

- Recommend monitoring patient monthly x 3 months
- If doing well and > 5% body weight reduction at 3 months, consider allowing patient to stay on longer than three months
- If longer than three months, monitor at least every 3 months with visit
- Limited long-term data (1-2 years)

Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: an endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2015;100(2):342-362. doi:10.1210/jc.2014-3415. doi:10.1210/jc.2015-1782
Lewis, K. H., Fischer, H., Ard, J., Barton, L., Bessesen, D. H., Daley, M. F., Desai, J., Fitzpatrick, S. L., Horberg, M., Koebnick, C., Oshiro, C., Yamamoto, A., Young, D. R., & Arterburn, D. E. (2019). Safety and Effectiveness of Longer-Term Phentermine Use: Clinical Outcomes from an Electronic Health Record Cohort. Obesity (Silver Spring, Md.), 27(4), 591–602. https://doi.org/10.1002/oby.22430

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Diethylpropion

- Diethylpropion (Tenuate)
- Approved in 1960's for short term use (3 months)
- Class: norepinephrine-releasing agent/sympathomimetic
- Dosage: 75 mg once daily
- Efficacy: 3.0 kg (6 – 52 weeks)
- Follow same guidelines as phentermine

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Orlistat

- Indications and dose
  - Approved by FDA, 1999
  - Approved in adolescents (age 12 years and older)
  - Indication: BMI ≥30 kg/m^2 or BMI ≥27 kg/m^2 with other risk factors
- Dosing
  - Rx: 120 mg TID with each meal (during or up to 1 hour after)
  - OTC: 60 mg TID with each meal (during or up to 1 hour after)

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Slide 40

LD0 Would this work as a current option for the source?

Lewis KH, Fischer H, Ard J, Barton L, Bessesen DH, Daley MF, Desai J, Fitzpatrick SL, Horberg M, Koebnick C, Oshiro C, Yamamoto A, Young DR, Arterburn DE. Safety and Effectiveness of Longer-Term Phentermine Use: Clinical Outcomes from an Electronic Health Record Cohort. Obesity (Silver Spring). 2019 Apr;27(4):591-602. doi: 10.1002/oby.22430. PMID: 30900410.

Larlene Dunsmuir, 2025-02-15T00:15:33.868

JR0 0 Added as a 2nd reference

Jill Racicot, 2025-02-25T07:33:36.165

Orlistat

- Advise patients
  - Nutritionally balanced, reduced-calorie diet; approximately 30% of calories from fat
  - Take a multivitamin containing fat-soluble vitamins at bedtime.

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Orlistat

- Contraindications and warnings
  - Contraindications
    - Pregnancy, chronic malabsorption syndrome, cholestasis
  - Warnings
    - Decrease cyclosporine exposure; rare cases of severe liver injury, increased levels of urinary oxalate
  - Adverse effects
    - Oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, oily evacuation, increased defecation and fecal incontinence

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Orlistat

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D0

Orlistat Plus Lifestyle Intervention for the Prevention of T2DM in Obese Patients

Four-year randomized placebo-control trial of 3,305 obese patients

https://diabetesjournals.org/care/article/27/1/155/26587/XENical-in-the-Prevention-of-Diabetes-in-Obese

DPP, Diabetes Prevention Program; T2DM, type 2 diabetes.

Torgerson JS, Hauptman J, Boldrin MN, Sjöström L. (2004). XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. Figure 2., Diabetes Care, 27(1):155-61.

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Orlistat Plus Lifestyle Intervention for the Prevention of T2DM in Obese Patients[20]

- Four-year randomized placebo-control trial of 3,305 obese patients
  - "DPP-type" intervention: Patients lost 3.0 kg
  - Orlistat + "DPP- type" intervention: Patients lost 5.8 kg

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Recently Approved Pharmacotherapies

Agent	Mechanism	Approval	Comments
Lorcaserin **Pulled from Market**	Specific 5-HT_{2C} (serotonin) receptor agonist	Approved June 2012 DEA Schedule IV	Generally well tolerated, not recommended in patients with severe or end-stage renal impairment
Phentermine/ Topiramate ER	Sympathomimetic Anticonvulsant (GABA receptor modulation, carbonic anhydrase inhibition, glutamate antagonism)	Approved July 2012 DEA Schedule IV	Requires dose titration; contraindicated in glaucoma; not recommended with history of kidney stones

DEA=Drug Enforcement Agency.

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LD0 Would this work?

Oh TJ. The Role of Anti-Obesity Medication in Prevention of Diabetes and Its Complications. J Obes Metab Syndr. 2019 Sep;28(3):158-166. doi: 10.7570/jomes.2019.28.3.158. Epub 2019 Mar 30. PMID: 31583380; PMCID: PMC6774449.

Larlene Dunsmuir, 2025-02-15T00:27:15.960

LD0 0 And, could it work for the next slide also?

Larlene Dunsmuir, 2025-02-15T00:44:44.063

JR0 1 Per Wendy - classic since it's a trial study

Jill Racicot, 2025-02-25T07:34:33.064

Phentermine/Topiramate ER

- Indication
  - BMI of ≥30 kg/m^2 (obese), or ≥27 kg/m^2 (overweight) with at least 1 weight-related comorbid condition (e.g., HTN, dyslipidemia, type 2 diabetes)
  - Approved for 12 years of age and older
- Dosing
  - Phentermine 3.75 mg/topiramate 23 mg extended-release daily for 14 days then increase to 7.5 mg/ 46 mg daily. Maximum dose is 15 mg/92 mg.
  - Discontinue if 5% weight loss is not achieved after 12 weeks on maximum daily dose of 15 mg/ 92 mg.

Extended release (ER)

Phentermine/Topiramate ER (Qsymia®). (2022). Prescribing information. https://qsymia.com/patient/include/media/pdf/prescribing-information.pdf

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Phentermine/Topiramate ER

- Contraindications
  - Pregnancy (Category X), glaucoma, hyperthyroidism, during or within 14 days of taking MAOIs

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Phentermine/Topiramate ER

- Warnings
  - Fetal toxicity
  - Increased heart rate
  - Suicide, mood and sleep disorders
  - Acute myopia and glaucoma
  - Cognitive impairment
  - Metabolic acidosis
  - Creatinine elevations
  - Hypoglycemia with diabetes meds
- Voluntary REMS program in place; pregnancy testing for those of childbearing potential advised before and during use

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Phentermine/Topiramate ER

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Phentermine/Topiramate ER on Weight Loss at 2 Years

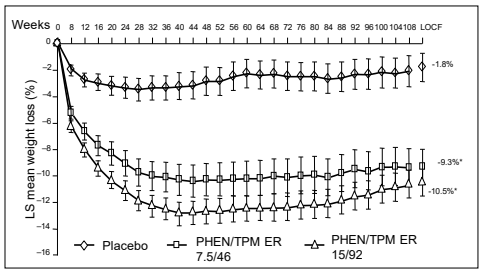

Image source: Used with permission from Wendy Wright.

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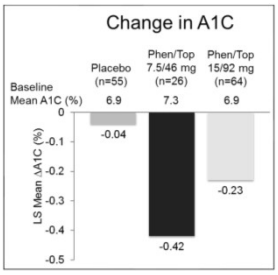
Effects of Phentermine/Topiramate ER in Patients with T2DM: Two Years of Treatment



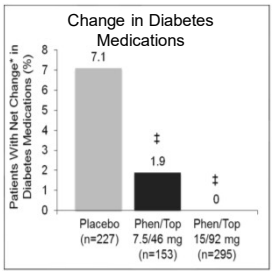


Image source: Used with permission from Wendy Wright.

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Phentermine/Topiramate ER: Most Commonly Reported Adverse Events21

Adverse Event (%) (N=3879)	Placebo	Phen/Top ER 7.5/46 mg
Paresthesia	1.9	13.7
Dry mouth	2.8	13.5
Constipation	6.1	15.1
Dysgeusia	1.1	7.4
Insomnia	4.7	5.8
Dizziness	3.4	7.2
Nausea	4.4	3.6

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Naltrexone ER/Bupropion ER

- Brand name – Contrave®
- Indication – Obesity
- Mechanism of action
  - Pro-opiomelanocortin (POMC) receptors in hypothalamus which is believed to regulate appetite
  - Mesolimbic dopamine circuit which is believed to control reward pathways associated with eating

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Naltrexone ER/Bupropion ER

- Dose: 8 mg/90 mg
- Titration
  - 1-pill in AM × 1-week, 1-pill BID × 1-week, 2 pills in AM and 1 in PM × 1 week, 2 pills BID
  - Take in the morning and evening.
  - Do not crush or chew.

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Naltrexone ER/Bupropion ER

- Efficacy
  - 43% vs. 17% lost 5% or more of body weight
  - 21% vs. 7% lost 10% or more of body weight
  - 0.6% decrease in A1C vs. 0.1% decrease in placebo group (individuals with Type 2 diabetes)
- Adverse effects
  - Nausea: 32.5% vs. 6.7%
  - Constipation: 19.2% vs. 7.2%
  - Headache: 17.6% vs. 10.4%

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Naltrexone ER/Bupropion ER

- Recommendations
  - Start slower than titration dose recommends.
  - Take more than 1-month to get to maximum dosage.
- Contraindications
  - Seizure disorders, anorexia or bulimia
  - Uncontrolled hypertension
  - Chronic opioids
  - MAOIs
  - Pregnancy

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Naltrexone ER/Bupropion

- Drug/drug interactions
  - Opioids: Blocks mu receptor sites
  - Other drugs metabolized by CYP2D6
- Drugs metabolized by CYP2D6
  - Bupropion inhibits CYP2D6 and can increase concentration of…
    - Antidepressants (e.g., selective serotonin reuptake inhibitors and many tricyclics)
    - Antipsychotics (e.g., haloperidol, risperidone, and thioridazine)
    - Beta-blockers (e.g., metoprolol)
    - Type 1C antiarrhythmics (e.g., propafenone and flecainide)

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Naltrexone ER/Bupropion ER

- Warnings
  - Monitor BP. Systolic BP rose 1–2 mm in clinical trials.
  - Monitor for suicidal ideations.
  - Can cause false positive drug test for amphetamines
- Advantage
  - Not scheduled (no DEA required)
- Cost
  - $70.00 × 2 months then $60.00 thereafter

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Liraglutide

- Brand name: Saxenda®
- Dosage: 3 mg daily
- Indication: Obesity
  - BMI: 30 kg/m^2 or higher or 27 kg/m^2 with obesity related comorbidity
  - Approved for ages 12 years and older: >60 kg
  - Start at 0.6 mg/day once weekly; increase by 0.6 mg/day once weekly.
- Mechanism of action: GLP-1R agonist
- Adverse effects: Nausea

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Liraglutide

- Efficacy
  - 62% of patients treated with liraglutide lost at least 5% of their body weight vs. 34% percent of patients treated with placebo.
  - Individuals with Type 2 diabetes had an average weight loss of 3.7% from baseline vs. placebo.
  - 49% of patients treated lost at least 5% of their body weight compared with 16% of patients treated with placebo.

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Liraglutide

- Evaluate patient at week 16.
  - If patient has not lost 4% or more of body weight, can consider discontinuation of drug.
- Carries all same warnings as liraglutide (Victoza®)
  - Medullary thyroid carcinoma
  - Pancreatitis
- Associated with a REMS program
  - As was/ is case with liraglutide (Victoza®)

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Liraglutide

- Now available in generic formulations
- Two manufacturers have received approval

https://www.managedhealthcareexecutive.com/view/fda-approves-first-once-daily-generic-of-victoza-for-type-2-diabetes

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Semaglutide

- Semaglutide (Wegovy®)
- Class: GLP-1 agonist; injectable
- Indication: BMI 30 kg/m^2 or greater or 27.0 kg/m^2 or higher with comorbidity
  - Approved 12 years of age and older
- Dose: 0.25 mg once weekly × 4 weeks; then 0.50 mg once weekly × 4 weeks; 1.0 mg once weekly × 4 weeks; 1.7 mg once weekly × 4 weeks; then a maximum of 2.4 mg once weekly

Semaglutide (Wegovy®). (2022). Prescribing information. https://www.novo-pi.com/wegovy.pdf

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WW0 https://www.managedhealthcareexecutive.com/view/fda-approves-t
Wendy Wright, 2025-01-05T13:34:54.727

Semaglutide

- Newest indication:
  - to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease and either obesity or overweight
  - CMS has announced coverage of semaglutide for a patient meeting the above criteria

WW0

https://www.novo-pi.com/wegovy.pdf

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Semaglutide

- Carries same warnings and precautions as GLP-1 agonists
- Okay in individuals with CKD
- Efficacy
  - 3 double-blinded placebo-controlled trials; 2116 patients; Up to 68 weeks
  - Percent of patients losing ≥5% of body weight (31.1 vs. 83.5; 30.2 vs. 67.4; 47.8 vs. 84.8)
  - Percent of patients losing ≥10% of body weight (12.0 vs. 66.1; 10.2 vs. 44.5; 27.1 vs. 73.0)

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Semaglutide

- Adverse effects
  - Nausea (44% vs. 16%)
  - Diarrhea (30% vs. 16%)
  - Vomiting (24% vs. 6%)
  - Constipation (24% vs. 11%)

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WW0 https://www.novo-pi.com/wegovy.pdf
Wendy Wright, 2025-01-05T13:38:50.227

Tirzepatide

- Tirzepatide (Zepbound™)
- Glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:
  - 30 kg/m^2 or greater (obesity) or
  - 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes mellitus, obstructive sleep apnea or cardiovascular disease)

https://uspl.lilly.com/zepbound/zepbound.html#pi accessed 01-13/2024

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Tirzepatide

- Newest indication:
  - Moderate – severe obstructive sleep apnea in adults with obesity
  - Trial: SURMOUNT-OSA
    - Trial: 65%-70% of participants had severe OSA
    - Average: more than 30 events/h on the apnea-hypopnea index (AHI) and a mean of 51.5 events/h.
    - 52 weeks: tirzepatide patient had 27-30 fewer events/h compared with 4-6 fewer events/h for those taking placebo.
    - Significantly more of those on tirzepatide achieved OSA remission or severity reduction to mild.
    - Tirzepatide: averaged 20% weight loss

https://www.medscape.com/viewarticle/obesity-drug-zepbound-approved-obstructive-sleep-apnea-2024a1000p20

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Tirzepatide

- Class: GIP/GLP-1 agonist
  - Works by increasing insulin secretion, decreasing glucagon secretion, increasing insulin sensitivity and delaying gastric emptying
- 3 doses available (5 mg, 10 mg, and 15 mg)
- Injected once weekly

https://uspl.lilly.com/zepbound/zepbound.html#pi accessed 01-13/2024

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WW0 https://www.medscape.com/viewarticle/obesity-drug-zepbound-ap
Wendy Wright, 2025-01-05T13:30:32.208

Tirzepatide

- Class: GIP/GLP-1 agonist (cont.)
  - Dosing
    - 2.5 mg SC once weekly × 4 weeks; then 5 mg once weekly × 4 weeks; then 7.5 mg once weekly × 4 weeks; then 10 mg once weekly × 4 weeks; then 12.5 mg once weekly × 4 weeks
    - Maximum: 15 mg once weekly
    - Administer any time of the day with or without regard to food
    - If dose is missed, patient has up to 96 hours to administer the dose; otherwise, should skip and administer next time the dose is due

https://uspl.lilly.com/zepbound/zepbound.html#pi accessed 01-13/2024

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Tirzepatide

- Clinical trials/efficacy:
  - Study 1 and Study 2
  - Average baseline weight: 100 – 105 kg
  - Study 1:
    - 5% weight reduction (15 mg): 90.9%
    - 10% weight reduction (15 mg): 83.5%
    - 15% weight reduction (15 mg): 70.6%
    - 20% or more weight reduction (15 mg): 56.7%

https://uspl.lilly.com/zepbound/zepbound.html#pi accessed 01-13/2024

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Tirzepatide

- Clinical trials/efficacy at 72 weeks:
  - Study 1 and Study 2
  - Average baseline weight: 100 – 105 kg
  - Study 2 (Patients also had diabetes):
    - 5% weight reduction (15 mg): 82.8%
    - 10% weight reduction (15 mg): 64.8%
    - 15% weight reduction (15 mg): 48.0%
    - 20% or more weight reduction (15 mg): 30.8%

https://uspl.lilly.com/zepbound/zepbound.html#pi accessed 01-13/2024

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Tirzepatide

- Precautions/warnings
  - No hepatic and renal dosing adjustments
  - Caution: History of gastroparesis or pancreatitis
  - Caution when adding to medications with narrow therapeutic index
  - Do not use in pregnancy; no data on impact in lactation

- Contraindications
  - Patients with medullary thyroid carcinoma or family history of such
  - Patients with multiple endocrine neoplasia syndrome

https://uspl.lilly.com/zepbound/zepbound.html#pi accessed 01-13/2024

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Contraception

- Advise females using oral contraceptives to switch to a non-oral contraceptive method or add a barrier method of contraception for 4 weeks after initiation and for 4 weeks after each dose escalation

https://uspl.lilly.com/zepbound/zepbound.html#pi accessed 01-13/2024

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Tirzepatide

- Adverse reactions (placebo, 5 mg, 10 mg, and 15 mg)
  - Nausea: (8%, 25%, 29%, 28%)
  - Diarrhea: (8%, 19%, 21%, 23%)
  - Vomiting: (2%, 8%, 11%, 13%)
  - Constipation: (5%, 17%, 14%, 11%)
- Cost: Approximately 1,400 for 4 weeks
  - Numerous copay cards are available online.

https://uspl.lilly.com/zepbound/zepbound.html#pi accessed 01-13/2024

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Recent Study

- Surmount 5
  - Patients lost an average of 20.2% of their weight with tirzepatide over 72 weeks versus 13.7% with semaglutide.

https://www.prnewswire.com/news-releases/lillys-zepbound-tirzepatide-superior-to-wegovy-semaglutide-in-head-to-head-trial-showing-an-average-weight-loss-of-20-2-vs-13-7-302322351.html Accessed 12-08-2024

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What else can you offer individuals if cost or insurance is an issue?

- Consider
  - Metformin (Glucophage®)
  - Liraglutide (Victoza®)
  - Semaglutide (Ozempic®, Rybelsus®)
  - Topiramate (Topamax®)

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Non-Systemic Hydrogel (Plenity®)

- Biodegradable oral non-systemic hydrogel which promotes fullness and may help to increase satiety to help with weight management.
- The capsules disintegrate in the stomach and release the enclosed hydrogel particles, which can then hydrate up to 100 times their original weight.
- When fully hydrated, the individual non-clustering hydrogel particles occupy about a quarter of average stomach volume.

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Non-Systemic Hydrogel (Plenity)

- The gel particles mix with ingested foods, creating a larger volume with higher elasticity and viscosity in the stomach and small intestine, promoting satiety and fullness.
- The hydrogel particles are partially degraded enzymatically in the colon, releasing most of the absorbed water, and subsequently being excreted in the feces.
- Regulated by the FDA as a class II medical device because it acts through mechanical modes of action.

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Case Study

- BMI: 34.2 kg/m^2
- BP: 118/84 mm Hg
- P: 90 bpm
- HEENT: Unremarkable

- Lungs: Clear
- Heart: S1S2; RRR
- PV: Unremarkable

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What medication would you consider?

What options do you have with her?

- Orlistat
- Phentermine
- Phentermine/topiramate
- Naltrexone ER/bupropion ER

- Liraglutide
- Semaglutide
- Tirzepatide

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Clinical implications

- Develop a workflow
  - NP identifies candidate
  - Patient calls insurance to see if the products are covered
    - We do this before we prescribe
  - Patient is booked with RN asap for instructions/teaching
  - Patient is then seen by NP generally at 1 month
  - Depending upon agent, continue monthly x 3 months then every 3 months
  - 3-4 months is the important visit: this is generally when decisions are made if this drug is helpful

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DO

Dietary Supplements for Weight Loss – A Systematic Review

- Five systematic reviews and meta-analyses, + 25 trials reviewed on the following…
  - Chitosan, chromium picolinate, Ephedra sinica, garcinia cambogia, glucomannan, guar gum, hydroxy-methylbutyrate, plantago psyllium, pyruvate, yerba maté, yohimbine
- Results: Evidence for reducing body weight is not convincing. None of the supplements reviewed can be recommended for OTC use.

Pittler, M.H., Ernst E. (2004). Dietary supplements for body-weight reduction: a systematic review. Am J Clin Nutr., 79(4):529-36. https://pubmed.ncbi.nlm.nih.gov/15051593/
Batsis, J. A., Apolzan, J. W., Bagley, P. J., Blunt, H. B., Divan, V., Gill, S., Golden, A., Gundumraj, S., Heymsfield, S. B., Kahan, S., Kopatsis, K., Port, A., Parks, E. P., Reilly, C. A., Rubino, D., Saunders, K. H., Shean, R., Tabaza, L., Stanley, A., Tchang, B. G., … Kidambi, S. (2021). A Systematic Review of Dietary Supplements and Alternative Therapies for Weight Loss. Obesity (Silver Spring, Md.), 29(7), 1102–1113. https://doi.org/10.1002/oby.23110

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“Questions?”

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Slide 86

LD0 Would this article work as a current option?

Batsis JA, Apolzan JW, Bagley PJ, Blunt HB, Divan V, Gill S, Golden A, Gundumraj S, Heymsfield SB, Kahan S, Kopatsis K, Port A, Parks EP, Reilly CA, Rubino D, Saunders KH, Shean R, Tabaza L, Stanley A, Tchang BG, Gundumraj S, Kidambi S. A Systematic Review of Dietary Supplements and Alternative Therapies for Weight Loss. Obesity (Silver Spring). 2021 Jul;29(7):1102-1113. doi: 10.1002/oby.23110. PMID: 34159755; PMCID: PMC8231729.

Larlene Dunsmuir, 2025-02-15T00:56:55.372

JR0 0 Added as a 2nd reference

Jill Racicot, 2025-02-25T07:38:47.849

End of Presentation
Thank you for your time and attention.

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