Overview of the Obesity Epidemic

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Conflict of Interest Disclosure

I disclose that:

- *I anticipate referencing the unlabeled / unapproved use of 3 medications for the treatment of obesity*
- *I have an affiliation with:*
  - *Medifast*
- *Obesity Medicine Association*

Learning Objectives

- Discuss the health consequences of obesity
- Identify the multiple factors that influence obesity
- Facilitate patient discussion about obesity
- Apply a comprehensive approach to obesity treatment

Definition of Obesity

Obesity is defined as a **chronic, relapsing, 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.

Adapted from Obesity Algorithm®, Obesity Medicine Association®

Measuring Obesity – Body Mass Index

Body Mass Index (BMI) = Body weight in kilograms / (Height in meters)^2

Overweight and Obesity Classification: Body Mass Index (BMI) in kg/m^2*	
	Normal weight (18.5 – 24.9)
	Overweight (25.0 – 29.9)
	Class I obesity (30.0 – 34.9)
	Class II obesity (35.0 – 39.9)
	Class III obesity (≥ 40)

Adapted from Obesity Algorithm®, Obesity Medicine Association®

* Different BMI cut-off points may be more appropriate for women versus men, among those of different races, and among individuals

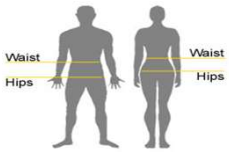
Measuring Obesity – Body Fat Composition

Percent Body Fat

Category	Female	Male
Essential	10-13%	2-5%
Athletic	14-20%	6-13%
Fitness	21-24%	14-17%
Acceptable	25-31%	18-24%
Obese	>31%	>25%

Measuring Obesity – Waist Circumference

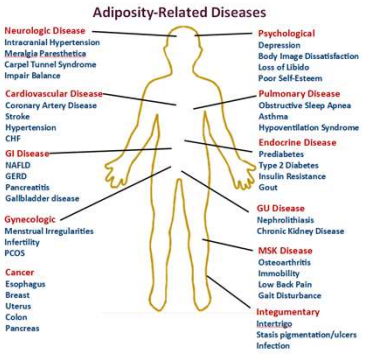
	Males	Females
Caucasian	40”	35”
African American	37”	31.5”
Latino	35.5”	31.5”
Asian	33.5”	31.5”



Question

- Where do you measure waist circumference?
  A. At Umbilicus
  B. Below umbilicus
  C. Iliac crests
  D. Maximum point of WC

Obesity is not about weight,
it’s about disease

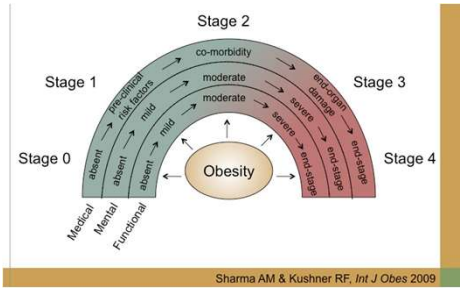


Edmonton Obesity Staging System

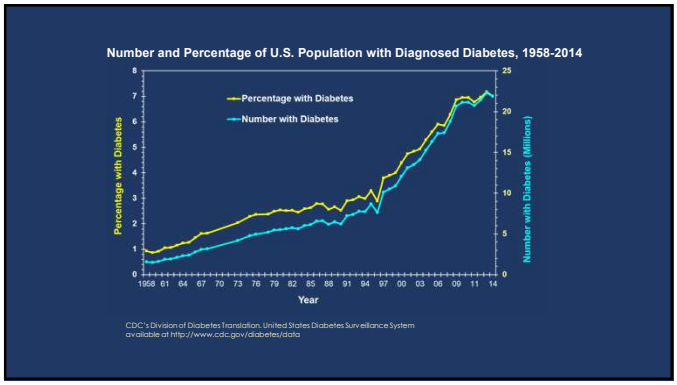
Staging according to medical consequences of obesity

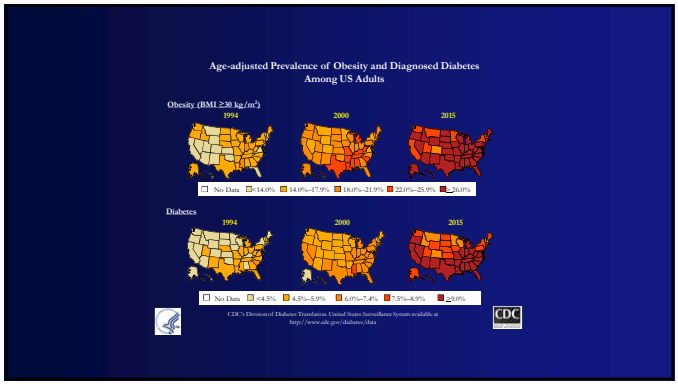
Stage	Risk Factors or Medical Conditions	Physical Symptoms	Psychological Symptoms
0	None	None	None
1	Subclinical – not requiring treatment	Mild symptoms	Mild – No treatment
2	Established Conditions Requiring Treatment	Moderate functional limitations	Moderate – depression/anxiety
3	Significant w/ end-organ damage	Significant functional limitations	Significant functional limitations
4	Severe – end stage	Severe – disabling	Severely disabling condition

Edmonton Obesity Staging System

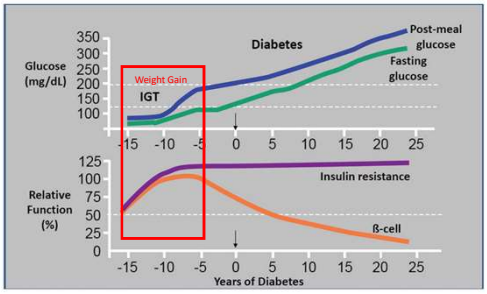


Sharma AM & Kushner RF, *Int J Obes* 2009





Developing Diabetes



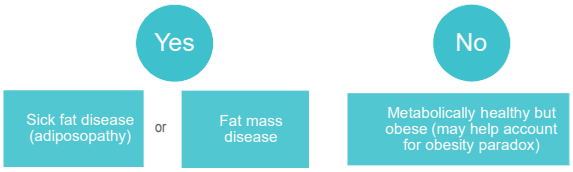
Information from Ramlo-Halsted & Clinical Diabetes, Spring 2000.

A patient with a BMI of 42 would be classified as?

- Overweight
- Class 1 obesity
- Class 2 obesity
- Class 3 obesity
- ~~Morbid obesity~~

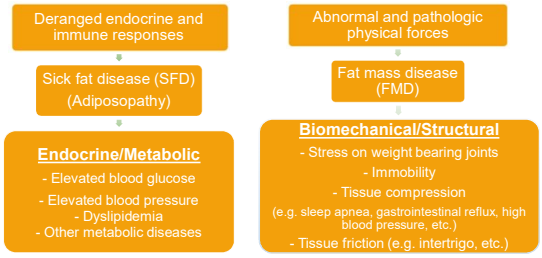
Health Consequences of Obesity

Is there a disease process present?



Adapted from Obesity Algorithm®, Obesity Medicine Association®

Health Consequences of Obesity



Adapted from Obesity Algorithm®, Obesity Medicine Association®

Obesity – Driving Factors

- What makes weight management so difficult?
  - Neurohormonal/Enterohormonal design

Leptin
Ghrelin
PYY
CCK
Orexin
GLP-1
Resistin
Adiponectin
..

Obesity – Driving Factors

- What makes weight management so difficult?
  - Genetics - >150 genes

Obesity – Driving Factors

- What makes weight management so difficult?
  - Food portions
  - Food choices
  - Taste

Obesity – Driving Factors

- What makes weight management so difficult?
  - Patient and physician perceptions
  - Media influence

Comprehensive Treatment of Obesity

- Nutrition
- Physical Activity
- Behavior
- Medications
- Surgery

Physical Activity

Physical Activity

- Exercise Activity Thermogenesis (EAT)
- Non-Exercise Activity Thermogenesis (NEAT)
  - Yard work
  - Extra steps
  - Stairs
  - Household chores
  - Standing

Physical Activity

- Exercise Rx

Exercise Rx CAMPBELL UNIVERSITY | Health Center

Name: _____ Date: _____

☐ **Aerobic Activity**

Type: Walk Jog Elliptical Swim Bike _____

Frequency (days/week): 2 3 4 5 6 7

Intensity: Light (A casual walk) Moderate (A brisk walk) Vigorous (Jogging or running)

Time (minutes/day): 10 20 30 60 60+

Make it fun: Music Buddy Dance _____

☐ **Strength Training**

- Do muscle strengthening exercises at least two days per week.
- Do exercises to strengthen all major muscle groups: legs, hips, back, chest, abdomen, shoulder, arms.
- Complete 8-12 repetitions (one set) for each exercise. Repeat the set three times for each exercise.
- These activities do not require going to a gym. You can use resistance bands or do body-weight exercises (e.g., push-ups, lungers).

☐ **Non-Exercise Activity Time (NEAT)**

- Park farther away from entrances.
- Take the stairs instead of the elevator/escalator.
- Stand instead of sitting.
- Set a steps/day goal _____
- Other: _____

Refills: Unlimited

Provider Signature: _____

Behavior

Behavior

- Why is it so difficult to discuss?
  - Judgment
  - Guilt
  - Shame
  - Blame
  - Failure

5A's of Obesity Management

Ask	• Ask for permission to discuss body weight. • Explore readiness for change.
Assess	• Assess BMI, waist circumference, and obesity stage. • Explore drivers and complications of excess weight.
Advise	• Advise the patient about the health risks of obesity, the benefits of modest weight loss (i.e., 5-10%), the need for long-term strategy, and treatment options.
Agree	• Agree on realistic weight-loss expectations, targets, behavioral changes, and specific details of the treatment plan.
Arrange/Assist	• Assist in identifying and addressing barriers; provide resources; assist in finding and consulting with appropriate providers; arrange regular follow up.

Behavior

- Broaching the Topic
  - Tying weight to clinical condition
    - Diabetes
    - Hypertension
    - Arthritis
    - OSA
  - Focus on health improvement not weight loss

Behavior – Weight Bias in Healthcare

- Perceptions of Patients Affected by Obesity
  - 53% report inappropriate comments from their doctors about their weight.
  - Doctors are the second most common source of stigma (69%).
  - BMI > 55: 68% report delayed seeking health care because of their weight due to disrespectful treatment, embarrassment, inadequate gowns, equipment and chairs…

Puhl R. Obesity. 2006. Amy NK. Int J Obes. 2006

Behavior

- Behavior Rx

Behavior Rx for Weight Management

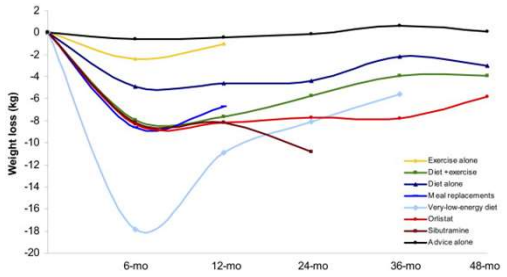
Patient Name_____ **Date** _____

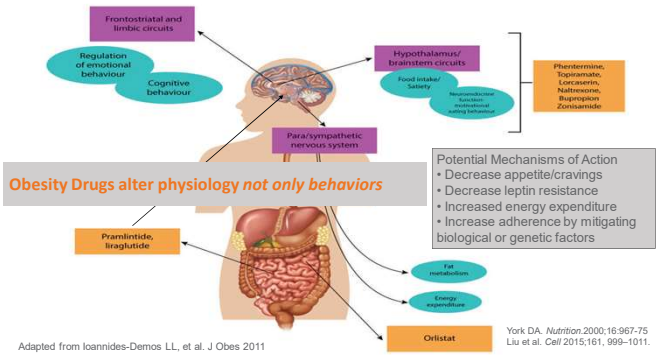
Self-monitoring
Weighing_____
Food intake – food diary calorie intake daily carb intake
Stress Management
Stress triggers for eating_____
Change strategy_____
Contingency Management
Biggest challenges to staying on program_____
Strategy to overcome challenge_____
Social Support
Support system_____
Potential saboteurs_____
Sleep Habits
Current hours of sleep_____
Change goal_____
Cravings
Strongest cravings – sugar, starches, fried food, sweet drinks _____
Change goal_____
Food Triggers
Common food triggers – stress, work, social, reward, relaxation____
Alternative strategies to food_____
_____

Provider _____

Medication

Treatment strategies for Obesity





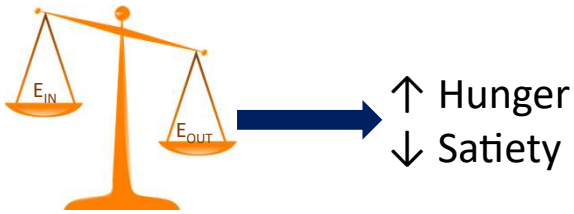
Potential Mechanisms of Action
- Decrease appetite/cravings
- Decrease leptin resistance
- Increased energy expenditure
- Increase adherence by mitigating biological or genetic factors

Adapted from Ioannides-Demos LL, et al. J Obes 2011

York DA. *Nutrition*.2000;16:967-75
Liu et al. *Cell* 2015;161, 999–1011.

Physiologic Response to a Calorie Deficit

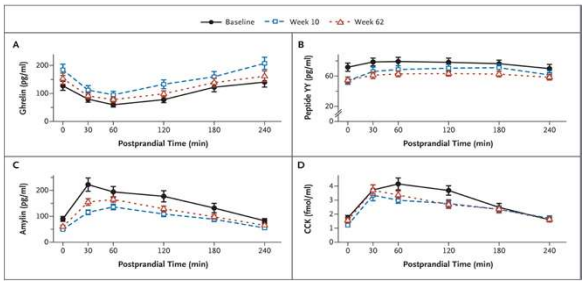
- Negative energy balance triggers a physiologic increase in hunger and decrease in satiety



Why Use Anti-Obesity Medication (AOM)?

- Obesity is a **chronic disease**
- Counter the **physiologic response** to energy deficit
- Weight maintenance is **more challenging** than weight loss
- Hormonal responses are **long-term**

Hormonal responses are long-term



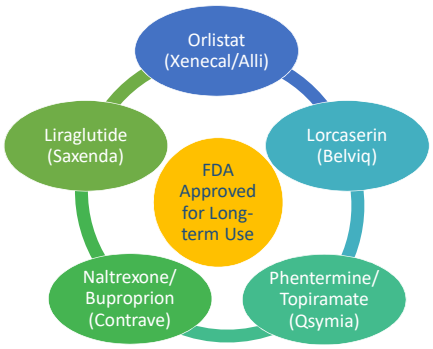
Sumithran P et al. N Engl J Med 2011;365:1597-1604

When to use Anti-obesity Medications

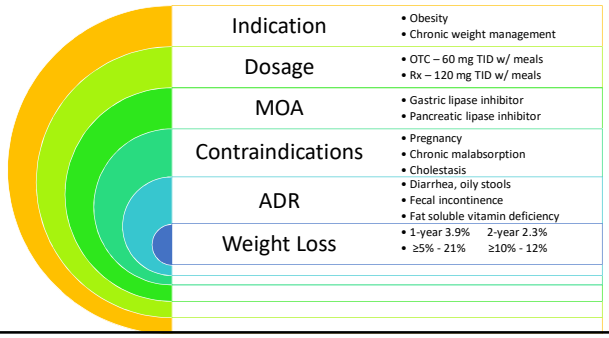
- General Recommendations
  - Indication for medication based on BMI
  - BMI ≥ 27 kg/m^2 + 1 or more adiposity related diseases (ARD)
  - BMI ≥ 30 kg/m^2
- Ignores presence of adiposity related diseases
- Ignores racial differences for BMI thresholds and ARD
- Ignores body composition

Documentation

- Best Practices
  - Follow **State Regulations**
  - **Previous** anti-obesity medication **use**
  - **Rationale** for mediation choice
  - **Vital signs** and **BMI** every visit
  - **Mood** and **appearance**
  - Rationale for **continued use**
  - **Include nutritional, physical activity and behavioral change recommendations**



Orlistat (Xenical, Alli)



Lorcaserin (Belviq)

Indication	• BMI ≥ 30 kg/m^2 • BMI ≥ 27 kg/m^2 + 1 ARD
Dosage	• 10 mg BID • XR 20 mg daily
MOA	• Selective serotonin 5HT2c agonist • Activates POMC neurons - ↑satiety
Contraindications	• Pregnancy • Hypersensitivity • Potential for serotonin syndrome
ADR	• Headache, dizziness, fatigue • Nausea, dry mouth, constipation • Hypoglycemia, back pain, cough
Weight Loss	• 5.8 Kg (12.8 lbs.) • ≥5% WL - 47% Placebo 22% • ≥10% WL - 22% Placebo 8.7%

DEA Schedule IV

Phentermine/Topiramate ER (Qsymia)

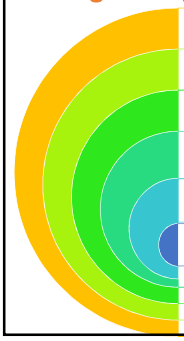
Indication	• BMI ≥ 30 kg/m^2 • BMI ≥ 27 kg/m^2 + 1 ARD
Dosage	• 3.75/23 mg x 14d → ↑7.5/46mg • If <3%WL at 12 weeks then increase • 11.25/69mg x 14d → ↑15/92mg
MOA	• Phentermine – sympathomimetic • Topiramate - ↑GABA / ↓carb. anhy.
Contraindications	• Pregnancy • Glaucoma, hyperthyoidism • Uncontrolled HTN
ADR	• Headache, dizziness, fatigue • Nausea, dry mouth, constipation • Hypoglycemia, back pain, cough
Weight Loss	• ≥5% WL - 67%; placebo 17% • ≥10% WL - 47%; placebo 7%

DEA Schedule IV - REMS

Naltrexone/Buproprion HCl ER (Contrave)

Indication	• BMI ≥ 30 kg/m^2 • BMI ≥ 27 kg/m^2 + 1 ARD
Dosage	• 8mg naltrexone/90mg buproprion • Titrate 1 qAM x 7d; then 1 BID x 7d • Then 2 qAM, 1qPM x 7d; then 2 BID
MOA	• Naltrexone – opioid antagonist • Buproprion -↓NE & dopamine uptake
Contraindications	• Pregnancy • Uncontrolled HTN, Seizure d/o • Opioid use, eating disorder, MAOI use
ADR	• Headache, dizziness, insomnia • Nausea, dry mouth, • Constipation, diarrhea
Weight Loss	• WL 5.4 & 8.1%; placebo 1.3% & 4.9% • ≥5% WL – 42&57%, placebo 17&43% • ≥10% WL – 21&35%, placebo 7&21%

Liraglutide (Saxenda)

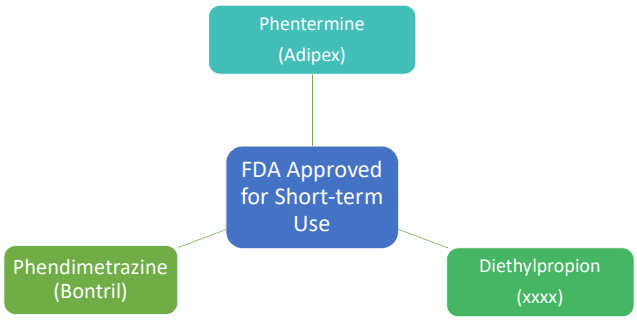


Indication	• BMI ≥ 30 kg/m² • BMI ≥ 27 kg/m² + 1 ARD
Dosage	• Titrate: 0.6mg SC daily x 7d, • then 1.2mg x 7d, then 1.8mg x 7d, • then 2.4mg x 7d, then 3.0mg x 7d
MOA	• GLP-1 agonist • Central satiety, ↓gastric emptying
Contraindications	• Pregnancy • Personal or FH medullary thyroid CA • MEN type 2, caution h/o pancreatitis
ADR	• N/V, diarrhea, constipation • Headache, dizziness, fatigue • Hypoglycemia, abdominal pain
Weight Loss	• WL 9.2% vs 3.5% placebo • ≥5% WL – 62%; placebo 34% • ≥10% - 34%; placebo 15%

Cardiovascular Outcomes with Anti-obesity Medications

Medication	LDL	TG	HDL	A1c	SBP
Phentermine/Topiramate CR	↓	↓	↑	↓	↓
Lorcaserin	↓	↓	–	↓	↓/–
Naltexone SR/Bupropion SR	–	↓	↑	↓	↑
Liraglutide 3.0mg	↓	↓	↑	↓	↓

Journal of the American College of Cardiology, Volume 68, Issue 8, August 2016
Cardiovascular Effects of the New Weight Loss Agents
Matthew H. Vorsanger et al



Case Study

- A 26-year-old man presents for weight loss. His weight is 339 lbs. and BMI is 48.69 kg/m^2. He relates that no diet has worked for him and that he is always hungry, even when he is not on a diet. Has a mostly sedentary job but takes an occasional walk. Patient on AOM
- 12/5/2017 - started phentermine ER ½ 37.5
- 2/6/2018 - dose increased to 30 mg
- 10/30/2018 - dose changed to 37.5 ½ bid

Case Study – Patient on Phentermine

Total Weight Loss – 112 lbs.

Total decrease in BMI – 16.1 kg/m^2

Phentermine (Adipex)

Indication	• BMI ≥ 30 kg/m^2 • BMI ≥ 27 kg/m^2 + 1 ARD
Dosage	• 8 mg ½ to 1 qd to tid • ER 15mg, 30mg, 37.5mg scored tab
MOA	• Sympathomimetic – centrally acting • NE ↑ release/↓ uptake → ↓appetite
Contraindications	• Pregnancy, Glaucoma, CVD • Uncontrolled HTN, hyperthyroidism
ADR	• Headache, dizziness, fatigue • Nausea, dry mouth, constipation • Hypoglycemia, back pain, cough
Weight Loss	• Limited data
DEA Schedule IV Controlled Substance	

Diethylproprion

Indication	• BMI ≥ 30 kg/m^2 • BMI ≥ 27 kg/m^2 + 1 ARD
Dosage	• 25mg tid • SR 75mg
MOA	• Sympathomimetic – centrally acting • NE ↑ release/↓ uptake → ↓appetite
Contraindications	• Pregnancy, Glaucoma, CVD • Uncontrolled HTN, hyperthyroidism
ADR	• Headache, dizziness, fatigue • Nausea, dry mouth, constipation • Hypoglycemia, back pain, cough
Weight Loss	• Limited data

DEA Schedule IV controlled substance

Phendimetrazine (Bontril)

Indication	• BMI ≥ 30 kg/m^2 • BMI ≥ 27 kg/m^2 + 1 ARD
Dosage	• 35mg capsule tid • SR 105mg capsule daily
MOA	• Sympathomimetic – centrally acting • NE ↑ release/↓ uptake → ↓appetite
Contraindications	• Pregnancy, Glaucoma, unstable CVD • Uncontrolled HTN, hyperthyroidism
ADR	• Headache, dizziness, fatigue • Nausea, dry mouth, constipation • Hypoglycemia, back pain, cough
Weight Loss	• Limited data

DEA Schedule III controlled substance

Medication Treatment

- Medications **not** FDA Approved for Weight Loss
  - Metformin
  - Topiramate
  - Naltrexone

Above all do no harm

Medications That Cause Weight Gain

- Diabetes Medications
  - Insulin
  - Sulfonylureas
- Steroids
- Chronic pain medication
- Anti-depressants
- Antipsychotic medications

Surgery

Bariatric Surgery

- Restriction
- Malabsorption
- Metabolic impact
  - Alters homones that effect appetite
  - Alters bile acid metabolism
  - Alters gut nutrient sensing
  - Alters glucose sensing

Sleeve Gastrectomy

Gastric Bypass (Roux-en-Y)

Laparoscopic Adjustable Gastric Band

Duodenal Switch

Bariatric Surgery

- Indications
  - BMI ≥ 40
  - BMI ≥ 35 + severe obesity related medical condition
  - ?BMI ≥ 30 + T2D
  - Patient prepared to commit to lifestyle change required after surgery

Bariatric Surgery

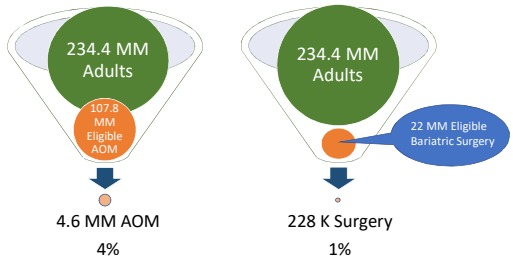
- Contraindications
  - Substance abuse
  - Eating disorder
  - Active psychiatric problem
  - Medically unstable
  - Women who plan to become pregnant w/in 12 months

Bariatric Surgery Patients Need Lifetime Monitoring!

	Vitamins							Minerals		
	A	B1	B9	B12	D*	E	K	Ca	Fe	Zn/Cu
RNY		X	X	X	X			X	X	
Sleeve		X	X	X	X				X	
LAGB		X			X					
BPD	X	X	X	X	X	X	X	X	X	X

*Vitamin D deficiency is seen in a significant number of patients with obesity at baseline. However, due to malabsorption, the risk is further increased post-op.
For a complete explanation of micronutrient deficiencies, refer to "Clinical Practice Guidelines for the Perioperative Nutritional, Metabolic, and Nonsurgical Support of the Bariatric Surgery Patient" at www.asmbs.org.

Current Treatment of Patients with Obesity



Summary

- Obesity rates have increased dramatically in the past 30 years
- Health consequences of obesity impact every organ system
- Approach to obesity treatment should include:
  - Nutritional intervention
  - Physical activity
  - Behavioral therapy
  - Pharmacotherapy
  - Surgery consideration
- Obesity is an undertreated disease

Resources for Obesity Medicine

- Obesity Medicine Association
  - obesitymedicine.org
- Obesity Algorithm
  - Obesitymedicine.org/obesity-algorithm/
- ASMBS
  - ASMBS.org
- The Obesity Society
  - Obesity.org

Supplement

Medication & Weight Change

Pharmacotherapy that May Alter Body Weight

Cardiovascular Medications

May increase body weight:
- Some beta-blockers
  - Propranolol
  - Atenolol
  - Metoprolol
- Older and/or less lipophilic dihydropyridine ("dipine") calcium channel blockers may increase body weight gain due to edema, compared to non-dihydropyridines and lipophilic dihydropyridines, and the increased edema may exacerbate obesity-related edema (and sleep apnea related peripheral edema), and also confound body weight as a measure of body fat
  - Nifedipine
  - Amlodipine
  - Felodipine

Diabetes Mellitus Medications

May increase body weight:
- Most insulins
- Sulfonylureas
- Thiazolidinediones
- Meglitinides

May decrease body weight:
- Metformin
- Glucagon-like peptide-1 agonists
- Sodium glucose co-transporter 2 inhibitors
- Alpha glucosidase inhibitors

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 Reference/s: [12, 27, 113, 114, 310]

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Pharmacotherapy that May Alter Body Weight

Hormones

May increase body weight:
- Glucocorticoids
- Estrogens

Variable effects on body weight:
- Progestins
  - Injectable or implantable progestins may have greatest risk for weight gain
  - May be dependent upon the individual
- Testosterone
  - May reduce percent body fat and increase lean body mass, especially if used to replace testosterone deficiency in men

Anti-seizure Medications

May increase body weight:
- Carbamazepine
- Gabapentin
- Valproate

May decrease body weight:
- Lamotrigine
- Topiramate
- Zonisamide

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 Reference/s: [113,119]

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Pharmacotherapy that May Alter Body Weight

Antidepressants

May increase body weight:
- Some tricyclic antidepressants (tertiary amines)
  - Amitriptyline
  - Doxepin
  - Imipramine
- Some selective serotonin reuptake inhibitors (e.g. paroxetine)
- Some irreversible monoamine oxidase inhibitors
  - Isocarboxazid
  - Phenelzine
- Mirtazapine

May decrease body weight:
- Bupropion

Variable effects on body weight:
- Some tricyclic antidepressants
  - Desipramine
  - Nortriptyline
  - Protriptyline
- Some SSRI
  - Citalopram
  - Escitalopram
  - Fluoxetine
  - Sertraline
- Some SSRI & SNRI
  - Desvenlafaxine
  - Duloxetine
  - Venlafaxine
- Some irreversible monoamine oxidase inhibitors (i.e., tranylcypromine)

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 Reference/s: [113,120-122]

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Pharmacotherapy that May Alter Body Weight

Mood Stabilizers

May increase body weight:
- Gabapentin
- Lithium
- Valproate
- Vigabatrin

Variable/neutral effects on body weight:
- Carbamazepine (sometimes reported to increase body weight)
- Lamotrigine (sometimes reported to decrease body weight)
- Oxcarbazepine

Migraine Medications

May increase body weight:
- Amitriptyline
- Gabapentin
- Paroxetine
- Valproic acid
- Some beta-blockers

May decrease body weight:
- Topiramate

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 Reference/s: [113, 120-122]

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Identify and Manage Concomitant Pharmacotherapy that Might Alter Body Weight

Antipsychotics

May substantially increase body weight:
- Clozapine
- Olanzapine
- Zotepine

May somewhat increase body weight:
- Asenapine
- Paliperidone
- Quetiapine
- Risperidone
- Lithium

Variable/neutral effects on body weight:
- Amisulpride
- Aripiprazole
- Haloperidol
- Lurasidone
- Ziprasidone

Hypnotics

May increase body weight:
- Diphenhydramine

May have limited effects on body weight:
- Benzodiazepines
- Melatonergic hypnotics
- Trazodone

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 Reference/s: [113, 120-122]

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Pharmacotherapy that May Alter Body Weight

Human Immunodeficiency Virus (HIV) Medications

May increase body weight:
- Some highly active antiretroviral therapies (HAART) protease inhibitors without HIV lipodystrophy

May decrease body weight:
- Some highly active antiretroviral therapies (HAART) protease inhibitors with HIV lipodystrophy

Chemotherapies

May increase body weight:
- Tamoxifen
- Cyclophosphamide
- Methotrexate
- 5-fluorouracil
- Aromatase inhibitors
- Corticosteroids

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 Reference/s: [113, 123,124]

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