UTAH SOCIETY OF
HEALTH-SYSTEM PHARMACISTS

Weigh to go! Updates in weight loss medications

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Disclosure

- **Relevant Financial Conflicts of Interest**
  - **CE Presenter, Adalie Tchividjian, PharmD:**
    - None
  - **CE mentor, Samantha Leonard, PharmD, BCPS:**
    - None
- **Off-Label Uses of Medications**
  - Metformin - Drug-induced obesity
  - Topiramate - binge eating disorder, drug-induced weight gain
  - Lorcaserin + phentermine - weight loss
  - Zonisamide - binge eating disorder
  - Tirzepatide, dulaglutide, semaglutide, liraglutide (GLP-1s) - obesity
  - Dapagliflozin, empagliflozin, canagliflozin (SGLT2) - weight loss

Pharmacist Learning Objectives

1. Analyze the risks and benefits of medications used for weight management
2. List the common additional indications for medications used for weight loss
3. Evaluate which patients are candidates for weight loss medications
4. Propose medication plan for weight management

Technician Learning Objectives

1. Define obesity
2. Distinguish medications that can be used for weight management
3. Recognize brand and generic names for medications used for weight loss

Introduction

Obesity Defined

Weight that is higher than what is considered healthy for a given height

$$BMI = \frac{weight\ (kg)}{height\ (m^2)}$$

BMI (kg/m²)	Weight Range
<18.5	Underweight
18.5 to <25	Healthy Weight
25 to < 30	Overweight
≥ 30	Obesity
30 to < 35	Obesity: Class 1
35 to < 40	Obesity: Class 2
40 or higher	Obesity: Class 3 (Severe)

Throughout the presentation, BMI will not include the kg/m² unit indicator

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Screening for Obesity

- BMI
- Body fat measurement
  - Waist circumference
    - Often used for patients with BMI ≥ 35 to assess cardiometabolic risk
  - Dual-energy X-ray absorptiometry (DEXA)
  - Bioelectrical impedance

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The Controversy of BMI

- As an indirect measure of obesity, BMI does not take into account age, sex, fat distribution, or muscle mass
  - For example, athletes with high muscle mass will have high BMI scores
- A 2001 study that compared BMI to DEXA scan results (X-Ray body scan that provides measurement of body fat, muscle mass, and bone health) showed:
  - 7% of women and 8% of men were incorrectly classified as obese using BMI
  - 32% of women and 41% of men had false-negative results using BMI

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Assess for Contributing Factors

- Comorbid conditions
  - Psychological
    - Depression/Anxiety/Trauma
    - Eating disorders
  - Endocrine Disorders
    - Hypothyroidism
    - Hypercortisolism (i.e. Cushing's disease)
    - Insulin Resistance due to Polycystic Ovarian Syndrome (PCOS)
- Diet
- Physical inactivity
- Sedentary lifestyle
- Medications*

Medications that can cause weight gain

Antipsychotics
Olanzapine, quetiapine, risperidone

Antidepressants
Mirtazapine, SSRIs (paroxetine, sertraline, escitalopram)
TCAs (amitriptyline, nortriptyline)

Antiepileptics
Gabapentin, valproic acid, lithium

Antihyperglycemics
Insulin, sulfonylureas, thiazolidinediones

Beta-blockers
Metoprolol, atenolol, propranolol

Glucocorticoids
Prednisone, methylprednisolone

Hormonal Agents
Medroxyprogesterone IM

Obesity-Associated Medical Conditions

- Overweight and obesity is linked with an increased risk of chronic health conditions, reduced quality of life, and earlier mortality
- Increased prevalence of:
  - Type 2 diabetes (T2DM)
  - Hypertension
  - Dyslipidemia
  - Metabolic syndrome
  - Osteoarthritis
  - Obstructive sleep apnea
  - Non-alcoholic fatty liver disease (NAFLD)

Shared Decision Making

- Ask permission to discuss weight-related topics
- Educate patient on risks of obesity and benefits of weight management
- Provide information in a manner that is tailored to patient's health literacy
- Use teach-back method

Patient must be agreeable to weight management measures

Educate on Risks of Obesity

	HbA_{1c}	fasting BG (mg/dL)
Diabetes	≥6.5%	≥126
Pre-Diabetes	5.7-6.4%	100-125
Normal	<5.7%	<100

CV RISK

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Non-Pharmacologic Management

Nutrition

Recommend Nutritional Consult

Educate:

- Nutrient dense foods
  - Whole grain (low glycemic index)
  - Eat carbohydrates with protein
  - Fresh fruits/veggies
  - Lean meats
  - Protein
  - High fiber
  - Low saturated fats

Limit alcohol and sugary beverages

MAKE SUSTAINABLE CHANGES

Physical Activity

joyful movement

Encourage patients to find ways of exercising that make them happy

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How Much?

Vigorous 75-150 min/week

Aerobic 150-300 min/week

Muscles 2x/week

What are your favorite ways to exercise your body?

Surgical Management

Bariatric Surgery vs. Cosmetic Procedures

Indications for Bariatric Surgery

American Society for Metabolic and Bariatric Surgery (ASMBS):

- BMI ≥ 35 regardless of presence of comorbidities
- BMI 30-34.9 with T2DM or cannot achieve weight loss with nonsurgical methods

Procedures

- Sleeve Gastrectomy
- Roux-en-Y Gastric Bypass
- Biliopancreatic diversion/Duodenal Switch
- Single Anastomosis Duodeno-ileostomy with Sleeve
- Intragastric Balloons
- One Anastomosis Gastric Bypass
- Adjustable Gastric Banding

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Post-Operative Management

- Slowly progress from liquid diet to soft solid foods to solid foods over the course of ~ 6 weeks
- Adequate fluid intake
- Emphasis on protein intake and limit of simple carbohydrates
- Micronutrient supplementation
  - Multivitamin
  - Vitamin B12
  - Vitamin C
  - Calcium
  - Iron
- Restricted activity for ~ 1 month following operation

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Complications

- Anastomotic leak
- Stenosis
- Bleeding
- Venous thromboembolism
- Small bowel obstruction
- Perforation
- Internal hernia
- Gallstone disease

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Outcomes

- Greater long-term weight loss than non-surgical management
- T2DM
  - Glycemic control
  - Remission
  - Reduction of microvascular and macrovascular risks
- Hypertension
  - Less medication needed for BP control
  - Remission
- Short and long term improvement of dyslipidemia
- Improves severity of sleep apnea

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Outcomes

- A 2023 study compared mortality of bariatric surgery patients vs non-surgery patients with a follow-up up to 40 years
  - All cause mortality
    - 16% lower in surgery group ($p < 0.001$)
  - Cause-specific mortality
    - Cardiovascular disease: Decreased by 29% ($p < 0.001$)
    - Cancer: Decreased by 43% ($p < 0.001$)
    - Diabetes: Decreased by 72% ($p < 0.001$)

Pharmacologic Management

Who qualifies for weight loss medications?

Patients with BMI ≥30

Patients with BMI ≥27 **and** an obesity-related comorbidity*

Lipase Inhibitor

ORLISTAT

MOA: Inhibits absorption of dietary fat by inhibiting gastric and pancreatic lipases

Orlistat

Brand Names	Alli®(OTC), Xenical® (Rx)
Indication	Approved for chronic weight management
Dose	OTC: 60 mg PO TID with meals RX: 120 mg PO TID with meals
Contraindications	Cholestasis, chronic malabsorption syndrome, pregnancy
Adverse Effects	Increased frequency and urgency of defecation, steatorrhea

- If taken with meal >30% fat, ↑ GI ADEs
- Take a daily multivitamin – separate from medication by at least 2 hours

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CNS Stimulant

PHENTERMINE, DIETHYLPROPION

MOA: Reduces appetite secondary to CNS effects, stimulates hypothalamus to release norepinephrine

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Phentermine

Brand Names	Adipex-P®, Lomaira® (Rx; C-IV)
Indication	Approved for short-term use (3 months) for: • BMI ≥ 30 or • ≥ 27 with an obesity related comorbidity
Dose	15 mg to 37.5 mg PO daily
Contraindications	(many) CV disease, history of drug abuse, pregnancy, MAOI use
Adverse Effects	Cardiac effects, CNS effects

- Individualize to achieve adequate response with lowest effective dose
- Take dose 30 minutes before breakfast (stimulant)
- Often combined with other weight loss medications (off-label)
- ISMP high-alert medication

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Diethylpropion

Brand Name	Tenuate® (Rx; C-IV)
Indication	Approved for short-term use (3 months) for: • BMI ≥ 30 or • ≥ 27 with an obesity related comorbidity
Dose	IR: 25 mg PO TID before meals +/- bedtime dose PRN ER: 75mg PO daily midmorning
Contraindications	Severe hypertension, glaucoma, history of drug abuse
Adverse Effects	Cardiac, CNS effects

- Should be prescribed in low quantities to minimize overdose possibility
- Discontinue if weight loss has not occurred within 4 weeks

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Antiseizure

TOPIRAMATE, ZONISAMIDE

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Topiramate

Brand Name	Topamax®
Indication	OFF LABEL: Monotherapy off-label for binge eating disorder and antipsychotic-induced weight gain
Mechanism of Action	Blocks Na+ channels, enhances GABA, etc. Mechanism for weight loss unclear
Dose	Initial 25mg or 50mg PO per day, increase weekly based on response and tolerability UP TO 400 mg/day
Adverse Effects	CNS effects, metabolic acidosis, kidney stones

- Must be renally dose-adjusted
- Nicknamed "dopamax" due to causing cognitive dysfunction
- Can cause birth defects if taken while pregnant
- Taper 25 mg/day increments weekly to discontinue

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Zonisamide

Brand Name	Zonegran®
Indication	Off-label: for binge-eating disorder
Mechanism of Action	Blocks Na and Ca channels Mechanism for weight loss unclear
Dose	100 mg PO daily x 7 days, increase weekly based on response and tolerability UP TO 600 mg/day
Contraindications	Sulfa allergy
Adverse Effects	CNS effects, GI effects

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CNS Stimulant + Antiseizure

PHENTERMINE/TOPIRAMATE

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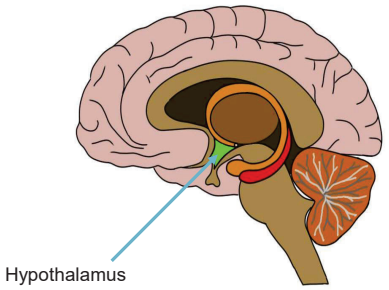
Mechanism of Action

Qsymia® increases norepinephrine, dopamine, and serotonin in the hypothalamus causing fullness, decreased appetite, and decreased cravings.



Phentermine/Topiramate

Brand Name	Qsymia® (Rx; C-IV)
Indication	Approved for chronic weight management
Dose	3.75/23 mg PO daily x 14 days, increase to 7.5/46 mg PO daily for 12 weeks then evaluate weight loss
Contraindications	Pregnancy, history of drug abuse
Adverse Effects	Dry mouth, upper respiratory infection, insomnia

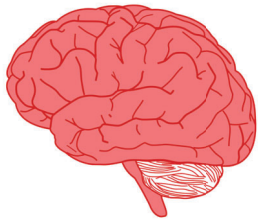
CLINICAL PEARLS

- Discontinue if patient hasn't lost 5% after 12 weeks at maintenance dose
- Take in the morning to avoid insomnia
- Avoid alcohol and drink lots of fluids
- Gradually discontinue (1 dose every other day for at least a week)
- REMS program

Opioid Antagonist + Antidepressant

NALTREXONE/BUPROPION

Mechanism of Action



Mesolimbic Reward System
Involved with feeling pleasure during rewarding experiences (i.e. eating), leading to cravings

Hypothalamus
Drives the urge to eat when activated

Naltrexone/Bupropion

Brand Names	Contrave®
Indication	Approved for chronic weight management
Dose	8/90 mg PO QAM x 7 days, escalate dose every 7 days to maintenance dose of 2 tabs BID
Contraindications	Acute opioid withdrawal, seizure disorder
Adverse Effects	Suicidal ideation, constipation, nausea/vomiting

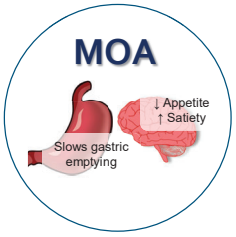
CLINICAL PEARLS

- Discontinue if patient hasn't lost 5% after 12 weeks at maintenance dose
- Bupropion sometimes used as monotherapy off-label

GLP-1 Receptor Agonist

LIRAGLUTIDE, SEMAGLUTIDE, EXENATIDE, TIRZEPATIDE, DULAGLUTIDE

GLP-1 Agonists: Brand/Generic



LIRAGLUTIDE	Saxenda® (Weight Loss) Victoza® (T2DM)
SEMAGLUTIDE	Wegovy® (Weight Loss) Ozempic® (T2DM) Rybelsus® (PO; T2DM)
EXENATIDE	Bydureon® (T2DM) Byetta® (T2DM) **Off-label: Weight Loss
DULAGLUTIDE	Trulicity® (T2DM) **Off-label: Weight Loss
TIRZEPATIDE*	Mounjaro® (T2DM) **Off-label: Weight Loss

*Type 2 Diabetes Mellitus = T2DM

GLP-1 Agonists: Dosing

LIRAGLUTIDE

Saxenda® (Weight Loss)
0.6 mg subq daily x 7 days, escalate dose every week to maintenance dose of 3mg subq daily

Victoza® (T2DM)
OFF LABEL*: 0.6 mg subq daily x 7 days, escalate dose every week to maintenance dose of 1.8mg subq daily

SEMAGLUTIDE

Wegovy® (Weight Loss)
0.25 mg subq weekly x 4 weeks, escalate dose every 4 weeks to maintenance dose 2.4 mg subq weekly

Ozempic® (T2DM)
OFF LABEL*: 0.25 mg subq weekly x 4 weeks, escalate dose every 4 weeks to maintenance dose 2 mg subq weekly

Rybelsus® (PO; T2DM)
OFF LABEL**: 3mg PO daily x 30 days, escalate dose every 30 days to maintenance dose of 14mg

*OFF LABEL FOR WEIGHT LOSS
**OFF LABEL FOR WEIGHT LOSS, BUT IN PHASE 3 TRIALS FOR THIS INDICATION
Images from proprietary websites: Saxenda.com and Wegovy.com – websites also contain videos on how to administer medication

GLP-1 Agonists: OFF LABEL Dosing

EXENATIDE

Byetta® (T2DM)
IMMEDIATE RELEASE: 5mg subq TWICE daily, may escalate dose to 10mg after one month if needed

Bydureon BCise® (T2DM)
EXTENDED RELEASE: 2mg subq weekly

DULAGLUTIDE

Trulicity® (T2DM)
0.75mg subq weekly, may escalate dose to 1.5mg after 4-8 weeks if needed

TIRZEPATIDE*

Mounjaro® (T2DM)
2.5 mg subq weekly x 4 weeks, escalate dose every 4 weeks to maintenance dose 15 mg subq weekly

Tirzepatide Clinical Study

Tirzepatide Once Weekly for the Treatment of Obesity[20]

Study Details

- Multicenter, double-blind randomized placebo-controlled trial
- Inclusion criteria:
  - BMI ≥ 30 or
  - BMI ≥ 27 and at least one weight-related complication (hypertension, dyslipidemia, OSA, cardiovascular disease)
  - Reported one or more unsuccessful dietary effort to lose weight
- 2539 participants

Results

	Result	P Value
Percentage change in body weight from baseline to week 72	Tirzepatide, 5 mg: -15.0 % Tirzepatide, 10 mg: -19.5 % Tirzepatide, 15 mg: -20.9 % Placebo: -3.1 %	P<0.001
Weight reduction of 5% or more at week 72	Tirzepatide, 5 mg: 85.1 % Tirzepatide, 10 mg: 88.9 % Tirzepatide, 15 mg: 90.9 % Placebo: 34.5 %	P<0.001

Adverse events: nausea, diarrhea, abdominal pain, vomiting

Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide Once Weekly for the Treatment of Obesity. *N Engl J Med*. 2022;387(3):205-216. doi:10.1056/NEJMoa2206038

GLP-1 Agonists: Contraindications/Adverse Effects

Contraindications
- History of pancreatitis
- Pregnancy
- Thyroid Tumors:
  - Medullary thyroid carcinoma (MTC) - thyroid C-cell tumors
  - Multiple endocrine neoplasia syndrome type 2 (MEN 2)

Adverse Effects
- Gastrointestinal
- Pancreatitis

GLP-1 Agonists: Administration

Subcutaneous administration
- Upper arm | Abdomen | Thigh
- Clean injection site with alcohol swab
- Depending on brand, pens can be single-use or multi-dose

Oral administration (Semaglutide - Rybelsus®)
- 1% bioavailable – take 30 minutes before ANYTHING else and with only <4 oz water

GLP-1 Agonists: Clinical Pearls

- Must use birth control while on a GLP-1
  - Stop using GLP-1 for 2 months before planning on becoming pregnant
  - Tirzepatide: May reduce efficacy of oral hormonal contraceptives due to delayed gastric emptying
- Consider discontinuation if 5% of baseline weight not lost within 3 months
- Administer missed weekly dose ASAP within 5 days
- Do not use with DPP4-inhibitors
- Can use with low $HbA1_c$ (doesn't cause hypoglycemia)
- In patients who do not tolerate a dosage increase, may consider delaying the increase for an additional 4 weeks

SGLT-2 Inhibitors

DAPAGLIFLOZIN, EMPAGLIFLOZIN, CANAGLIFLOZIN

MOA: Sodium-glucose co-transporter 2 inhibitor, promotes renal excretion of glucose

SGLT-2 Inhibitors

DAPAgliflozin	Farxiga® T2DM, Heart Failure, Chronic Kidney Disease (CKD)
EMPAgliflozin	Jardiance® T2DM, Heart Failure
CANAgliflozin	Invokana® T2DM

CLINICAL PEARLS

- Do not use if GFR < 30:
  - empagliflozin
  - canagliflozin
- Do not use if GFR < 45:
  - dapagliflozin
- Try to avoid if A1C > 10%

Dose	Dose for weight management not defined (off-label)
Contraindications	Dialysis
Adverse Effects	Diuresis, vulvovaginal candidiasis, diabetic ketoacidosis

Used for weight management **OFF LABEL

Sodium-Glucose Co-Transporter-2 Inhibitors in Non-Diabetic Adults With Overweight or Obesity[23]

Study Details

- Systematic review and meta-analysis
- Inclusion criteria:
  - RCTs
  - Overweight/obese adults without diabetes
  - SGLT2 inhibitor as monotherapy and placebo as control
  - Standardized diet and physical activity advice
  - Reporting body weight and BMI as primary outcome
- 6 studies; 872 participants

Results

	Result	P Value
Body weight change (SGLT2 vs placebo)	MD: 1.42 kg 95% CI: -1.70 to -1.14	P<0.00001
BMI change (SGLT2 vs placebo)	MD: -0.47 kg/m² 95%CI: -0.63 to -0.31	P<0.00001

Adverse events: SGLT2 inhibitors treatment suffered more genital/vulvovaginal mycotic infection and nausea

Miscellaneous

METFORMIN, PRAMLINITIDE, METRELEPTIN

Metformin

Brand Name	Glucophage®, Glumetza®
Indication	T2DM Off-label: Drug-induced obesity
Mechanism of Action	• Decreases hepatic glucose production, intestinal absorption of glucose, and improves insulin sensitivity • Decreases appetite
Dose	IR: 750 mg to 2 g PO daily in 2 divided doses ER: 1 g to 2 g PO daily
Contraindications	Diabetic ketoacidosis, lactic/metabolic acidosis, renal failure
Adverse Effects	Gastrointestinal effects, lactic acidosis, vitamin B12 deficiency

CLINICAL PEARLS

- Increase dose slowly to reduce GI effects
- Do not use if GFR < 30

Pramlintide

Brand Name	SymlinPen®
Indication	Type 1 and T2DM Off-label: weight management
Mechanism of Action	Prolongs gastric emptying, reduces postprandial glucagon secretion, centrally-mediated appetite suppression
Dose	Dose for weight management not defined (off-label)
Contraindications	Gastroparesis
Adverse Effects	Severe hypoglycemia

CLINICAL PEARLS

- Subcutaneous injection usually given before each major meal
- Ensure to counsel patient on signs, symptoms, and treatment of hypoglycemia

Metreleptin

Brand Name	Myalept®
Indication	Lipodystrophy Off-label: weight management
Mechanism of Action	• Recombinant human leptin analog that binds to/activates human leptin receptor • Reduces food intake
Dose	Dose for weight management not defined (off-label)
Adverse Effects	Anti-metreleptin antibody development, lymphoma

CLINICAL PEARLS

- Subcutaneous injection, patient must draw dose out of vial
- REMS program

Current Trials

- Rybelsus (oral semaglutide)
- CagriSema (cagrilintide/semaglutide)
- Ecnoglutide
- Mazdutide
- Retatrutide
- ARD-101

Place in Therapy

Medication	Average Weight Loss	Considerations
Tirzepatide (Mounjaro®)*	~20%	• Weekly injection • Used for T2DM (not currently FDA approved for weight loss)
Semaglutide (Wegovy®)*	~15%	• Weekly injection • Approved for weight management and T2DM
Liraglutide (Saxenda®)*	~10%	• Daily injection • Approved for weight management and T2DM
Phentermine/Topiramate (Qsymia®)	7-10%	• CV and CNS adverse effects • Avoid using in cardiovascular disease
Naltrexone/Bupropion (Contrave®)	~4%	• GI upset and increases blood pressure • Cannot be use in patients with seizure disorders
Orlistat (Alli®, Xenical®)	3-5%	• GI adverse effects

*GLP-1 receptor agonists have cardiovascular and renal benefits

Other options: phentermine, diethylpropion, topiramate, zonisamide, SGLT-2 inhibitors, metformin, pramlintide, metreleptin, and other GLP-1 receptor agonists

Place in Therapy

- Consider other co-morbidities
  - Indications/Contraindications
- Patient preference for route of administration
- History of treatment failure
- Insurance coverage

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