

# Obesity Algorithm<sup>®</sup>

2016-2017

# Disclaimer and Permissions

## Disclaimer

The Obesity Algorithm<sup>®</sup> guidelines were originally presented by the Obesity Medicine Association (OMA) in 2013 and have since been updated yearly to include the latest treatments and trends in the field of obesity medicine. They were developed to assist health care professionals in the management and care for patients with overweight and obesity. The Obesity Algorithm is not intended to be a substitute for a medical professional's independent judgment and should not be considered medical advice. The content herein is based on medical literature and the clinical experiences of obesity medicine specialists. In areas regarding inconclusive or insufficient scientific evidence, the authors used their professional judgment.

The Obesity Algorithm is a working document that represents the state of obesity medicine at the time of publication. OMA encourages medical professionals to use this information in conjunction with, and not as a replacement for, their best clinical judgment. The presented recommendations may not be appropriate in all situations. Any decision by practitioners to apply these guidelines must be made in light of local resources and individual patient circumstances.

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# Peer Review

Since its original release in 2013, the Obesity Algorithm has undergone peer review by medical professionals and providers, facilitated by:

- Public posting on the web with free access and free download
- Presentations and discussions at OMA meetings
- Presentations and discussions at other scientific sessions and conferences
- Citations in medical literature

Throughout the year, OMA receives comments based on widespread exposure amongst world-wide colleagues (e.g., scientific and clinical peers), as well as via online public access. OMA members are encouraged to provide feedback. This 2016-2017 version of the Obesity Algorithm incorporates worldwide input, as well as interim scientific and clinical trial data.

# Major Updates Included in the 2016-2017 Version

- General updates and text edits
- Obesity terminology and health care office environment
- Obesity genetic syndromes (complementary to the OMA Pediatric Obesity Algorithm)
- Obesity paradox
- Body composition assessment
- Energy expenditure assessment
- Diet patterns (“diets”)
- Gastrointestinal hormones
- Expanded section on FDA-approved bariatric procedures
- Macro and micronutrients in post-bariatric surgery patients
- Microbiome
- References

# Authors and Citation

**Core Authors:** Harold E. Bays, MD, FTOS, FACC, FACE, FNLA; Jennifer C. Seger, MD, FOMA; Craig Primack, MD, FACP, FAAP, FOMA; William McCarthy, MD, FOMA; Joshua Long, MD, FASMBS; Stacy L Schmidt PhD; Sunil Daniel, MD, FTOS; Julie Wendt, MD; Deborah B. Horn, DO, MPH, MFOMA; Eric C. Westman, MD, MHS, MFOMA

**Contributing Authors:** Nihar Shah MD, FACP, and Thomas Clark, MS, MD, FACS, FASMBS

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To provide clinicians with an overview of principles important to the care of patients with increased and/or dysfunctional body fat, based upon scientific evidence, supported by medical literature, and derived from the clinical experiences of members of the Obesity Medicine Association.

# Process

- The Obesity Algorithm was derived from input by volunteer OMA members consisting of:
  - Clinicians
  - Clinical trialists
  - Researchers
  - Academicians
- The Obesity Algorithm project has never received industry funding
- The authors have never received payment for their contributions

# Intent of Use

The Obesity Algorithm is intended to be a “living document” updated once a year (as needed). It is intended to be an educational tool used to translate the current medical science and the experiences of obesity specialists to better facilitate and improve the clinical care and management of patients with overweight and obesity.

This algorithm *is not* intended to be interpreted as “rules” and/or directives regarding the medical care of an individual patient.

While the hope is many clinicians may find this algorithm helpful, the final decision regarding the optimal care of the patient with overweight and obesity is dependent upon the individual clinical presentation and the judgment of the clinician who is tasked with directing a treatment plan that is in the best interest of the patient.

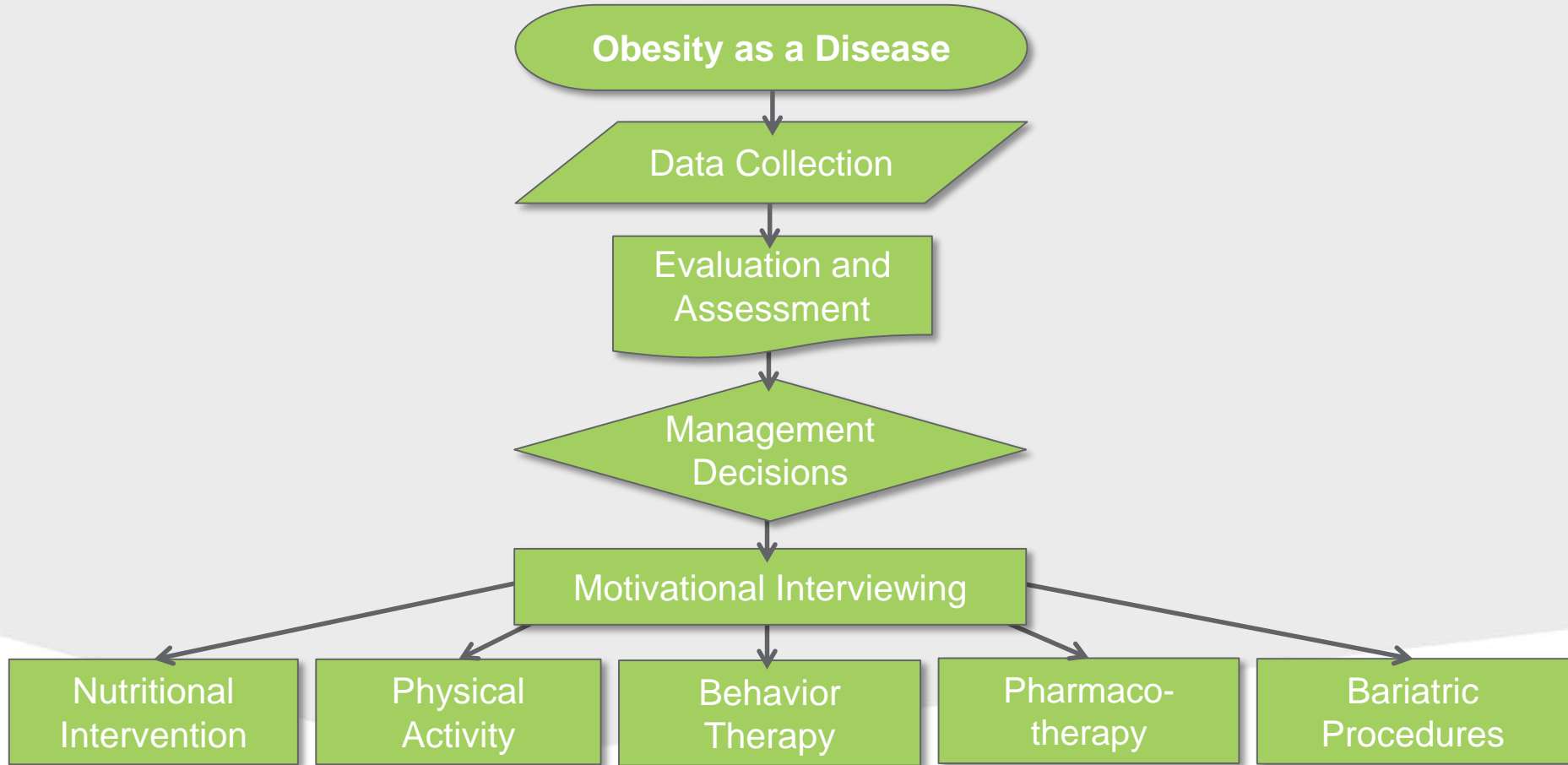
The Obesity Algorithm is listed by the American Board of Obesity Medicine as a suggested resource and study-aid for the obesity medicine certification exam. ([abom.org/exam-resources](http://abom.org/exam-resources))



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# Obesity Algorithm



# Obesity Defined as a Disease

## The Obesity Medicine Association's 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.”

# Obesity Is a Disease When...

- The patient has excessive body fat, as assessed by reliable measures
- Excessive body fat is caused by genetic or developmental errors, infections, hypothalamic injury, adverse reactions to medications, nutritional imbalance, and/or unfavorable environmental factors
- Multiple pathogenic adipocyte and/or adipose tissue endocrine and immune dysfunctions contribute to metabolic disease (adiposopathy or “sick fat” disease)
- Multiple pathogenic physical forces from excessive body fat cause stress damage to other body tissues (fat mass disease)

The adverse health consequences of increased body fat are not simply “co-morbidities” or “associated risk factors”

# Obesity Terminology

“**People-first**” language recognizes the potential hazards of referring to or labeling individuals by their disease. Thus, “**patient who is overweight or has obesity**” or “**patient with overweight or obesity**” are preferred over “obese patient.” This is similar to the standard with other diseases, such as diabetes mellitus, wherein “patient with diabetes” is preferred over “diabetic patient.”

## Encouraged Terms

- Weight
- Unhealthy weight
- Overweight
- Body mass index
- Affected by obesity

## Discouraged Terms

- Morbidly obese
- Obese
- Fat

# Obesity Health Care Office Environment

Clinicians and staff should be trained to avoid hurtful comments, jokes, or being otherwise disrespectful, as patients with obesity may be ashamed or embarrassed about their weight.

## Positive Office Space

- Sturdy, armless chairs and high, firm sofas in waiting rooms
- Sturdy, wide exam tables that avoid or prevent tipping
- Sturdy stool or step with handles to help patients climb onto the exam table
- Tables/chairs/toilet seats should sustain higher body weights
- Extra-large patient gowns
- Split toilet seat; provide a specimen collector with a handle
- Reading materials in the waiting room that focus on healthy habits, rather than physical looks or being “thin”

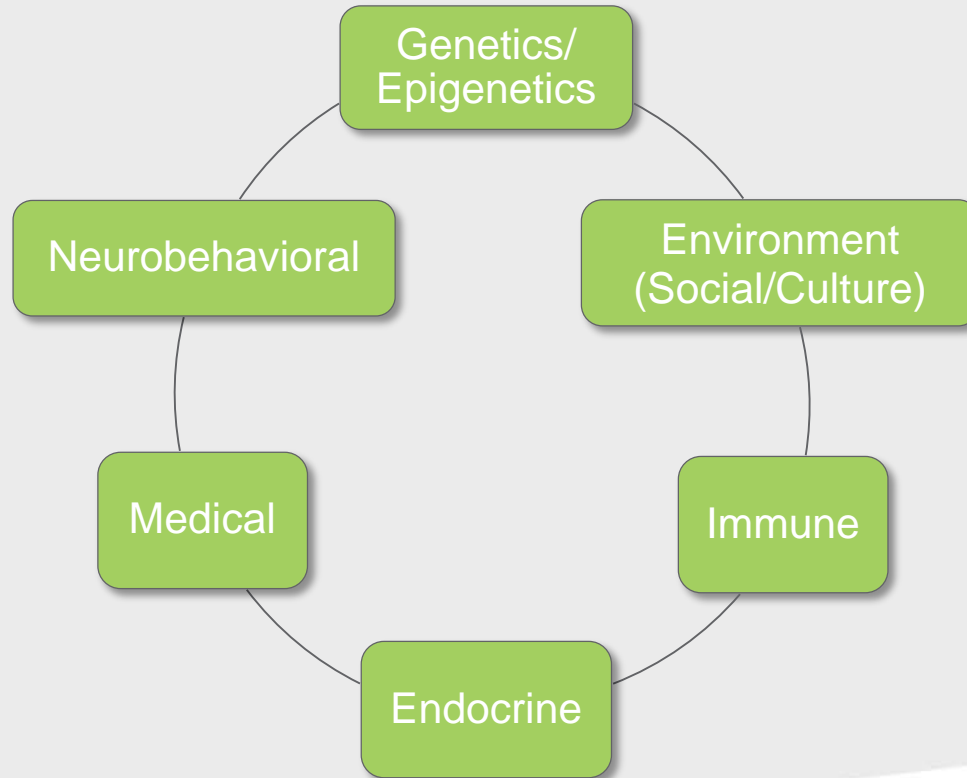
## Appropriate Medical Devices

- Large adult blood pressure cuffs or thigh cuffs on patients with an upper-arm circumference greater than 34 cm
- Extra-long needles to draw blood
- Large vaginal specula
- Weight scales with the capacity to measure patients who weigh more than 400 pounds

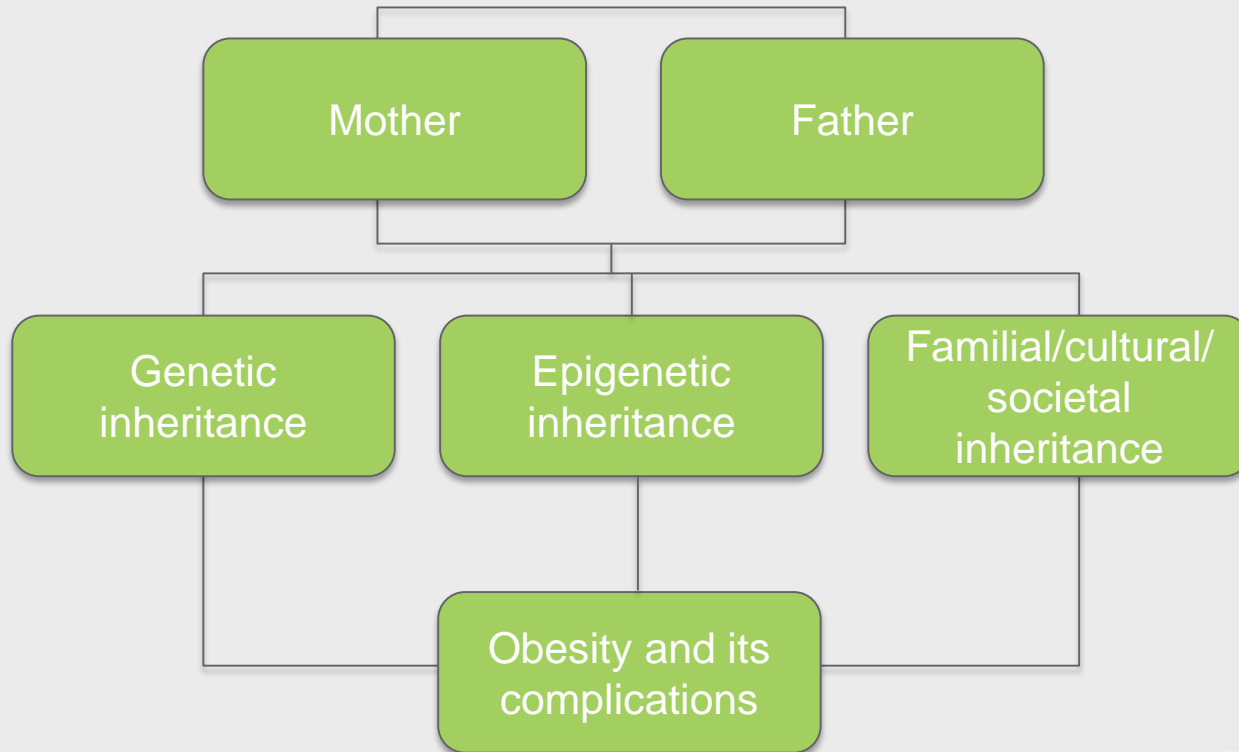
# Obesity as a Multifactorial Disease



# Obesity as a Multifactorial Disease



# Multifactorial Inheritance Factors Contributing to Obesity



# Genetics: Melanocortin 4 Receptor Deficiency

## Clinical Presentation

- Obesity, especially in families
- Hyperphagia and obesity early in childhood
- Insulin resistance
- Increase in bone mineral density (“big boned”)
- Accelerated linear growth
- Reduced sympathetic nervous activity

## Genetic Abnormality

- Autosomal dominant or recessive
- Most common known genetic defect predisposing to obesity
- Polymorphism of gene localized to chromosome 18q22

## Clinical Presentation

- Obesity, often hyperphagic
- Short stature
- Weak muscle tone
- Poor growth
- Small hands/feet
- Delayed development
- Underdeveloped genitals (often with infertility)
- Behavioral/emotional challenges
- Mild to moderate intellectual impairment
- Insatiable appetite
- Narrow forehead
- Almond-shaped eyes
- Triangular mouth
- Often with fair skin and light-colored hair

## Genetic Abnormality

- Not inherited
- Most cases involve loss of function of a portion of chromosome 15
- Often reported as the most common human genetic "obesity syndrome"

# Genetics: Albright's Hereditary Osteodystrophy

## Clinical Presentation

- Obesity
- Short stature
- Rounded face
- Skeletal defects: shortened fourth metacarpals and other bones of the hands and feet
- Dental hypoplasia
- Soft-tissue calcifications/ossifications
- Pseudohypoparathyroidism (hypocalcemia, hyperphosphatemia)

## Genetic Abnormality

- Associated with molecular defect in the gene (GNAS1), which encodes for the alpha subunit of the stimulatory G protein

## Clinical Presentation

- Obesity
- Metabolic abnormalities (e.g., type 2 diabetes mellitus, high blood pressure, dyslipidemia)
- Blindness (retinal dystrophy and pigmentary retinopathy)
- Anosmia
- Hearing loss
- Dysmorphic extremities: polydactyly and short or fused fingers and toes
- Poor coordination
- Dental abnormalities
- Intellectual disability
- Behavioral/emotional challenges
- Hypogonadism (with infertility)
- Renal cystic disease; renal insufficiency, which may lead to end-stage renal disease

## Genetic Abnormality

- Autosomal recessive
- Mutations of at least 16 genes (BBS genes) applicable to cilia involved in:
  - Cell movement
  - Chemical signaling
  - Sensory input (sight, hearing, and smell)

## Clinical Presentation

- Obesity
- Developmental delay
- Intellectual disability
- Small head size
- Narrow hands and feet with slender fingers
- Weak muscle tone
- Retinal dystrophy
- Joint hypermobility
- Thick hair and eyebrows
- Thick eyelashes
- “Open mouth” expression with incisoral prominence
- Low white blood cell count
- Overly friendly behavior

## Genetic Abnormality

- Typically auto recessive
- Mutation of the VPS13B gene (COH1 gene)

## Clinical Presentation

- Mainly in males
- Intellectual disability
- Seizure disorders
- Large earlobes
- Shortened toes
- Small genitalia
- Gynecomastia

## Genetic Abnormality

- X-linked disorder
- Mutation of the zinc finger gene POF1B (located on the X chromosome)



# Genetics: Other Genetic Syndromes Associated with Obesity

- Leptin deficiency
- Leptin receptor deficiency
- Src homology 2 B adapter protein 1 (SH2B1) mutations
- Carboxypeptidase E mutations
- Prohormone convertase-1 deficiency
- Proopiomelanocortin deficiency
- Proprotein convertase subtilisin kexin 1/3 deficiency
- Brain derived neurotrophic factor (BDNF) deficiency
- TrkB deficiency
- Sim1 deficiency
- Maternal uniparental disomy of chromosome 14
- Trisomy 21 (Down's Syndrome)

- Fragile X syndrome
- Turner's syndrome
- Alstrom syndrome
- Carpenter syndrome
- Macrosomia, Obesity Macrocephaly Ocular abnormalities (MOMO) syndrome
- Rubinstein-Taybi syndrome
- Rapid-onset Obesity with Hypothalamic dysfunction
- Hypoventilation and Autonomic Dysregulation (ROHHAD syndrome)
- Deletions/mutations of various other gene loci 17 and polymorphisms of fat mass and obesity associated (FTO) gene located on chromosome 16.

# Obesity: Extragenetic Etiology/Causes

## Extragenetic

- Environment (family, home, geographic location)
- Culture
- Lack of optimal nutrition and physical activity
- Disrupted sleep (e.g., poor quality, too little, or too much)
- Adverse consequences of medications
- Mental stress
- Neurologic dysfunction (central nervous system trauma, hypothalamic inflammation, leptin resistance)
- Viral infections
- Gut microbiota neurologic signaling and transmission of pro-inflammatory state

# Obesity: Epigenetic Etiology/Causes

**Epigenetics:** Alterations in gene expression without alteration in the genetic code

## Pre-pregnancy

- Pre-conception paternal or maternal overweight/obesity may influence epigenetic signaling during subsequent pregnancy:
  - Increased risk of overweight/obesity in offspring
  - Increased risk of other diseases (e.g., cardiovascular disease, cancer, diabetes, mellitus, etc.) in offspring

## Pregnancy

- Especially in the presence of gestational diabetes mellitus, unhealthy maternal nutrition in women who are pregnant and overweight or with obesity may increase placental nutrient transfer to fetal circulation:
  - Glucose
  - Lipids and fatty acids
  - Amino acids
- Increased maternal nutrient transport may alter fetal gene expression:
  - Covalent modifications of deoxynucleic acid and chromatin
  - May impact stem cell fate
  - May alter postnatal biologic processes involved in substrate metabolism
  - May increase offspring predisposition to overweight/obesity and other diseases

## Post-pregnancy

- Adverse effects of epigenetic pathologies may help account for generational obesity
- Improvement in generational obesity in offspring will likely require generational change in nutrition and physical activity in prior generations of parents

# Overall Obesity Management Goals

# Within Subsets of Patients with Overweight and/or Obesity

Deranged endocrine and  
immune responses



## Sick Fat Disease (SFD) (Adiposopathy)

Endocrine/metabolic:

- Elevated blood glucose
- Elevated blood pressure
- Dyslipidemia
- Other metabolic diseases

Abnormal and pathologic  
physical forces

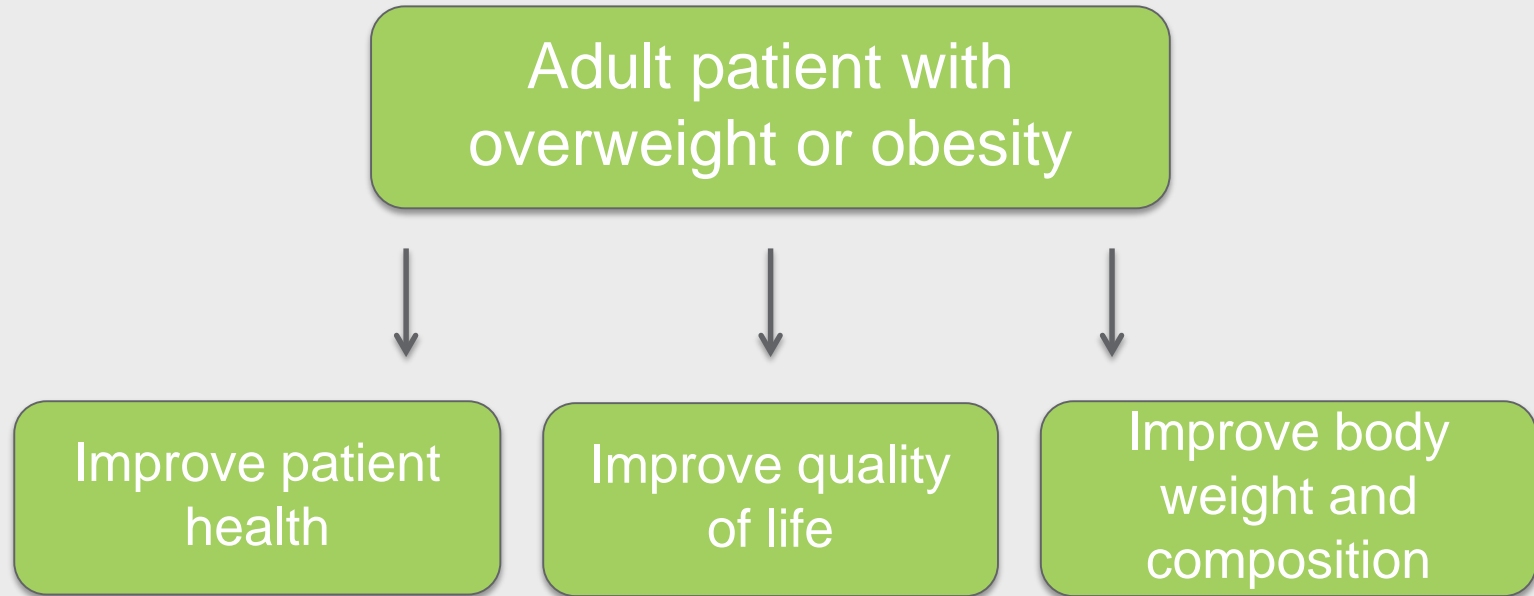


## Fat Mass Disease (FMD)

Biomechanical/structural:

- Stress on weight-bearing joints
- Immobility
- Tissue compression (i.e., sleep apnea, gastrointestinal reflux, high blood pressure, etc.)
- Tissue friction (i.e., intertrigo, etc.)

# Overall Management Goals



# Obesity Classification

# Body Mass Index: Increase Body Fat (Adiposity)

Body mass index (BMI) in kilograms per meters squared (kg/m<sup>2</sup>)\*

**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

\*Different BMI cut-off points may be more appropriate based upon gender, race, and ethnicity



# Percent Body Fat: American Council on Exercise Classification

## American Council on Exercise Classification: Percent body fat\*

### Essential Fat

Women: 10-13%  
Men: 2-5%

### Athletes

Women: 14-20%  
Men: 6-13%

### Fitness

Women: 21-24%  
Men: 14-17%

### Acceptable

Women: 25-31%  
Men: 18-24%

### Obesity

Women:  $\geq 32\%$   
Men:  $\geq 25\%$

\*Based on “expert opinion;” cut-off points not scientifically validated

# Percent Body Fat: U.S. Army Regulations

## U.S. Army regulations: Percent body fat (%BF)

### Men %BF Calculator (Age, height, & tape measure of neck and waist)

#### Maximum allowable %BF to join Army

- Age 17-20 24%
- Age 21-27 26%
- Age 28-39 28%
- Age 40+ 30%

#### Maximum allowable %BF after entry

- Age 17-20 20%
- Age 21-27 22%
- Age 28-39 24%
- Age 40+ 26%

### Women %BF Calculator (Age, height, & tape measure of neck, waist, and hip)

#### Maximum allowable %BF to join Army

- Age 17-20 30%
- Age 21-27 32%
- Age 28-39 34%
- Age 40+ 36%

#### Maximum allowable %BF after entry

- Age 17-20 30%
- Age 21-27 32%
- Age 28-39 34%
- Age 40+ 36%

# Waist Circumference: Increased Body Fat (Adiposity)

Obesity classification:  
Waist circumference (WC)\*

**Abdominal Obesity - Men**

$\geq 40$  inches  
 $\geq 102$  centimeters

**Abdominal Obesity - Women**

$\geq 35$  inches  
 $\geq 88$  centimeters

\*Different WC abdominal obesity cut-off points are appropriate for different races (i.e.,  $\geq 90$  centimeters for Asian men and  $\geq 80$  centimeters for Asian women)

# Obesity: Summary Diagnostic Metrics and Diagnostic Codes

**Body Mass Index**  
≥ 30 kg/m<sup>2</sup>

**Percent Body fat**  
Women: ≥ 32%  
Men: ≥ 25%

**Abdominal Obesity:**  
**Women**  
≥ 35 inches  
≥ 88 centimeters

**Abdominal Obesity: Men**  
≥ 40 inches  
≥ 102 centimeters

## Overweight and Obesity E66

- Code first obesity complicating pregnancy, childbirth and the puerperium, if applicable (O99.21-)
- Use additional code to identify body mass index (BMI), if known (Z68.-)

### Excludes:

- adiposogenital dystrophy (E23.6)
- lipomatosis NOS (E88.2)
- lipomatosis dolorosa [Dercum] (E88.2)
- Prader-Willi syndrome (Q87.1)

## E66.0 Obesity Due to Excess Calories

- E66.01 Morbid (severe) obesity due to excess calories
- E66.09 Other obesity due to excess calories
- E66.1 Drug-induced obesity
- E66.2 Morbid (severe) obesity with alveolar hypoventilation
- E66.3 Overweight
- E66.8 Other obesity
- E66.9 Obesity, unspecified

# Body Mass Index (BMI)

## Advantages

- Increased BMI generally correlates with metabolic and fat mass diseases in population studies
- Commonly used
- Reasonably reproducible
- Low cost
- Adequate measure for epidemiological studies
- Adequate screening metric for most patients

## Disadvantages

- May not correlate with metabolic and fat mass diseases in an individual patient
- Does not account for muscle mass
- May over-diagnose obesity in muscular individuals, under-diagnose patients with sarcopenia
- BMI cut-off points do not distinguish between men and women, nor ethnic and racial considerations
- Should be used as part of the clinical evaluation, and not the sole measure of obesity for all patients

# Percent Body Fat

## Advantages

- More specific assessment of body fat
- May be a reasonable longitudinal measure, especially in patients who may not be losing weight, but engaged in resistance exercise training, and thus may be losing body fat, and increasing muscle

## Disadvantages

- Some measurement techniques are not always accurate, nor easily reproducible (i.e., single site skinfold calipers)
- Electronic body fat measurements may be expensive, and as with calipers, the accuracy and reproducibility is dependent upon the equipment and software, as well as the expertise of the technician
- Cut-off points not validated to correlate to metabolic disease

# Waist Circumference

## Advantages

- Well-correlated to metabolic disease
- Direct anatomical measure of adipose tissue deposition, with an increase in waist circumference reflective of adipose tissue dysfunction
- Low cost

## Disadvantages

- Measurement not always reproducible
- Waist circumference is not superior to BMI in correlating to metabolic disease in patients with BMI  $\geq 35$  kg/m<sup>2</sup>
- Racial/ethnic differences

# Which Is the “Best” Measure of Obesity?

## Population Assessment

- Body mass index (BMI), waist circumference (WC), and percent body fat (%BF) similarly correlate with prevalence of metabolic syndrome

## Individual Assessment

- BMI is a reasonable initial screening measurement for most patients
- WC provides additional information regarding adipose tissue function/dysfunction and predisposition to metabolic disease among individuals with BMI < 35 kg/m<sup>2</sup>
- %BF may be more useful in patients with extremes in muscle mass (i.e., individuals with sarcopenia or substantial increases in muscle mass), and thus may be a more accurate measure of body composition when assessing the efficacy of interventions directed towards change in muscle mass



# Fat Mass Disease: Abnormal and Pathologic Physical Forces

# Clinical Manifestations: Fat Mass Disease

## Cardiovascular

- Congestive heart failure and cor pulmonale
- Varicose veins
- Thromboembolic events (i.e., pulmonary embolus, stroke)
- Hypertension (i.e., compression of kidney)

## Pulmonary

- Dyspnea
- Obstructive sleep apnea
- Hypoventilation/Pickwickian syndrome
- Asthma

## Neurologic

- Intracranial hypertension (pseudotumor cerebri) due to increased intra-abdominal pressure and sleep apnea, with impaired central venous return.
- Stroke (see “cardiovascular”)
- Nerve entrapment (i.e., meralgia paresthetica, carpal tunnel syndrome)

# Clinical Manifestations: Fat Mass Disease

## Musculoskeletal

- Immobility
- Osteoarthritis (e.g. knees, hips)
- Low back pain
- Myalgias
- Altered center of gravity
- Impaired balance

## Gastrointestinal

- Gastroesophageal reflux
- Hernias

## Integument

- Striae distensae (skin stretch marks)
- Stasis pigmentation
- Venous stasis ulcers
- Cellulitis
- Skin tags
- Intertrigo (i.e. bacterial, fungal skin fold infections)
- Carbuncles

# Clinical Manifestations: Fat Mass Disease

## Psycho-Social

- Depression
- Hopelessness
- Low self-esteem
- Body-image dissatisfaction
- Diminished sex drive
- Impaired intimacy and sexual relationships
- Decreased work productivity
- Increased work absenteeism

## Negative Self or External Perceptions

- “Unmotivated”
- “Weak-willed”
- “Less intelligent”
- “Less attractive”
- “Unsuccessful”
- “Overindulgent”
- “Lazy”

## Biases

- Society
- Family
- Workplace
- Harassment
- Bullying

# Sleep Disorders and Obesity: Obstructive Sleep Apnea\*

## History

- Snoring (usually loudly)
- Insomnia
- Restless sleep
- Sudden waking with choking or gasping
- Headaches
- Daytime sleepiness
- Fatigue
- Increased risk of motor vehicle accidents
- Forgetfulness
- Mood changes
- Lack of interest in sexual behavior
- Gastroesophageal reflux

\*Other sleep disorders associated with obesity include insomnia and restless leg syndrome.

# Sleep Disorders and Obesity: Obstructive Sleep Apnea

## Physical Findings

- Increased neck circumference
  - Men > 17 inches
  - Women > 16 inches
- Head abnormalities
  - Modified Mallampati score of 3 or 4
  - Retrognathia
  - Lateral peritonsillar narrowing
  - Macroglossia
  - Tonsillar hypertrophy
  - Enlarged uvula
  - High arched/narrow palate
  - Nasal abnormalities
  - Overbite
- Cardiopulmonary abnormalities
  - Peripheral edema
  - Cardiac dysrhythmia
  - High blood pressure

# Sleep Disorders and Obesity: Obstructive Sleep Apnea

## Diagnosis

- Questionnaires:
  - Berlin Sleep Questionnaire
  - Epworth Sleepiness Scale
  - STOP-Bang Questionnaire
    - **STOP** = **S**noring, **T**iredness, **O**bserved apnea and high blood **P**ressure)
    - **Bang**: **B**MI, **a**ge, **n**eck circumference, **g**ender
- Testing
  - In-lab overnight sleep studies
    - Apnea hypopnea index (AHI)
      - 5-15/hour = mild sleep apnea
      - 15-30/hour = moderate sleep apnea
      - > 30/hour = severe sleep apnea
  - Home sleep test
  - Multiple sleep latency test

## Adverse Consequences of Untreated Obstructive Sleep Apnea

- Worsening obesity
- Congestive heart failure
- Atrial fibrillation
- Nocturnal dysrhythmias
- Stroke
- High blood pressure
- Type 2 diabetes mellitus
- Pulmonary hypertension

# Sleep Disorders and Obesity: Obstructive Sleep Apnea

## Treatment

- Reduction of fat mass
- Behavior therapy to improve sleep patterns
- Oral appliances
  - Mandibular reposition devices
  - Tongue retaining devices
- Nasal expiratory positive airway
- Continuous positive airway pressure
- Adaptive servo-ventilation
- Surgery
  - Laser-assisted uvulopalatoplasty
  - Radiofrequency ablation
  - Palatal implants
  - Electrical stimulation of upper airway muscles



# Adiposopathy (Sick Fat Disease): Abnormal Endocrine and Immune Responses

# Anatomic Changes

- Positive caloric balance may lead to adipocyte hypertrophy with variable increases in adipocyte number, as regulated by intracellular:
  - Sterol regulatory element binding protein-1 (SREBP1),
  - Peroxisome proliferator-activated receptor (PPAR) gamma
  - CCAAT-enhancer binding proteins (C/EBPs)

# Anatomic Changes

- When adipogenesis (proliferation and differentiation) is impaired in peripheral subcutaneous adipose tissue (SAT), then inadequate storage of excess energy in SAT may result in energy overflow and increased circulating free fatty acids
  - Worsening adipocyte hypertrophy and adipocyte dysfunction
  - Increasing (“ectopic”) fat deposition in other depots
    - Visceral fat
    - Subcutaneous SAT
    - Pericardiac fat
    - Perivascular fat
  - Increasing (“ectopic”) fat deposition in other body organs
    - Liver
    - Muscle
    - Pancreas
    - Heart
    - Kidney

# Functional Changes

- Increased adipocyte hypertrophy and adipose tissue accumulation may contribute to:
  - Adipocyte and adipose tissue hypoxia
  - Increased adipose tissue immune cell infiltration
  - Increased adipocyte apoptosis
  - Increased reactive oxygen species and oxidative stress
  - Extracellular matrix abnormalities
  - Intraorganelle dysfunction (e.g., mitochondrial and endoplasmic reticulum stress)
  - Changes in adipose tissue neural network and innervations

# Adiposopathic Endocrinopathies

- Angiogenesis
- Adipogenesis
- Extracellular matrix dissolution and reformation
- Lipogenesis
- Growth factor production
- Glucose metabolism
- Production of factors associated with the renin-angiotensin system
- Lipid metabolism
- Enzyme production
- Hormone production
- Steroid metabolism
- Immune response
- Hemostasis
- Element binding (e.g., sterol regulatory element-binding proteins, and calcium)
- Multiple receptors:
  - Traditional peptides and glycoprotein hormones
  - Nuclear hormones
  - Cytokines or adipokines with cytokine-like activity
  - Growth factors
  - Catecholamine receptors

# Adiposopathic Immunopathies

- Proinflammatory adipose tissue factors
  - Factors with cytokine activity (e.g., leptin)
  - Acute-phase response proteins (e.g., C-reactive protein)
  - Proteins of the alternative complement system
  - Chemotactic or chemo-attractants for immune cells
  - Eicosanoids and prostaglandins (e.g., PGE2)
- Anti-inflammatory adipose tissue factors (e.g., adiponectin)

# Obesity, Health, and Harmony of Function of Body Organs

Adiposopathy most often results in metabolic disease when accompanied by:

- Dysfunction other body organs
- Limitations of the metabolic “flexibility” of other body organs to mitigate the pathogenic metabolic, endocrine, and immune responses promoted by obesity

Metabolic health is dependent upon the interactions or crosstalk with adipose tissue and other body organs:

- Liver
- Muscle
- Pancreas
- Immune system
- Heart and vasculature
- Brain
- Endocrine glands
- Intestine
- Other body organs

# Metabolic Manifestations of Adiposopathy

- High blood glucose (prediabetes mellitus, type 2 diabetes mellitus)
- High blood pressure
- Metabolic syndrome
- Adiposopathic dyslipidemia
  - Increased triglyceride levels
  - Decreased high-density lipoprotein cholesterol levels
  - Increased atherogenic particle number (increased apolipoprotein B)
  - Increased proportion of small, dense, low-density lipoprotein particles
  - Increased triglyceride-rich lipoproteins
  - Increased lipoprotein-remnants
- Insulin resistance
- Hepatosteatorosis (fatty liver)
- Hyperuricemia and gout
- Cholelithiasis
- Acanthosis Nigricans
- Nephrolithiasis
- Glomerulopathy
- Pro-thrombotic predisposition
- Neuropsychiatric diseases (such as worsening depression due to adiposopathic immune and endocrine responses)
- Asthma (due to adiposopathic immune and endocrine responses)
- Worsening of other inflammatory diseases (osteoarthritis, atherosclerosis, etc.)



# Gender-specific Manifestations of Adiposopathy

## Women

- Hyperandrogenemia
- Hirsutism
- Acne
- Polycystic ovarian syndrome
- Menstrual disorders
- Infertility
- Gestational diabetes mellitus
- Preeclampsia
- Thrombosis

## Men

- Hypoandrogenemia
- Hyperestrogenemia
- Erectile dysfunction
- Low sperm count
- Infertility

# Obesity and Adiposopathy Increases the Risk of Cancers

- Bladder cancer
- Brain cancer
- Breast cancer (postmenopausal)
- Cervical cancer
- Colon cancer
- Endometrial/uterine cancer
- Esophageal cancer
- Gallbladder cancer
- Head and neck cancer
- Kidney/renal cancer
- Leukemia
- Liver cancer
- Multiple myeloma
- Non-Hodgkin lymphoma
- Ovarian cancer
- Pancreatic cancer
- Prostate cancer (prognosis is worse, not necessarily increased risk)
- Stomach cancer
- Thyroid cancer

# Adiposopathic and/or Fat Mass Pathologies:

## Genitourinary and Reproductive Manifestations

### Genitourinary

- Urinary stress incontinence
- Pelvic prolapse (e.g. cystocele, rectocele, uterine prolapse, vault prolapse)

### Reproductive Pre-pregnancy

- Men
  - Buried or hidden penis
  - Erectile dysfunction
  - Psychological barriers to sexual behavior
  - Infertility
- Women
  - Psychological barriers to sexual behavior
  - Infertility, anovulation, polycystic ovary syndrome

### Reproductive Pregnancy

- Gestational diabetes mellitus
- Preeclampsia
- Increased risk of miscarriage and stillbirth
- Overdue pregnancy
  - Increased need for induction
  - Increased need and complications of cesarean section in women (delayed healing and wound infection)
- Large for gestational age offspring
- Thrombosis
- Obstructive sleep apnea

# Obesity Paradox

# Obesity Paradox

## ANATOMIC OBESITY PARADOX

- Are some fat depots protective while others are “paradoxically” pathogenic?

## PHYSIOLOGIC OBESITY PARADOX

- Are some individuals who are overweight or with obesity “paradoxically” healthy?
- Do some individuals who are normal weight, or only mildly overweight, “paradoxically” have metabolic disease?

## DEMOGRAPHIC (GENDER AND RACE) PARADOX

- Are women at a “paradoxically” lower age-adjusted cardiovascular disease risk than men?
- Are some races “paradoxically” at increased risk for metabolic diseases for the same amount of body weight?

## THERAPEUTIC OBESITY PARADOX

- Can adding body fat “paradoxically” treat metabolic diseases typically associated with too much body fat?
- Does an increase in fat mass always predispose to metabolic disease?
- Does a decrease in fat mass always improve metabolic disease?

## CARDIOVASCULAR OUTCOMES OBESITY PARADOX

- Why are individuals who are modestly overweight often report to have a better prognosis after cardiovascular disease (CVD) events and cardiovascular procedures?

## ATHEROSCLEROSIS “OUTSIDE-TO-IN” OBESITY PARADOX

- What is the role of pericardial and perivascular adipose tissue in promoting atherosclerosis?

## THERAPEUTIC APPROACH OBESITY PARADOX

- How do clinicians best navigate the apparent paradox of “blame” versus “accountability” in obesity management?

# Obesity Paradox: General Concepts

- Obesity increases mortality
- Obesity increases morbidity
- More than one “obesity paradox” exists
- Obesity paradoxes are less paradoxical when viewed from the perspective of both fat mass *and* fat function

## Are some fat depots protective while others are “paradoxically” pathogenic?

### Peripheral Subcutaneous Adipose Tissue (SAT) Can Be Protective

- Provides storage of energy
- Physical padding
- Thermal insulation
- During positive caloric balance, if adipocyte proliferation and differentiation are sufficient to mitigate adiposopathic adipocyte hypertrophy, endocrinopathies, inflammation, and lipotoxic energy overflow to other fat depots and other body organs, then an increase in body fat may not be as pathogenic in promoting metabolic disease

## Are some fat depots protective while others are “paradoxically” pathogenic?

### Peripheral Subcutaneous Adipose Tissue (SAT) Can Be Pathogenic

- Fat mass diseases
- During positive caloric balance, if adipocyte proliferation and differentiation are ***not*** sufficient to mitigate adiposopathic adipocyte hypertrophy, endocrinopathies, inflammation, and lipotoxic energy overflow to other fat depots and other body organs, then this may increase the risk of metabolic diseases such as diabetes mellitus, high blood pressure, and dyslipidemia.
- SAT is ~80% of total fat mass
  - Majority of adipose tissue-derived systemic free fatty acids originate from SAT, with extrahepatic lipotoxicity potentially contributing to insulin resistance in muscle
  - Majority of adipose tissue-derived free fatty acids in the portal system originate in SAT (not VAT), with lipotoxicity potentially contributing to insulin resistance in the liver
- An increase in abdominal SAT is associated with adiposopathic predisposition to metabolic disease, not unlike VAT



**Are some fat depots protective while others are “paradoxically” pathogenic?**

## **Visceral Adipose Tissue (VAT) Can Be Protective**

- Provides storage of energy
- Physical padding to protect against mechanical damage to abdominal organs
- May protect against peritoneal catastrophes (perforated visceral organs)
- Thermal insulation

## Are some fat depots protective while others are “paradoxically” pathogenic?

### Visceral Adipose Tissue (VAT) Can Be Pathogenic

- VAT adipocytes have higher basal lipolysis than SAT adipocytes
  - Increased sensitivity to catecholamines
  - Decreased sensitivity to insulin
  - Direct portal access to the liver
- More active expression of adiposopathic endocrinopathies than SAT
- More active expression of adiposopathic immunopathies than SAT
- More associated with increased risk of metabolic disease, possibly because increased visceral adiposity reflects dysfunctions of all fat depots

## Are some fat depots protective while others are “paradoxically” pathogenic?

- Both subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) are potentially protective and pathogenic
- SAT and VAT mass and function are interdependent
- Both SAT and VAT express adiposopathic endocrinopathies and immunopathies when promoting metabolic diseases
- An increase in visceral adiposity is a surrogate marker for the dysfunction of SAT and other fat depots
- An increase in visceral adiposity is a surrogate marker for global fat dysfunction, helping to account for its association with metabolic diseases
- Central obesity is a clinical measure that reflects both an increase in visceral fat and an increase in subcutaneous abdominal fat

Are some fat depots protective while others are “paradoxically” pathogenic?

## Benign Multiple Symmetrical Lipomatosis

- Increased fat accumulation in the subcutaneous adipose tissue regions of the arms, legs, shoulders, and neck.
- Increased proliferation of small adipocytes in subcutaneous adipose tissue
- Increased secretion of anti-inflammatory adipokines (e.g. adiponectin)
- Typically, glucose or lipid disorders do not develop

## Inherited Lipodystrophy

- Variable lack of body fat and impaired adipose tissue function (e.g., low adiponectin levels and inability to adequately store fat)
- High circulating free fatty acids (lipotoxicity)
- Hyperglycemia and dyslipidemia

# Physiologic Obesity Paradox

**Are some individuals who are overweight or with obesity “paradoxically” healthy?  
Do some individuals who are normal weight, or only mildly overweight  
“paradoxically” have metabolic disease?**

## **“Metabolically Healthy But Obese” Phenotype**

- Defined as individuals who respond to positive caloric balance without pathogenic adipose tissue dysfunction sufficient to result in metabolic disease
- The prevalence of MHO is decreased with greater intensity of metabolic assessment
- MHO may still experience fat mass disease, sleep apnea, and increased risk of cancers
- With aging, MHO are at greater risk of future development of metabolic disease

## **“Metabolically Obese Normal Weight” Phenotype**

- Defined as normal-weight individuals who express metabolic diseases typically associated with an increased in body fat
- Some individuals may express adiposopathy with increased body fat not outside the upper range of normal
- Some individuals may have dysfunction of other body organs that are disharmonious in their physiologic interactions with adipose tissue (“metabolic inflexibility”)

# Demographic (Gender and Race) Obesity Paradox

**Are women at a “paradoxically” lower age-adjusted cardiovascular disease risk than men?**

**Are some races “paradoxically” at increased risk for metabolic diseases for the same amount of body weight?**

## **For the Same Age and Weight, Men Have a Higher Rate of CVD Compared to Women**

- Cardiovascular disease (CVD) is the most common cause of death in women and men
- During positive caloric balance:
  - Men often expand fat deposition via the more pathogenic adipocyte hypertrophy and android or “apple” fat distribution.
  - Women often expand fat deposition via the less pathogenic adipocyte proliferation and gynoid or “pear” fat distribution

# Demographic (Gender and Race) Obesity Paradox

**Are women at a “paradoxically” lower age-adjusted cardiovascular disease risk than men?**

**Are some races “paradoxically” at increased risk for metabolic diseases for the same amount of body weight?**

**For the Same Increase in Body Fat, Individuals of Asian Descent Have an Increased Risk for Type 2 Diabetes Mellitus, Metabolic Syndrome, and Cardiovascular Disease Compared to Other Races**

- Greater adipocyte size; reduced number of adipocytes
- Increased visceral adiposity
- Increased free fatty acid and leptin levels
- Increased pro-inflammatory factors (e.g., C-reactive protein), and decreased anti-inflammatory factors (e.g., adiponectin)
- Increased insulin resistance
- Asians require a lower cut-off point for the clinical determination of overweight and obesity

Can adding body fat “paradoxically” treat metabolic diseases typically associated with too much body fat?

Does an increase in fat mass always predispose to metabolic disease?

Does a decrease in fat mass always improve metabolic disease?

- **Peroxisome proliferator-activated receptor agonists (thiazolidinediones)** increase the proliferation and differentiation of adipocytes, increasing fat mass, providing increased adipocyte functionality, and are approved as glucose-lowering agents
- **Weight loss with human immune virus antiretroviral (HIV) therapy** may result in HIV lipodystrophy, with impairment in adipocyte differentiation, reduction in mean fat cell size, possible decrease in adipocyte proliferation, decrease in subcutaneous adipose tissue accumulation, relative increase in visceral adipose tissue accumulation, and increased risk of hyperglycemia and dyslipidemia.



# Therapeutic Obesity Paradox

**Can adding body fat “paradoxically” treat metabolic diseases typically associated with too much body fat?**

**Does an increase in fat mass always predispose to metabolic disease?**

**Does a decrease in fat mass always improve metabolic disease?**

## **Transplantation of Fat in Lipoatrophic Mice**

- Lipoatrophic mice have virtually no white adipose tissue
- Severe hyperglycemia.
- Fat transplant improves hyperglycemia, hyperinsulinemia, and muscle insulin sensitivity

## **Liposuction of Subcutaneous Adipose Tissue (SAT)**

- Removal of SAT does not improve hyperglycemia, high blood pressure, and dyslipidemia

**Why are individuals who are modestly overweight often reported to have a better prognosis after cardiovascular disease (CVD) events and cardiovascular procedures?**

## **The Obesity CVD Paradox May Be Risk-factor Dependent**

- Individuals who are modestly overweight may have improved CVD prognosis only if they are physically fit
- Cigarette smoking decreases body weight (especially with chronic lung disease), but increases CVD risk

# Cardiovascular Disease Outcomes Obesity Paradox

**Why are individuals who are modestly overweight often reported to have a better prognosis after cardiovascular disease (CVD) events and cardiovascular procedures?**

## **The Obesity CVD Paradox May Reflect Different Cardiovascular Pathologies**

- The pathophysiology applicable to obesity and adiposopathy may differ from other pathophysiologies leading to CVD events; the prognosis may differ as well
- Inherent vasculopathies predisposing to CVD events may be independent of body weight, be of greater severity, and have poorer outcomes compared with CVD events that occur due to obesity
- Familial hypercholesterolemia (FH) is an inherited disorder that is independent of body weight, results in severe elevations in cholesterol, and which has a disproportionately high rate of (premature) CVD morbidity and mortality
- A patient with FH who is a heavy smoker and not overweight may be at greater risk for an ST segment elevated myocardial infarction (STEMI) than a nonsmoker without FH who is overweight or with obesity

**Why are individuals who are modestly overweight often reported to have a better prognosis after cardiovascular disease (CVD) events and cardiovascular procedures?**

## **The Obesity CVD Paradox Might Be Partially Explained by Enhanced Cardiovascular Autorepair Potential**

- Adipocytes, blood vessels, and cardiomyocytes share a similar lineage of mesenchymal stem cells
- Individuals who are overweight often have a greater reservoir of adipose tissue mesenchymal cells
- After an acute CVD event, increased circulating reparative mesenchymal cells might conceivably migrate to the injured myocardial site, and assist with cardiovascular tissue repair

# Cardiovascular Disease Outcomes Obesity Paradox

**Why are individuals who are modestly overweight often reported to have a better prognosis after cardiovascular disease (CVD) events and cardiovascular procedures?**

## **The Obesity CVD Paradox Might Be Partially Explained by a Disproportional Attention Directed towards CVD Prevention among Patients with Obesity**

- Patients with obesity often have medical conditions that prompt earlier access and more frequent access to medical care
- In the global management of patients with obesity, preventative interventions may be disproportionately implemented, perhaps involving earlier and more frequent CVD diagnostic procedures, and initiation of therapeutic agents proven to reduce CVD
- Obesity increases the risk of type 2 diabetes mellitus (T2DM); while it remains unclear the degree by which glucose-lowering reduces CVD risk, patients with T2DM are often treated with antihypertensive, lipid-altering, and perhaps antithrombotic agents that reduce CVD morbidity and mortality

# Atherosclerosis “Outside-to-In” Obesity Paradox

## What is the role of pericardiac and perivascular adipose tissue in promoting atherosclerosis?

Atherosclerosis is most often described as an “*inside-to-in*” pathogenic process wherein atherogenic apoB containing lipoproteins enter the subendothelia, become oxidized, and then help promote inflammation, plaque formation, and ultimately, plaque rupture leading to CVD events

## What is the role of pericardiac and perivascular adipose tissue in promoting atherosclerosis?

### An “Outside-to-in” Atherogenic Model Suggests That Adiposopathic Adipose Tissue Surrounding the Heart and Arteries Also Contributes to Atherosclerosis

- Coronary calcium correlates to epicardial fat
- Coronary calcium scoring is used to assess atherosclerosis
- Adipose tissue surrounding the heart and arteries may serve as a local supplier of toxic, free fatty acids to the myocardium, and thus contribute to “fatty heart”
- Pericoronary adipose tissue may serve as a supply site for oxidized low density lipoproteins in coronary plaques, possibly via transport through the interstitial space

## What is the role of pericardiac and perivascular adipose tissue in promoting atherosclerosis?

### An “Outside-to-in” Atherogenic Model Suggests That Adiposopathic Adipose Tissue Surrounding the Heart And Arteries Also Contributes to Atherosclerosis

- Adipose tissue surrounding the heart and arteries may secrete factors that alter endothelial cells and function
- “Sick” epicardial adipose tissue may have reduced anti-inflammatory secretions (e.g., reduced adiponectin) and increased pro-inflammatory adipokine secretion that can be transported into vessel walls via transcellular passing or diffusion (vasocrine regulation)
- Adipose tissue surrounding the heart and arteries may help supply macrophages to an expanded adventitial vas vasorum, resulting in even greater pro-atherogenic inflammatory signaling



## How do clinicians best navigate the apparent paradox of “blame” versus “accountability” in obesity management?

- Individual responsibility can encompass both “blame” and “accountability”
- “Blame” often goes beyond assigning responsibility and often leads to condemnation and accusations, with the intent to elicit guilt
  - Promoting guilt is often counterproductive in changing behavior
- “Accountability” most often refers to record keeping and shared decision-making
  - Promoting accountability is a critical component towards modifying behavior
  - A lack of acknowledging individual responsibility may invite counterarguments and reduce feelings of empathy by others
  - A reluctance to recommend accountability via record keeping and shared decision-making may deprive the patient of an important behavior modification technique

# Stress and Obesity: Cause and Effect

# Psychological or Medical Stress

## Stress Responses

- Cognitive changes
  - Increased (e.g., some cases of emergent stress)
  - Decreased (e.g., some cases prolonged stress)
- Physiological changes
- Behavioral changes
- Pain
  - Potential analgesia with emergent stress
  - Potential worsening of pain with chronic stress

# Psychological or Medical Stress: Endocrine Response

## Emergent “Fight or Flight” Response

(Increased Sympathomimetic Activity)

- Increase in short-term sympathetic nervous system activation
- Increased catecholamines (e.g., norepinephrine and epinephrine)
- Cardiovasculopulmonary responses
  - Increased blood pressure
  - Vasoconstriction
  - Increased heart rate and contractility
  - Impaired blood flow to kidney
  - Bronchial dilation
- Metabolic responses
  - Potential increase in glucose levels (increased insulin resistance, increased hepatic glycogenolysis, and increased hepatic gluconeogenesis)
  - Increased adipose tissue lipolysis

# Psychological or Medical Stress: Endocrine Response

## Submit and Stay Response

(Increased hypothalamic pituitary axis activity)

### Increased Longer-term Stress Hormone Release

- Increased corticotropin-releasing hormone
- Increased adrenocorticotropin
- Increased arginine, vasopressin, and oxytocin
- Increased blood cortisol

### Metabolic Responses to Increased Cortisol

- Potential increase in glucose levels (increased insulin resistance and increased hepatic gluconeogenesis)
- Increased blood pressure
- Increased adipose tissue lipolysis (cortisol is a catabolic hormone)

# Medical or Psychological Stress: Immune Response

## Acute Response (Catecholamine-mediated)

- Immune effects can be mixed, but in general, may enhance immune response:
  - Demargination of leukocytes from vascular endothelia increases leukocyte blood concentration
  - Increased:
    - Innate immune response
    - Adaptive immune response
    - T-lymphocyte cytokine response

## Prolonged Response (Glucocorticoid-mediated)

- Immune effects can be mixed, but in general, may dysregulate immune response:
  - Decreased leukocyte mobilization with decrease in leukocyte blood concentration
  - Decreased:
    - Innate immune response
    - Adaptive immune response
    - T-lymphocyte cytokine response

# Chronic Psychological Stress and Eating Behavior

## Limbic System

(Thalamus, hypothalamus, amygdala, hippocampus)

- Chronic stress-induced endocrinopathies and immunopathies may adversely affect the limbic system
- Hypothalamic dysfunction (such as with trauma) is an important cause of obesity

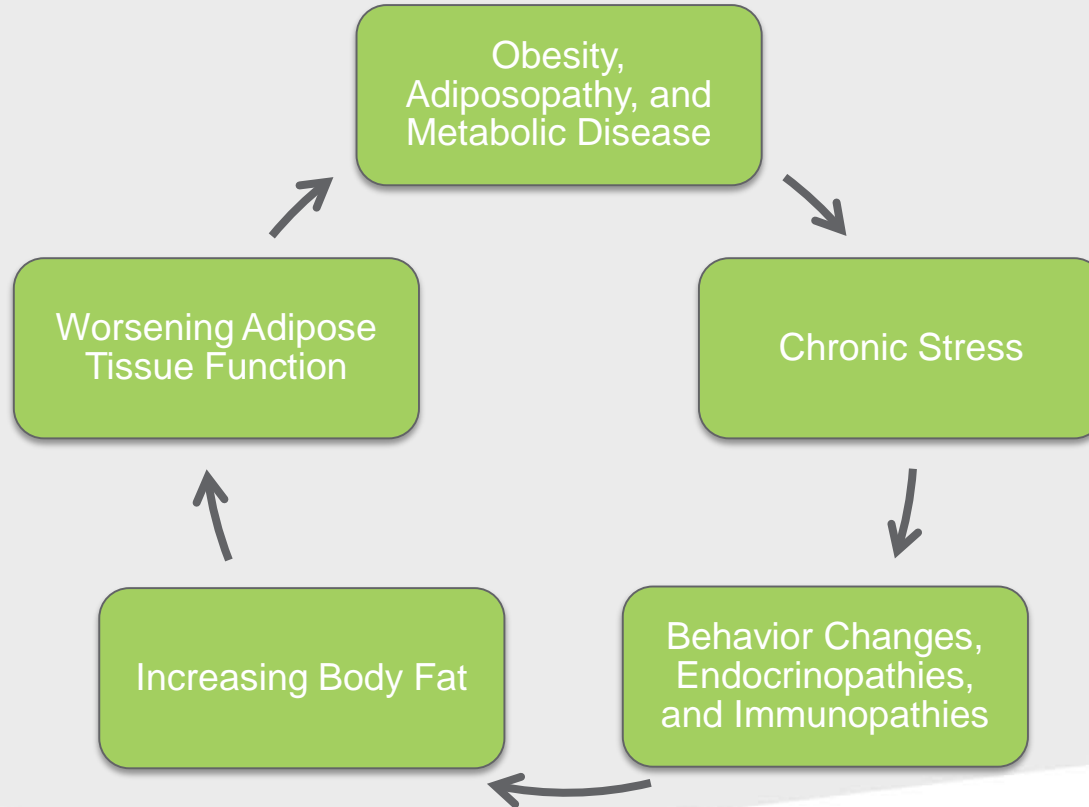
## Cerebrum

(Frontal, parietal, occipital, and temporal lobes)

- Priority replacement: personal, work, or emotional priorities may overtake priorities relative to nutrition, physical activity, and/or health
- Chronic stress-induced endocrinopathies and immunopathies may adversely affect the cerebrum
- Gourmand Syndrome
  - While not necessarily a stress disorder, Gourmand Syndrome is illustrative of how cerebral disorders may affect eating behaviors
  - Occurs with damage to right frontal lobe (trauma/stroke)
  - Post-injury passion for gourmet foods

Enhanced desire for hyperpalatable foods

# Adiposopathy Stress Cycle





# Patient Evaluation: History

## Medical History and Review of Systems

- Age, gender, race, ethnicity
- Fat mass disease (i.e., osteoarthritis, sleep apnea)
- Adiposopathy (i.e., type 2 diabetes mellitus, high blood pressure)
- Eating disorders
- Mental stress
- Sleep pattern
- Other medical and surgical conditions
- Medication and food allergies
- Medications that may affect body weight
- Cigarette smoking
- Alcohol intake
- Recreational drug use (e.g., marijuana, cocaine)

## Family History

- Family members affected by obesity
- Applicable familial medical diseases

## Support Systems

- Person who selects and purchases food
- Availability and involvement of family and friends
- Educational access to healthy nutrition and physical activity (e.g., current knowledgebase, availability of Internet, knowledge centers, etc.)

## Socioeconomic and Cultural History

- Economic status
- Social status
- Cultural background
- Occupation
- Family structure
- Parenting behavior
- Marital status
- Living situation
- Abuse (physical, mental, sexual)
- Geographic location (e.g., urban food desert)

## Meals and Snacks

- Timing
- Frequency (via questionnaire)
- Nutritional content
- Preparer of food
- Access to foods
- Location of home food consumption (i.e., eating area, television, computer, etc.)
- Location of away food consumption (i.e., workplace restaurants, fast food, etc.)

## Behavior

- Previous nutritional attempts to lose weight and/or change body composition
  - If unsuccessful or unsustainable, what were short- and long-term barriers to achieving or maintaining fat weight loss
- Triggers (hunger, cravings, anxiety, boredom, reward, etc.)
- Nighttime eating
- Binge eating
- Emotional eating
- Family/cultural influences
- Community influences
- Readiness for change

## Records

- Food and beverage diary, including type of food or beverage consumed and amount consumed
  - 72-hour recall
  - Keep food and beverage record for a week and return for evaluation
- Electronic application tools

# Physical Activity History

- Success and/or failure of previous physical activity/exercise efforts
- If no longer engaged in a routine physical activity/exercise regimen:
  - When? (Date of change)
  - What? (Cause of change)
  - Why? (Identify barriers to re-engagement)
- Current physical activity (FITTE)
  - Frequency
  - Intensity
  - Time or Duration
  - Type
  - Enjoyment (physical activity/exercise preferences)
- Current fitness level, endurance capacity, mobility, and equipment needs
- Access to locations amenable to increased physical activity/exercise (e.g., gym, workplace, exercise facilities, bicycle paths and walk ways, urban or rural home setting)
- Perceived barriers to increased physical activity

# Physical Activity History

Examples of common medical conditions that should be evaluated before prescribing an exercise program:

- Diseases of the heart, lung, musculoskeletal, and other body systems
- Metabolic diseases having potential risks with increased physical activity:
  - Atherosclerotic coronary heart disease (worsening ischemia)
  - Diabetes mellitus (hypoglycemia)
  - High blood pressure (increase blood pressure with resistance training)

# Routine Preventive Medical Care

Ensure individual with overweight or obesity receives standard preventive medical care, which, depending upon gender and age, may include:

- Breast exam (and mammogram as applicable)
- Pelvic exam
- Pap smear
- Testicular exam
- Rectal exam and stool for occult blood (sigmoidoscopy or colonoscopy as applicable)
- Immunizations

# Patient Evaluation: Physical Exam

# Physical Exam

## Vital Signs

- Height with bare or stocking feet measured with a stadiometer
- Weight using calibrated scale and method consistent from visit to visit (i.e., light indoor clothing or gown)
- Body mass index
- Waist circumference
  - Standing using superior iliac crest
  - May not provide additional diagnostic information among patients with BMI > 35 kg/m<sup>2</sup>
- Blood pressure using appropriately sized cuff
- Pulse
- Neck circumference

## General Physical Exam

- Comprehensive physical exam
- Special emphasis on physical exam of the nose, throat, neck, lung, heart, abdomen, musculoskeletal system, and integument



# Patient Evaluation: Laboratory and Diagnostic Testing

# Laboratory: Routine

## Adiposity-relevant Blood Testing

- Fasting blood glucose
- Hemoglobin A1c
- Fasting lipid levels
  - Triglycerides
  - Low-density lipoprotein (LDL) cholesterol
  - High-density lipoprotein (HDL) cholesterol
  - Non-HDL cholesterol
- Liver enzymes and other liver blood tests
  - Aspartate aminotransferase (AST)
  - Alanine aminotransferase (ALT)
  - Alkaline phosphatase
  - Total bilirubin
- Electrolytes (i.e., potassium, sodium, calcium, phosphorous, etc.)
- Renal blood testing (i.e., creatinine, blood urea nitrogen, etc.)
- Uric acid
- Thyroid stimulating hormone (TSH)
- Vitamin D levels

## General Laboratory Testing

- Complete blood count
- Urinalysis
- Urine for microalbumin

# Laboratory: Individualized Blood Testing

- Glucose tolerance testing
- Fasting insulin testing
- Fasting proinsulin, C-peptide, and insulin if hyperinsulinemia is suspected as a secondary cause of obesity (e.g. insulinoma, nesidioblastosis, etc.)
- One milligram (mg) overnight dexamethasone cortisol suppression test, 24-hour urine collection for (free) cortisol, or repeated measures salivary cortisol collection at 11:00 PM if endogenous hypercortisolism is suspected as a secondary cause of obesity
- Prolactin, estradiol, follicle-stimulating hormone, luteinizing hormone, and pregnancy test in women with unexplained oligomenorrhea or amenorrhea
- Testosterone and other androgen levels (i.e., dehydroepiandrosterone sulfate/DHEAS) for women with hirsutism or polycystic ovarian syndrome
- Testosterone (and if low to a clinically significant degree: possibly prolactin, follicle-stimulating hormone, and luteinizing hormone) for men with impotence or physical findings of hypogonadism
- Apolipoprotein B and/or lipoprotein particle number, especially if triglyceride levels are elevated
- Iron studies (iron, total iron binding capacity, ferritin)
- High-sensitive C-reactive protein (hs-CRP)

# Diagnostic Testing: Individualized

- Magnetic-resonance imaging or computed tomography of the brain if a structural lesion of the pituitary/hypothalamus is suspected (i.e., craniopharyngioma, pituitary tumor)
- Resting electrocardiogram
- Cardiac stress testing
- Echocardiogram
- Coronary calcium scores
- Cardiac positron emission tomography imaging (computed tomography)
- Ankle-brachial index
- Sleep studies
- Imaging studies of the liver (i.e., ultrasound)
- Anaerobic threshold/ $\text{VO}_2$  testing
- Resting metabolic rate (RMR)

# Diagnostic Testing: Individualized

## Body Composition

- Dual-energy X-ray absorptiometry (DEXA), ideally with visceral fat assessment
- Bioelectric impedance
- Near-infrared interactance
- Whole-body air displacement plethysmography (BOD POD)
- Myotape measurements (to assess muscle mass as well as wrist and neck size for use in percent body fat equations)
- Caliper percent body fat measurements (e.g., three-site skinfold calculations)
- Underwater weighing
- Quantitative magnetic resonance (QMR)
- Computerized tomography (single slice or volume method)
- Deuterium dilution

## Emerging Science Testing

- Leptin
- Adiponectin
- Leptin-to-adiponectin ratio
- Free fatty acids
- Immune markers
  - Tumor necrosis factor
  - Interleukin 1 and 6
- Infectious testing
  - Gut microbiota
  - Adenovirus assays
  - Evaluation for other microbes

# Body Composition

# Body Compartments: Fat-free Mass versus Lean Body Mass

**Fat free mass**\* is total body mass less any body fat. It includes:

- Water
- Mineral
- Protein and glycogen

\*Usually what is directly measured by two compartment techniques, such as DEXA

**Lean body mass**\* is total body mass less adipose tissue. It includes:

- Water
- Mineral
- Protein and glycogen
- Essential fat in organs, central nervous system, and bone marrow

\*Usually differs from fat-free mass by only ~5%, slightly less in men, slightly more in women)

# Body Compartments

## Two Compartment:

- Fat mass
- Fat-free mass
- Can be assessed by:
  - Dual-energy x-ray absorptiometry (DEXA)
  - Underwater, or hydrostatic weighing
  - Air displacement plethysmography (BOD POD)
  - Bioelectrical impedance (BIA)
  - Skin fold thickness-derived calculations
  - Deuterium dilution

## Three Compartment:

- Fat mass
- Total body water
- Fat-free dry mass (bone and protein)

(Although DEXA measures two compartments at a time, it can assess the “three compartments” of fat mass, lean soft tissue mass, and bone mineral mass. Similarly, assuming total body water is a constant proportion of fat free mass may allow BIA to estimate more compartments (e.g., fat free mass, fat mass, and total body water)

## Four Compartment:

- Fat mass
- Total body water
- Bone mineral
- Protein
- Can be assessed by combination of two compartment assessments, such as hydrostatic weighing, plus dual-energy x-ray absorptiometry (DEXA), plus deuterium dilution or hydrostatic weighing, plus DEXA, plus bioimpedance spectroscopy

## Six Compartment:

- Fat mass
- Total body water
- Bone mineral
- Non-Bone mineral
- Protein
- Glycogen
- **Fat mass** = stored and essential lipids
- **Water** = usually largest single component of body mass
  - ~55% intracellular
  - ~45% extracellular
- **Minerals** = calcium, phosphorous, magnesium, etc.
- **Protein & glycogen** = “residual”



# Body Compartments: Measurement Summary

Method	Accuracy*	Expense	Limitations
Calipers	User dependent	Inexpensive	Not optimal measuring technique for patients with very high body mass index
Dual-energy X-ray absorptiometry (DEXA)	Accurate	Relatively expensive	Not all DEXA (1) distinguish visceral versus subcutaneous fat, or (2) accommodate patients with very high body mass index
Air displacement (BOD POD)	Accurate with some potential variability	Inexpensive	Clothing and hydration dependent
Bioelectrical impedance	Accurate with some potential variability	Inexpensive	Hydration dependent
Under water weighing densitometry	Accurate	Relatively inexpensive	Time consuming, requires water submersion, and depends upon adequate lung exhalation
Computerized Tomography / Magnetic Resonance Imaging	Accurate	Expensive	Not all CT & MRI can accommodate individuals with very high body mass index
Deuterium dilution hydrometry	Accurate	Relatively inexpensive	Not readily available for commercial use

\*The accuracy of all methods depends on the degree of training, and quality of equipment.

# Body Compartments: Measurements

- **Cadaver analysis** is the only true “gold standard” for body composition assessment
- **Body weight or body mass index** are not direct measures of body composition
- **Skinfold calipers** can be used to estimate proportion of body fat
- **Hydrodensitometry (underwater weighing)** estimates proportion of body fat based upon the Archimedes principle that the buoyant force of a body immersed in fluid is equal to the weight of the displaced fluid.
  - Lean tissues (bone and muscle) are more dense than water, and a person with more muscle will weigh more underwater
  - Fat is less dense than water, and a person with more body fat will weigh less underwater
  - Two-compartment model

# Body Compartments: Dual Energy X-Ray Absorptiometry (DEXA)

- Depending on software, DEXA can measure both body fat and bone-mineral density
- Low risk of radiation exposure, ~5% of standard chest X-ray
- Results may vary from machine to machine, and technician to technician
- Greatest accuracy achieved with appropriate user training, standard operating procedures, and routine calibration
- Greatest utility may be for serial measurements on the same machine by same technician
- DEXA can measure abdominal visceral fat

# Body Compartments: Dual Energy X-Ray Absorptiometry (DEXA)

- Monoenergetic X-Ray measures an homogenous absorber component
- Dual-energy X-Ray quantitates densities of two absorber components
- In body areas with no bone, DEXA can measure the “two compartments” of fat mass and lean soft tissue mass
- In body areas with bone, DEXA can measure the “two compartments” of soft tissue mass and bone mineral mass
- By combining these two analyses, DEXA can provide data regarding three compartments (fat, lean tissue, and bone)

# Body Compartments: Whole Body Plethysmography (BOD POD)

- Plethysmos = Greek for enlargement
- Measures body volume by air displacement
- Displacement principles similar to water displacement by hydrodensitometry weighing
- No strenuous exercise two hours before procedure
- No eating or drinking one hour before procedure
- Light clothing (tight swimsuit is preferred)
- Two-compartment model

# Body Compartments: Bioelectrical Impedance Analysis (BIA)

- BIA measures impedance by body tissues to flow of electrical current (electrical resistance = impedance)
- Electrical current passes more easily through water and muscle and less easily through fat
- Many BIA analyses assume fat-free mass has a constant proportion of water (~70%)
- Preparation: remove all metal, eliminate body waste prior to procedure, and avoid exercise causing sweat eight hours before, avoid large amounts of caffeine or alcohol 12 hours before
- While often considered a two-compartment model (fat versus fat-free mass), the assumption that total body water is a constant proportion of fat-free mass may allow estimation of more compartments (e.g., fat-free mass, fat mass, and total body water)

# Body Compartments: Deuterium Dilution

- In adults, intra and extracellular water constitutes ~70% of Fat Free Mass (FFM)
- With an estimate of total body water (TBW), the amount of Fat Mass can, in turn, be estimated via Body Mass minus FFM
- Deuterium is a stable (non-radioactive) isotope of hydrogen ( $^2\text{H}$ ), administered as deuterium oxide ( $^2\text{H}_2\text{O}$ )
- After mixing with body water, deuterium is eliminated from the body in urine, saliva, sweat and human milk
- One technique is to collect post-dose saliva samples 3 and 4 hours after the deuterium oxide is administered
- While correction is required for some deuterium that distributes to non aqueous tissues, TBW (kg) can be calculated by the dose of  $^2\text{H}_2\text{O}$  (mg) /  $^2\text{H}$  in saliva (mg/kg) less baseline (pre-dose)  $^2\text{H}$
- Two-compartment model

## Body Compartments: CT and MRI

- Both computerized tomography (CT) and magnetic resonance imaging (MRI) accurately measure adipose tissue and skeletal muscle
- CT increases exposure to ionizing radiation, a potential clinical concern with repeat CT testing
- MRI = No radiation exposure
- Both CT and MRI accurately assess visceral and hepatic fat



# Energy Expenditure

# Energy Expenditure: Components Overall

In moderately sedentary individuals, components of total energy expenditure:

- 70% resting metabolic rate
- 20% physical activity
- 10% dietary thermogenesis

# Energy Expenditure: Component Variability

With the exception of individuals engaged in physical exercise outside typical study populations, the coefficient of variation in humans regarding energy expenditure:

- Resting metabolic rate = 5 – 10%
- Physical exercise = 1 – 2%
- Diet-induced thermogenesis = 20%

# Energy Expenditure: Component of NEAT

Often the widest variance in energy expenditure among individuals is non-exercise activity thermogenesis (NEAT)

- Working, fidgeting, and other activities of daily living, not including physical exercise
- Can range between 150-500 kcal/day, which is often greater than bouts of physical exercise
- NEAT can help explain perception that some individuals:
  - Are “naturally skinny”
  - Can maintain body weight compared to others, even with the same caloric intake and same exercise activity

# Energy Expenditure: Metabolic Rate

## Basal Metabolic Rate

- Energy expended while fasting, rested, and supine in a thermoneutral environment
- Increased with increased body weight

## Resting Metabolic Rate

- Energy expended at rest, does not require overnight supine measurement
- Increased with increased body weight

# Energy Expenditure: Measurement via Direct and Indirect Calorimetry

## Direct Calorimetry

- Measures heat generated by an organism
- Measures differences in temperature of water entering and leaving the chamber via a heat exchanger
- Value of generated heat can estimate total energy expenditure
- Enclosed chamber/calorimeter

## Indirect Calorimetry

- Estimates basal energy expenditure and resting energy expenditure via measuring oxygen consumption and carbon dioxide production
- A metabolic cart is an electronic device, typically on a mobile push “cart,” that measures O<sub>2</sub> consumption (VO<sub>2</sub>) and CO<sub>2</sub> production (VCO<sub>2</sub>)
  - Computer system
  - Monitor
  - Breathing tubes

# Energy Expenditure: Direct Calorimetry Formula

Total energy expenditure = ~60% from heat + ~40% from ATP production



- Utilized by direct calorimetry
- Requires knowledge of generated heat, such as through the differences in water temperature entering and leaving a chamber

# Energy Expenditure: Indirect Calorimetry Formulas

**Abbreviated Weir equation: Energy expenditure =  $VO_2 + VCO_2$**   
[Weir equation: Energy expenditure =  $VO_2 + VCO_2 - \text{Nitrogen (urine)}$ ]



- Utilized by indirect calorimetry
- Requires knowledge of:
  - Oxygen consumption ( $VO_2$  in -  $VO_2$  out)
  - $CO_2$  production (expired  $CO_2$ )
  - (Nitrogen level for full Weir equation)
- Assumes  $FIO_2 + FIN_2 = 1$
- Inhaled ambient air = 21%  $O_2$  + 79%  $N_2$  + less than 1%  $CO_2$



# Energy Expenditure: Indirect Calorimetry Formulas

$$\text{Respiratory quotient (RQ)} = \text{CO}_2 \text{ production} / \text{O}_2 \text{ consumption}$$



- Utilized by indirect calorimetry to assess proportion of metabolized fuels
- RQ for carbohydrates = 1.0
- RQ for fats = 0.7
- RQ for proteins = variable
- Overfeeding = increase in RQ to as high as 1.3 due to lipogenesis
- Underfeeding and ketosis = decrease in RQ due to lipolysis
- In treating severe chronic obstructive lung disease, increasing the proportion of dietary fats (relative to carbohydrates) decreases CO<sub>2</sub> production and decreases amount of energy spent on respirations
- Higher RQ may be predictive of future increase in fat mass

# Energy Expenditure: Measurement by Doubly Labeled Water

## Background

- Estimates carbon dioxide production, which is reflective of energy expenditure via tissue respiration (carbon dioxide from body cells is exchanged for oxygen in blood)
- Oxygen component will decay quicker because oxygen is lost as both CO<sub>2</sub> (in expired air) + H<sub>2</sub>O (urine and sweat)
- Hydrogen component will decay slower because hydrogen is lost only as H<sub>2</sub>O

## Measurements

- Doubly labeled water is administered orally using traceable hydrogen isotope (deuterium or <sup>2</sup>H) and oxygen isotope (<sup>18</sup>O)
- The difference found in body fluids (sampling urine, saliva, or blood) is used to calculate the body's production of CO<sub>2</sub> over time

# Energy Expenditure: Measurement by Non-calorimetric Methods

- **Resting metabolic rate energy expenditure** can be estimated by calculations
  - Age
  - Gender
  - Weight
  - Height
  - Harris-Benedict and Mifflin St. Jeor Equation = age, gender, weight, height
  - Maintenance of Hemodialysis Energy (MHDE) Equation for dialysis patients
- **Physical activity energy expenditure** can be estimated by:
  - Physical activity records as input data to validated energy-expenditure tables
  - Calculations based on heart rate
  - Motion sensors (e.g., pedometers)
  - Accelerometers (uniaxial, bi-axial, tri-axial)
    - Wearable technologies such as watches or attachment to belt around waist or ankle

# Treatment

## Medical Management and Coordination

Nutrition

Physical Activity

Behavior Therapy

Pharmacotherapy

Bariatric Surgery

# Treatment of Adult Patients with Overweight or Obesity

- Treat adipocyte and adipose tissue dysfunction, which treats sick fat disease (SFD or adiposopathy)
- Treat excessive body fat, which treats fat mass disease (FMD)
- Treating diseases due to increased body fat and its adverse metabolic and biomechanical consequences may improve patient health, quality of life, body weight, and body composition

# Identify and Manage Secondary/Contributing Causes of SFD and FMD

## Conditions that may promote fat mass gain:

### Genetic Syndromes

- Isolated (i.e., Prader Willi)
- Familial (melanocortin 4 receptor deficiency)

### Medical Conditions

- Hypothalamic damage
- Immobility
- Insulinoma
- Some cases of untreated hypothyroidism
- Hypercortisolism (Cushing's disease)
- Sleep disorders

### Psychological and Behavioral Conditions

- Mental stress
- Depression
- Anxiety
- Post-traumatic stress syndrome
- Binge-eating disorder
- Night-eating syndrome
- Eating disorders not otherwise specified

# Concomitant Medications



# Identify and Manage Concomitant Pharmacotherapy That Might 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

# Metformin

## **May help improve adiposopathic disorders:**

- Insulin resistance
- Polycystic ovarian syndrome
- Fatty liver
- Cardiovascular disease (especially when compared to sulfonylurea)

## **May help treat complications of other concurrent drug treatments:**

- Antipsychotic-related weight gain
- Human immunodeficiency virus (HIV) protease inhibitor-associated abnormalities (i.e., HIV lipodystrophy)

## **May help reduce the overall cancer rate and help improve the treatment of multiple cancers:**

- Colon
- Ovary
- Lung
- Breast
- Prostate

**May enhance effects of gastrointestinal hormones applicable to weight loss (e.g., glucagon-like peptide-1, Peptide YY)**

# Identify and Manage Concomitant Pharmacotherapy That Might 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

# Identify and Manage Concomitant Pharmacotherapy That Might Alter Body Weight

## 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 (secondary amines)
  - Desipramine
  - Nortriptyline
  - Protriptyline
- Some selective serotonin reuptake inhibitors
  - Citalopram
  - Escitalopram
  - Fluoxetine
  - Sertraline
- Some serotonin and norepinephrine re-uptake inhibitors
  - Desvenlafaxine
  - Duloxetine
  - Venlafaxine
- Some irreversible monoamine oxidase inhibitors (i.e., tranylcypromine)

# Identify and Manage Concomitant Pharmacotherapy That Might 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

# Identify and Manage Concomitant Pharmacotherapy That Might Alter Body Weight

## Antipsychotics

May substantially increase body weight:

- Clozapine
- Olanzapine
- Zolpidem

May somewhat increase body weight:

- Asenapine
- Chlorpromazine
- Iloperidone
- Paliperidone
- Quetiapine
- Risperidone
- Sertindole
- 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

# Identify and Manage Concomitant Pharmacotherapy That Might 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

# General Nutrition



The principles outlined here pertain to general nutrition and may not apply to the individual patient.

# Carbohydrates

- Carbohydrates contain 4 kcal/gram
- Carbohydrates can serve as a source of energy and as well cellular structural elements such as hyaluronic acid and proteoglycans
- Carbohydrates may contain sugars, starch and/or fiber
- The digestion and absorption of carbohydrates results in monosaccharide (glucose, fructose, galactose) molecules
- Carbohydrates are not an essential macronutrient, as the liver and kidney can synthesize glucose
- Calorie deficiency can lead to marasmus (insufficient calories), but there is *no known carbohydrate deficiency*
- USDA DRI for carbohydrate is 130 grams/day

# Fat

- Fat contains 9 kcal/gram
- Fats or lipids are a diverse group of compounds used as an energy source and for many metabolic processes:
  - Immune response (omega-3 fatty acids)
  - Cell membrane structure (phospholipids)
  - Brain tissue (cerebrosides)
  - Synthesis of bile acid, cholesterol, vitamin D, steroid hormones
  - Insulation
- Several fatty acids cannot be made by the body and these “essential” fatty acids must be consumed in the diet
- Fatty acid deficiency can lead to a disease state
- USDA DRI for fat is at least 30 grams/day

# Protein

- Protein contains 4 kcal/gram
- Protein contains amino acids and serves as the major structural building blocks of the human body: bone, muscle, skin, brain, nucleic acids
- Essential amino acids are those which cannot be made by the human body and must be consumed in the diet
- Some amino acids can be used as an energy source (converted to glucose or ketones when needed)
- Protein deficiency can lead to a disease state (Kwashiorkor is sufficient calories but insufficient protein)
- USDA DRI (Dietary Reference Intake) for protein is 0.8 to 2.0 grams/kg/day depending upon age, gender, physical activity

# Insulin Controls Fat Metabolism

- Insulin promotes fatty acid and triglyceride synthesis (lipogenesis) and storage, and it inhibits fat breakdown (lipolysis)
- Foods that cause a rise in blood glucose, such as sugars, starches, or amino acids will stimulate the secretion of insulin from the pancreas
- A diet that lowers the amount of insulin secreted is beneficial for weight loss

# Nutritional Therapy for Obesity

# Principles of Healthy Nutrition

## Limit:

- Highly processed foods of minimum nutritional value: sweets, “junk foods,” cakes, cookies, candy, pies, chips
- Energy-dense beverages: sugar-sweetened beverages, juice, cream

## Encourage:

- Consumption of healthy proteins and fats, vegetables, leafy greens, fruits, berries, nuts, legumes, whole grains
- Complex carbohydrates over simple sugars: Low glycemic index over high glycemic index foods
- High-fiber foods over low-fiber foods
- Reading labels rather than marketing claims

Managing the *quality* of calories is important when reducing the quantity of calories, such as during weight loss.

Factors related to improved outcomes:

Evidence-based

Quantitative

Patient adherence

Patient preference

Qualitative



# Choosing Nutritional Therapy for Obesity

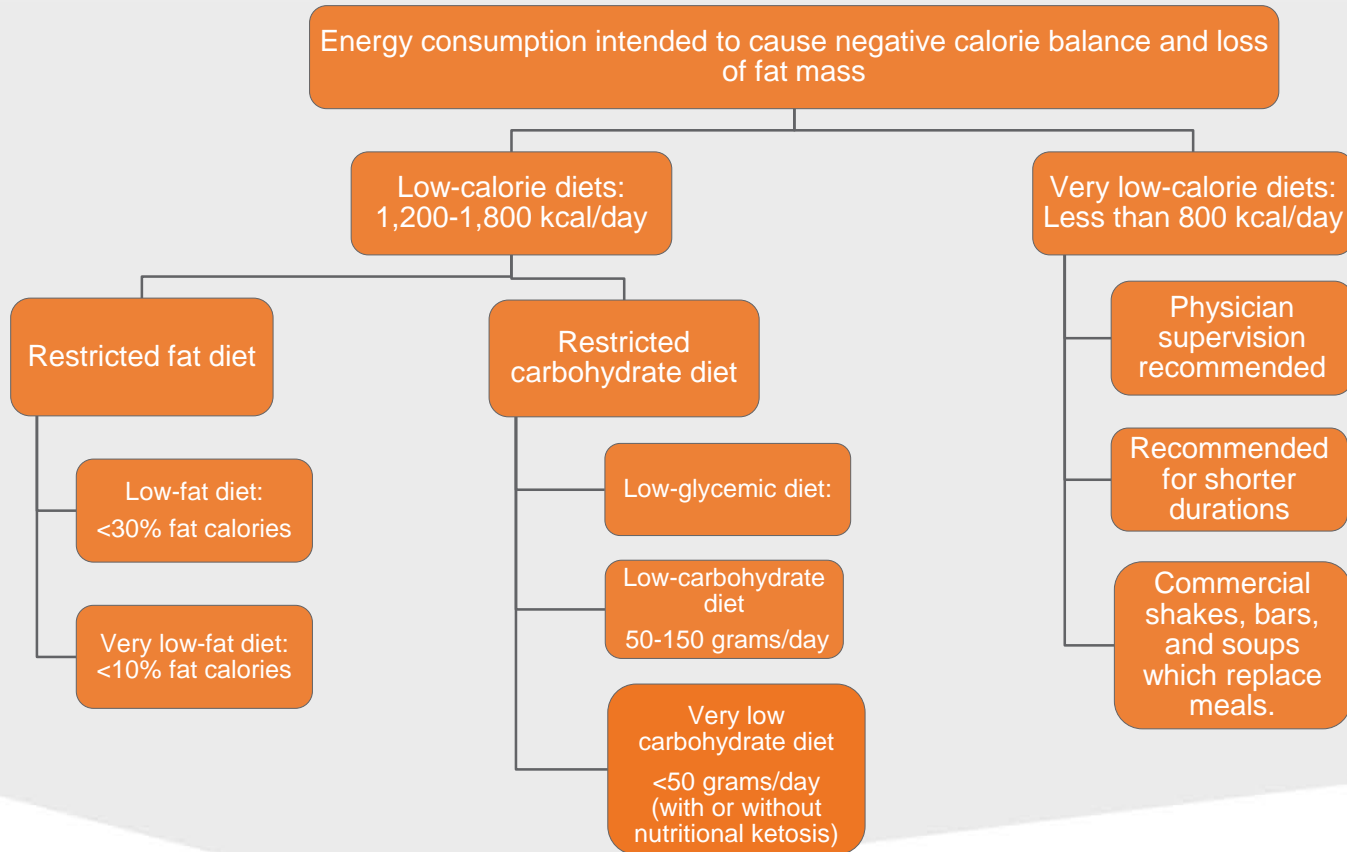
The most appropriate nutritional therapy for weight loss should be safe, effective, and one to which the patient can adhere.

- Encourage foods that result in a negative caloric balance to achieve and maintain a healthy weight
- Consider the following:
  - Individual food preferences, eating behaviors, and meal patterns
  - Cultural background, traditions, and food availability
  - Time constraints and financial issues
  - Nutritional knowledge and cooking skills

# Choosing Nutritional Therapy for Obesity

- Nutritional approaches for weight loss typically focus on the caloric manipulation of the three macronutrients: carbohydrate, fat, or protein
- Very low-calorie diets contain less than 800 kcal/day and require close medical supervision for safety reasons
- Low calorie diets range from 1200-1800 kcal/day (1200-1500 for women, 1500-1800 for men)
- Restricting dietary fat leads to a greater reduction in total and LDL cholesterol, whereas restricting dietary carbohydrate leads to a greater reduction in serum triglycerides and an increase in HDL-cholesterol
- Reduction of carbohydrates can lead to a greater reduction in serum glucose and hemoglobin A1C

# Nutritional Therapy for Obesity



# Low-calorie Diets: Restricted-carbohydrate Diet

Low-carbohydrate diet defined as 50-150 grams of carbohydrates per day.  
Very low-carbohydrate diet defined as <50 grams of carbohydrates per day.

## Weight Loss

- May produce modestly greater weight loss compared to fat-restricted dietary intake for the first 6 months, wherein afterwards, the net weight loss may be similar to other calorie restricted nutritional interventions
- May assist with reducing food cravings

## Metabolic Effects

- Reduces fasting glucose, insulin and triglycerides
- Modestly increases high-density lipoprotein cholesterol levels
- May increase low-density lipoprotein cholesterol levels
- May modestly reduce blood pressure
- The metabolic effects noted above may occur with or without weight loss
- In patients with epilepsy, a very low carbohydrate ketogenic diet (VLCKD) may reduce seizures
- LCKD may possibly improve diabetes mellitus complications (i.e., nephropathy)

## Risks

- May produce carbohydrate cravings within the first few days of implementation, which may be mitigated by artificial sweeteners or adding low-glycemic-index foods
- May induce gout flare if history of gout
- May present challenges in patients undergoing dietary protein restriction (severe kidney disease)

# Low-calorie Diets: Restricted-fat Diet

Defined as 10-30% of total calories from fat.

## Weight Loss

- After six months, fat-restrictive, low-calorie nutritional intervention generally produces the same amount of weight loss compared to the “low-carb diet”

## Metabolic Effects

- May reduce fasting glucose and insulin levels
- Modestly decreases low-density and high-density lipoprotein cholesterol levels
- May modestly reduce blood pressure

## Risks

- Hunger control may present challenges, which may be mitigated with weight-management pharmacotherapy
- If fat restriction results in a substantial increase in carbohydrate consumption, and if weight loss is not achieved, an increase in carbohydrate dietary intake may potentially contribute to hyperglycemia, hyperinsulinemia, hypertriglyceridemia, and reduced levels of high-density lipoprotein cholesterol

# Very Low-calorie Diets

Defined as less than 800 kcal/day, typically implemented utilizing specifically formulated meal-replacement products *supervised by a trained clinician.*

## Weight Loss

- Produces more rapid weight loss than low calorie (low-fat or carbohydrate restricted) diets due to the lower energy intake

## Metabolic Effects

- Reduces fasting glucose, insulin and triglycerides
- May modestly increase high-density lipoprotein cholesterol levels
- May modestly decrease low-density lipoprotein cholesterol
- Reduces blood pressure

## Risks

- Fatigue, nausea, constipation, diarrhea, hair loss, and brittle nails
- Cold intolerance, dysmenorrhea
- Small increase in gallstones, kidney stones, gout flare
- If insufficient mineral intake, then may predispose to palpitations and cardiac dysrhythmias, muscle cramps
- Weight regain *will* occur if patients are not taught how to maintain healthy eating when transitioning to non-meal replacement

# Dietary Patterns

Includes many dietary patterns but must be calorically restricted to effectively treat obesity.  
Weight loss and metabolic effects vary.

- Mediterranean diet
- Therapeutic lifestyle diet
- DASH (Dietary Approaches to Stop Hypertension)
- Atkins diet
- Ornish diet
- Paleo diet
- Vegetarian diet
- Commercial diet programs

# Trans Fats

Trans fats are created through a process of hydrogenating polyunsaturated fats (vegetable oils) into more saturated fats, allowing for higher melting temperatures more desirable for processed foods, cooking and frying.

- ***Partially hydrogenated vegetable oils*** were developed because they favorably affected taste in applicable foods and were less expensive than saturated fats from animals (lard)
  - Some early shortenings (fats) were made from partially hydrogenated vegetable oil (cottonseed and soybean oil), originally contained 50% trans fats, and were marketed as being a healthier alternative to animal fat, because they were derived from “vegetables”
  - Although it contains partially hydrogenated palm and soybean oils, common shortenings now contain minimal trans fats, soybean oil, fully hydrogenated palm oil (i.e., 3 grams saturated fats, 6 grams polyunsaturated fats, 2.5 monounsaturated fats)
- Trans fats may increase low-density lipoprotein cholesterol, reduce high-density lipoprotein cholesterol, and increase the risk of cardiovascular disease (myocardial infarction and stroke), type 2 diabetes mellitus, and certain cancers
- While the FDA has banned partially hydrogenated oil by 2018, trans fats can still be found in ***some*** cakes, pies, cookies (especially with frosting), biscuits, microwavable breakfasts, stick margarine, crackers, microwave popcorn, cream-filled candies, doughnuts, fried fast foods, and frozen pizza



# Mediterranean Diet

The Mediterranean Diet is not a defined “diet,” but rather a generalized term to describe several meal pattern variants often found in Greece, Italy, and Spain. The Mediterranean Diet has the most consistent and robust scientific support in reducing atherosclerotic cardiovascular disease risk.

## Encouraged

- Olive oil as main source of fat
- Vegetables, fruit, legumes, whole grains, nuts, and seeds
- Moderate intake of red wine
- Moderate consumption of seafood, fermented dairy products (cheese and yogurt), poultry, and eggs

## Discouraged

- Limit consumption of high amounts of red meat, meat products, and sweets\*

\*Olive oil is a staple of most definitions of the Mediterranean diet; however, some Mediterranean cuisine includes lard and butter for cooking, and olive oil for dressing salads and vegetables

# Therapeutic Lifestyle Change Diet (TLC)

The TLC Diet is a low-fat meal-plan variant that was recommended by the National Cholesterol Education Program, Adult Treatment Panel. It is the “diet” most often utilized in the conduct of lipid clinical trials.

## Encouraged

- Total fat: 25–35% of daily calories
  - Polyunsaturated fat: Up to 10% of total daily calories
  - Monounsaturated fat: Up to 20% of total daily calories
- Carbohydrate: 50% to 60% of total calories
- Soluble fiber: At least 5-10 grams a day, preferably 10-25 grams a day
- 2 grams per day of plant stanols or sterols through foods or dietary supplements

## Discouraged

- Limit saturated fat: < 7% of total calories
- Limit cholesterol: < 200 mg a day
- Avoid foods with *trans* fatty acids.

The Atkins Diet is illustrative of a carbohydrate-restricted nutritional intervention which promotes utilization of fat for energy and generates ketosis, which may reduce appetite.

## Encouraged

- **The induction phase** allows no more than 20 grams of carbohydrate per day from non-starchy vegetables and leafy greens; encourages adequate proteins from foods such as beef, pork, bacon, fish, chicken, eggs, and cheese, to reduce insulin levels and generate ketosis.
- **The ongoing weight loss phase** allows a wider variety of vegetables, seeds and nuts, and low-glycemic fruits (i.e., strawberries and blueberries).
- **The pre-maintenance phase**, after the goal weight is achieved, allows carbohydrate intake to be slowly increased as long as weight gain does not occur.
- **In the maintenance phase**, 60 to 90 grams of carbohydrates per day is allowed, which may allow legumes, whole grains, and fruits.
- All phases encourage a balance of saturated, monounsaturated, and polyunsaturated fatty acids.

## Discouraged

Avoid:

- Processed and refined foods
- Foods with a high glycemic index
- Foods rich in *trans* fatty acids

In all but the maintenance phase, limit:

- Cereals, breads, and grains
- Dairy products, except cheese
- Starchy vegetables
- Most fruits

The Ornish Diet is illustrative of a fat-restricted nutritional intervention.

## Encouraged

- Foods are best eaten in their natural form
- Vegetables, fruits, whole grains, and legumes
- One serving of a soy product each day
- Limited amounts of green tea
- Fish oil 3-4 grams each day
- Small meals eaten frequently throughout the day

## Discouraged

- Limit dietary fat: < 10% of total daily calories
- Limit dietary cholesterol:  $\leq 10$  mg per day
- Limit sugar, sodium, and alcohol
- Avoid animal products (red meat, poultry, and fish) and caffeine (except green tea)
- Avoid foods with *trans* fatty acids, including vegetable shortening, stick margarines, and commercially prepared foods, such as frostings; cake, cookie, and biscuit mixes; crackers and microwave popcorn; and deep-fried foods
- Avoid refined carbohydrates and oils

# DASH Diet

The “Dietary Approaches to Stop Hypertension” (DASH) is a diet pattern promoted by the U.S. National Heart Lung and Blood Institute, primarily to treat high blood pressure.

## Encouraged

- Vegetables, fruits, and whole grains
- Fat-free or low-fat dairy products
- Fish, poultry, and lean meats
- Nuts, seeds, and legumes
- Fiber and the minerals calcium, potassium, and magnesium

## Discouraged

- Limit sodium: 1,500-2,300 mg per day
- Limit total fat: ~27% of total daily calories
- Limit saturated fat: <6% of total daily calories
- Limit cholesterol:  $\leq 150$  mg per day for a 2,100-calorie eating plan
- Avoid red and processed meats
- Avoid sugar-sweetened beverages
- Avoid foods with added sugars

# Paleolithic Diet

Paleolithic nutritional intervention is based upon a diet pattern presumed to exist during the Paleolithic period (lasting 3.4 million years, and ending 6000-2000 BC). It differs from some other diets in that it excludes grains, dairy, and processed foods.

## Encouraged

- Fresh vegetables, fruits, and root vegetables
- Grass-fed lean red meats
- Fish/seafood
- Eggs
- Nuts and seeds
- Healthful oils (olive, walnut, flaxseed, macadamia, avocado, and coconut)

## Discouraged

Avoid:

- Cereal grains
- Legumes, including peanuts
- Dairy products
- Potatoes
- Processed foods
- Refined sugar, refined vegetable oils, and salt

# Vegetarian Diet

A vegetarian nutritional intervention includes a meal plan consisting of foods that come mostly from plants.

## Encouraged

- Vegetables
- Fruits
- Whole grains
- Legumes
- Seeds
- Nuts
- May include eggs and milk

## Discouraged

- Fowl
- Fish
- Beef
- Pork
- Lamb

# Vegetarian Diet Variants

**Vegan (“Total Vegetarian”)**: Only plant-based foods (e.g., fruits, vegetables, legumes, grains, seeds, and nuts) with no animal proteins or animal by-products, such as eggs, milk, or honey

**Lacto-vegetarian**: Plant foods plus some or all dairy products (e.g., cheese)

**Lacto-ovo Vegetarian (or Ovo-lactovegetarian)**: Plant foods, dairy products, and eggs

**Semi or Partial Vegetarian**: Plant foods and may include chicken or fish, dairy products, and eggs, but not red meat

**Pescatarian**: Plant foods and seafood



# Physical Activity

# Physical Activity to Improve Health

## Adiposopathy (Sick Fat Disease)

- Assist with weight maintenance
- Assist with weight loss
- Improve body composition
- Improve adiposopathic psychological disturbances
- Possibly improve adipocyte function (“train” fat cells)
  - Improve insulin sensitivity
  - Increase mitochondrial biogenesis
  - Increase browning (“beiging”) of fat cells

## Non-adipose Parameters

- Improve metabolic health
- Improve musculoskeletal health
- Improve cardiovascular health
- Improve pulmonary health
- Improve mental health (e.g., mood, happiness, sense of well-being)
- Improve sexual health

# Medical Evaluation to Ensure Safety before Beginning New Exercise Program

- Assess current physical activity level
- Assess readiness
- Agree upon patient expectations and goals with written “contract”
- Assess potential need for medical testing/evaluation (i.e., cardiac stress testing, pulmonary function tests, musculoskeletal assessment, etc.)
- Assess mobility, fitness, and potential equipment needs or modifications
- Potential adjustment of medications
  - Before start of physical activity plan
  - During implementation of physical activity plan
- Optimal default
  - Back-up plan

## Unable to Walk

- Seated exercise program
- Arm exercises (i.e., arm cycling)
- Swimming/aquatic exercises (e.g., shallow or deep water exercises)
- Gravity-mediated physical activity
- Consider physical therapy evaluation
  - Recommend rehabilitation & physical therapy guided activity program
  - Set physical activity goals
  - Assess special equipment needs

## Limited Mobility, Able to Walk

- Walking
- Swimming/aquatic exercises (e.g., shallow or deep water exercises)
- Gravity-mediated physical activity
- Assess for special equipment needs

## No Substantial Limitations to Mobility

- Exercise/physical activity prescription plan driven by patient and guided by clinician
- Assess for special equipment needs

# Priority: Increase Energy Expenditure

## Dynamic (Aerobic) Training

- Some physical activity is better than none
- At least 150 minutes (2.5 hours) per week of moderate physical activity or at least 75 minutes (1.25 hours) per week of vigorous intensity aerobic exercise = most health benefits, promote modest weight loss, and prevent weight gain
- > 300 minutes (5 hours) per week of moderate physical activity or 150 minutes (2.5 hours) per week of vigorous intensity aerobic exercise = promote more robust weight loss and prevent weight regain after weight loss

## Resistive (Anaerobic) Strength Training

- Percent body fat better assessment of body composition than BMI
- Utilize appropriate weight-lifting technique
- Emphasize “core” muscle exercises
- Using a variety of free weights, machines, and resistance bands may elicit less boredom and provide greater flexibility regarding scheduling and location
- Short-term sore muscles may be expected
- Sore joints suggests poor technique, with possible need for medical evaluation and physical activity modification
- Prioritize muscle mass metrics (e.g., myotape measurements) versus amount of weight lifted

# Priority: Increase Energy Expenditure and Decrease Sedentary Time

## Leisure Time Physical Activity

- Engage in competitive sport activities involving substantial physical activity, best if on a routine basis
- Engage in non-competitive sports such as running, hiking, cycling, cross-fit training, etc.
- Outdoor warm-weather physical activity in sunlight may facilitate negative caloric balance and have other health benefits, but need to avoid excessive sun exposure
- Engage in physical activity sport-alternatives, such as dancing

## Transportational/Occupational Non-exercise Activity Thermogenesis (NEAT)

- Walk short distances instead of automated transportation
- Take stairs instead of elevator
- Carry overnight travel bags instead of using rollers
- Active work environment (i.e., standing desks, walking desks)
- Avoid prolonged inactivity
  - Take breaks from inactivity
  - Walk, stand, incidental movements

# Exercise Prescription

- Exercise prescription (FITT-VP)
  - Frequency
  - Intensity
  - Time or duration
  - Type or mode
  - Volume or total energy expenditure of the exercise
  - Progression of the exercise
- Exercise prescription (FITTE)
  - Frequency
  - Intensity
  - Time spent
  - Type
  - Enjoyment level

# Metabolic Equivalent Tasks (METs)

- METs are used to assess the intensity of physical exercise:  $\text{Kcal} = \text{METs} \times \text{weight} \times \text{time}$
- Equal to the amount of energy expended during one minute while lying down at rest
- Equal to ~3.5 milliliters of oxygen consumption per kilogram of bodyweight per minute (3.5 ml/kg/min)
- Oxygen consumption may be decreased with increased age
- Standing = 2 METs
- Walking 4 miles per hour = 4 METs
- Running 10 miles per hour = 16 METs



# Tracking Progress

- Daily activity logs (written or electronic)
- Pedometer/accelerometer logs
- Dynamic training metrics (i.e., miles run, laps swam, etc.)
- Resistance training metrics (i.e., muscle-circumference measurements, reps, sets, etc.)
- Percent body fat measurements

# Motivational Interviewing

# Motivational Interviewing: Stages of Change



# Motivational Interviewing: Focus

## Collaboration

- Working together to find and implement pragmatic solutions
- Not focusing on who is right and who is wrong

## Evocation

- Drawing out the patient's thoughts and ideas regarding solutions
- Not telling the patient what to do

## Autonomy

- Empowering the patient to own the solution
- Not the authoritarian power of the clinician

# Motivational Interviewing: Principles

Express empathy

Avoid  
argumentation

Develop  
discrepancy

Resolve  
ambivalence

Support self-  
efficacy

# Express Empathy

- Communicate
- Understand
- Collaborate
- Support
- Encourage
- Listen

# Avoid Arguments: Resistance

## Types of Resistance

- Resistance in changing behavior may arise when the patient:
  - Views the problem or solution differently than the clinician
  - Feels the clinician is being too judgmental and/or authoritative
- Types of resistance
  - Arguing
  - Denying
  - Ignoring
  - Interrupting

## Roll with Resistance

- Rolling with resistance avoids arguments and confrontations by choosing not to challenge patient actions and statements that suggest resistance to change
- May be especially useful during initial interactions with the patient

## Therapeutic Paradox

- Therapeutic paradox is analogous to “reverse psychology,” wherein the clinician makes a statement seemingly in support of no change in hopes the patient will make an argument for change
  - *“It sounds like now is not the best time for you to make changes.”*
  - *“You seem to be saying you have a lot going on right now that keeps you from making changes, so what do you think is the best way for us to move forward at this time?”*

# Avoid Arguments: Roll with Resistance Examples

## Reflection

- Simple reflection: *“You don’t think you can lose weight right now.”*
- Amplified reflection: *“People worry too much about your weight; your current body weight is not really a problem.”*
- Double-sided reflection: *“You had previously suggested you were committed to weight loss, but now you no longer feel commitment is necessary.”*

## Shifting Focus

- *“Your conflict with your contractor is obviously stressful to you, but you are a bit ahead of me; I would like for us to go back and talk about what led to your entries in your diet diary.”*

## Reframing

- *“I get the sense that when your family expresses concern about your body weight, they do so in a way that makes you angry. Maybe their intent is not to frustrate you but rather meant to reflect how much they care for you.”*

## Siding with the Negative

- *“You previously gave us permission to discuss your body weight. But now you seem resistant to talk about it, much less talk about change. At this point, I am not sure you would be able to change even if you wanted to change.”*



# Discrepancy and Ambivalence

## Identify Discrepancy

- Discrepancy explores the mismatch between where patients are today and where they want to be in the future
- Contrasts current behavior and life goals
- Can involve acknowledging positive and negative aspects of current behavior
- Can promote motivation for change



## Amplify Discrepancy

- Amplifying discrepancy can help resolve ambivalence
- May facilitate thoughts of change



## Resolve Ambivalence (defined as uncertainty in the desire for change)

- Resolution of ambivalence helps facilitate change
- Can involve discussing:
  - Benefits for change
  - Risks of change
  - Benefits and risk of no change

# Motivational Questioning: Evoking Change-talk Examples

## Elicit Talk of Change

- *“Why do you want to change?”*
- *“How important is it that you change?”*
- *“What values are most important to you?”*
- *“How do your actions fit your values?”*
- *“How do you plan to change?”*
- *“How confident are you that you can change?”*

## Exploring Past and Future

- *“How were things better in the past?”*
- *“What may happen if things stay the same?”*
- *“How would you like for things to change within the next year?”*
- *“What are the best ways for you to change in the next year?”*

## Query Extremes

- *“How accurate is this statement: ‘Some might think your current actions are so important to you that you won’t give them up, no matter what the cost?’”*
- *“What is the worst case scenario if you do not change?”*
- *“What is the best case scenario if you do change?”*

# Change Metric Examples

## Importance of Change

- *“On a scale of 1-10, where one is not important and 10 is most important, how important is it for you to change?”*
- *“Why are you not at a lower/higher number?”*

## Readiness to Change

- *“On a scale of 1-10, where one is not ready to change and 10 is absolutely ready to change, how ready are you to change?”*
- *“Why are you not at a lower/higher number?”*

## Confidence in Ability to Change

- *“On a scale of 1-10, where one is not at all confident and 10 is absolutely confident, how confident are you in your ability to change?”*
- *“Why are you not at a lower/higher number?”*

# Decision-balancing Examples

- *“Write down some of the good things and bad things about your current eating and physical activity levels.”*
- *“It sounds like you enjoy many aspects about what has led to your current body weight, but now you have reasons why this needs to change.”*

# Self-efficacy: Affirmation

## Supporting Self-efficacy

- Motivational interviewing assumes the patient is capable of making change
- Change is promoted by focusing on past patient successes and highlighting existing patient skills and strengths
  - *“You have lost weight. What do you think were the main things you did to achieve this?”*
  - *“How do you feel about your success?”*

## Affirmation

- *“Your weight loss shows a real commitment toward improving your health.”*
- *“It is clear you have made some real changes.”*
- *“It seems that despite a lot of things happening, you have managed to stay on course, and that is really impressive.”*
- *“Although you have not lost weight, the fact you have returned reflects how serious you are about losing weight.”*

# Self Efficacy: Advice/Feedback and Summary Examples

## Advice/Feedback

- *“What do you know about how body fat can affect your...?”*
  - *Blood sugar/pressure/cholesterol*
  - *Heart*
  - *Breathing*
  - *Bones and joints*
  - *Possible pregnancy*
  - *Quality of life*
  - *[Other clinical consequences experienced by the patient]*

## Summary

- *“From what you’ve said, you want to lose weight mainly because you are concerned about your health and because your family is concerned.”*
- *“It seems that with your commitment to the weight-management plan, and with support from your family, most everyone agrees that overall you are making great progress.”*
- *“Although you had made progress in the past, your weight went up a bit this time. But it is good you did not get so discouraged as to cancel your appointment.”*

# Motivational Interviewing Techniques: Micro-Counseling (OARS)

## Open-ended Questions

- Avoids binary answers such as “yes” or “no”
- Invites expression of elaborative thoughts
- May help patient explore reasons for and possibility of change

## Affirmation

- An expressed recognition of the patient’s strengths and how these strengths can be applied to implement favorable change
- Affirmations to the patient by the clinician should be:
  - Relevant
  - Genuine

## Reflections

- Careful listening can often be the most effective form of empathy
- After careful listening, the clinician is better able to:
  - Facilitate evocation
  - Develop discrepancy
  - Amplify and resolve ambivalence
  - Offer collaboration
  - Support self-efficacy

## Summaries

- Each counseling session should conclude with a summary of:
  - What was discussed
  - Shift attention from negative past failures and toward positive but realistic future goals
  - Establish metrics to measure success of future goals
  - Outline follow-up plans

# Motivational Questioning: General Approach Examples

## Open-ended Questions

- *“If you don’t mind, can you tell me why are you here today?”* (Incorporates permission.)
- *“What do you hope we can accomplish today?”*
- *“What do you realistically think we can accomplish today?”*

## Reflective Listening

- *“From what you are telling me, it sounds like you (or your family/friends) want you to lose weight, but you...”*
  - *“. . . have concerns.”*
  - *“. . . are unsure how.”*
  - *“. . . are unsure if you need to.”*
  - *“. . . are unsure if you want to.”*
  - *“. . . are unsure if you can.”*
  - *“. . . are unsure if you are committed to change.”*

## Normalizing

- *“While no situation is the same, in general, many people often have problems losing weight.”*
- *“Many people feel like you: they want to lose weight but find it difficult.”*
- *“Many people have repeatedly tried to lose weight in the past before they were finally successful.”*



# Motivational Interviewing Techniques: 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 percent), 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.

# Motivational Interviewing Techniques: FRAMES

Feedback about Personal Risk

Responsibility of Patient

Advice to Change

Menu of Strategies

Empathetic Style

Self-efficacy

# Behavior Therapy

# Why Do People Eat Like They Do?

## Physiologic

- Strong biologic forces that resist weight loss
  - Weak biologic forces that resist weight gain
  - Hypothalamic dysfunction
    - Trauma
    - Inflammation
  - Hunger before meals
  - Lack of satiety after meals
  - Eating to facilitate sleep
- Five senses central nervous system signaling:
    - Sight of food
    - Smell of food
    - Hear talk of food, sounds of food (cooking, wrapper opening)
    - Taste of food
    - Feel of lack of food (i.e., vibration of “empty stomach,” borborygmi, texture, size)

# Why Do People Eat Like They Do?

## Mental Stress

- Chronic stress-induced limbic (e.g., hypothalamic) endocrinopathies and immunopathies
- Chronic stress-induced cerebral endocrinopathies and immunopathies
- Chronic stress-induced priority replacement of personal, work, or emotional priorities that overtake nutritional and physical activity priorities

## Timing and Emotions

- Timing
  - It's mealtime
  - Special occasions
  - Holidays
- Emotions
  - Surrogate for love and/or affection
    - For self
    - For others (children and friends)
  - Celebrate happiness
  - Soothe sadness
  - Avoidance: Cooking or eating can be a successful accomplishment, preferable to more challenging activities or situations
  - Treat:
    - Boredom
    - Fatigue
    - Stress

# Why Do People Eat Like They Do?

## Environment

- Others are eating
- Food is available
- Offers of free food
- Highly researched and effective advertisements for energy dense foods
- Perceived obligations
  - Family gatherings
  - Business meetings
  - Clean-plate syndrome

## Information Gap

- Lack of education about proper nutrition
- Challenges regarding access to nutritional information, especially when eating out
- Caloric content
- Nutritional content
- Marketing messages
  - “low fat”
  - “whole grain”
  - “no added sugar”
  - “natural sugar”
  - “cholesterol free”

# Why Do People Eat Like They Do?

## Reward

- Eating as a remuneration for an accomplishment or “good day”
- Eating as compensation for a “bad day”
- Eating for pleasure, not because of hunger
- Over-consumption of palatable food may affect the brain’s reward system
  - Stimulates opioid release
  - Decreases biologic stress response
  - May ultimately simulate addiction-like reward deficits, which promotes compulsive eating

# Why Do People Eat Like They Do?

## Eating Disorders

- Binge-eating disorder
- Bulimia nervosa
- Night-eating syndrome



# Eating Disorders and Obesity: Binge-eating Disorder

## Diagnosis:

- Frequent episodes of consuming large amounts of food more than once per week for at least three months
  - No self-induced vomiting (purging)
  - No extra exercising
  - Feelings of lack of self control, shame, and guilt
- Occurs in 2-3 percent of U.S. adults
- Often considered the most common eating disorder
- May occur in up to 50 percent of patients with severe obesity
- Eating Attitudes Test may assist with diagnosis

## Treatment:

- Often requires treatment by a qualified clinician
- Cognitive behavior therapy
- Lisdexamfetamine dimesylate is the only pharmacotherapy with an FDA indication to treat binge-eating disorder
- Although not FDA indicated for this use, clinical trials suggest other pharmacotherapies may be efficacious
  - Some selective serotonin reuptake inhibitors
  - Topiramate

# Lisdexamfetamine Dimesylate: Indications and Use

- Lisdexamfetamine dimesylate is a central nervous system stimulant indicated for the treatment of:
  - Moderate to severe binge-eating disorder (BED)
  - Attention Deficit Hyperactivity Disorder (ADHD)
- Limitations:
  - Not indicated for weight loss; safety and effectiveness for the treatment of obesity have not been established
- Drug Enforcement Agency Schedule II drug
- Dosing for BED: Once in the morning with or without food. Avoid afternoon doses. Capsule may be opened and mixed with yogurt, water, or orange juice (see drug interactions).
  - Starting dose = 30 mg every morning for one week
  - Titration dose = 50 mg every morning for one week
  - Top dose = 70 mg every morning
  - Recommended dose = 50-70 mg every morning
  - Severe renal impairment: Maximum dose is 50 mg per day
  - End-stage renal disease: Maximum dose is 30 mg per day

# Lisdexamfetamine Dimesylate

## Potential Drug Interactions

- Agents that alter urinary pH can alter blood levels of amphetamine
  - Acidifying agents decrease amphetamine blood levels (e.g., ascorbic acid)
  - Alkalinizing agents increase amphetamine blood levels (e.g., sodium bicarbonate)
- Concurrent administration with monoamine oxidase (MAO) inhibition may contribute to hypertensive crisis

## Pharmacokinetics

- Lisdexamfetamine is rapidly absorbed from the gastrointestinal tract, converted to dextroamphetamine and l-lysine primarily in the blood due to the hydrolytic activity of red blood cells
- Lisdexamfetamine is not metabolized by cytochrome P450 enzymes
- Approximately 96 percent of oral dose radioactivity is recovered in the urine (42 percent related to amphetamine, 25 percent to hippuric acid, and 2 percent to intact lisdexamfetamine)
- Plasma elimination half-life is less than one hour

# Lisdexamfetamine Dimesylate: Potential Adverse Experiences

## Most Common Adverse Reactions:

- Anorexia
- Anxiety
- Decreased appetite
- Decreased weight
- Diarrhea
- Dizziness
- Dry mouth
- Irritability
- Insomnia
- Nausea
- Upper abdominal pain
- Vomiting
- Increased heart rate
- Constipation
- Feeling jittery

# Lisdexamfetamine Dimesylate: Contra-indications

- Central nervous system stimulants (amphetamines and methylphenidate-containing products), including lisdexamfetamine dimesylate, have high potential for abuse and dependence
- Risk of abuse should be assessed prior to prescribing
- Patients should be monitored for signs of abuse and dependence while on therapy
- Known hypersensitivity (e.g., anaphylactic reactions, Stevens-Johnson Syndrome, angioedema, and urticarial) to amphetamine products or other ingredients in lisdexamfetamine dimesylate
- Use with monoamine oxidase (MAO) inhibitor or within 14 days of the last MAO inhibitor dose

# Lisdexamfetamine Dimesylate: Warnings

- Serious cardiovascular reactions
  - Due to reports of sudden death in children and adolescents with serious heart problems, as well as sudden death, stroke, and myocardial infarction in adults, avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious health arrhythmia, or coronary artery disease.
- Blood pressure or heart rate increases
  - Blood pressure and pulse should be monitored. Benefits and risks should be considered before use in patients for whom blood pressure increases may be problematic.
- Psychiatric adverse reactions
  - May cause psychotic or manic symptoms in patients with no prior history or exacerbation of symptoms in patients with pre-existing psychosis. Evaluate for bipolar disorder prior to stimulant use.
- Suppression of growth
  - Height and weight should be monitored in pediatric patients during treatment.
- Peripheral vasculopathy, including Raynaud's phenomenon
  - Stimulants are associated with peripheral vasculopathy, including Raynaud's phenomenon. Careful observations for digital changes is necessary during treatment with stimulants.

# Eating Disorders and Obesity: Bulimia Nervosa

## Diagnosis:

- Cycle of recurrent binge eating and compensatory purging, laxative abuse, diuretic abuse, extra exercising, fasting, or strict dieting
- Occurs in approximately 1% of adults (mostly women)
- Russell sign: Calluses and abrasions on dorsum of the hands caused by repeated contact with the teeth during self-induced vomiting
- Laboratory: Hypokalemia due to hypomagnesemia

## Treatment:

- Often requires treatment by a qualified clinician
- Fluoxetine is an FDA-approved pharmacotherapy for bulimia nervosa
- Although not FDA-indicated for this use, topiramate and naltrexone may be efficacious

# Eating Disorders and Obesity: Night-eating Syndrome

## Diagnosis:

- At least 25% of daily food consumption (often greater than 50%) consumed after evening meal
- Recurrent awakenings from sleep that require eating to go back to sleep, often involving carbohydrate-rich snacks
- Little interest in breakfast (morning anorexia)
- Night-eating syndrome may occur in as much as 5% of the U.S. population

## Treatment:

- Behavioral therapy regarding nutritional timing and content



# Why Don't People Engage in Routine Physical Activity?

## Physiologic

- Musculoskeletal, neurologic, pulmonary, cardiac, and other health disorders
- Pain or soreness
- Fatigue
- Conveniences which limit the physiologic need for physical activity
  - Automated transportation (i.e., cars, buses, etc.)
  - Elevators and escalators
  - Online shopping
  - Automated equipment that lessens manual labor

## Lack of Time

- Work commitments
- Family responsibilities
- Time preferentially allotted for other entertainments with minimal energy expenditure
  - Television
  - Movies
  - Video games
  - Internet
  - Watching sports

# Why Don't People Engage in Routine Physical Activity?

## Disinterest

- “Exercise is boring”
- Past failures to achieve exercise goals
- Past failures in observing body changes
- Concerns of being seen:
  - In workout clothes
  - In gyms surrounded by others more fit
- Desire to avoid perspiration
  - General appearance
  - Hair
  - Odor

## Environment

- Lack of:
  - Others (family, friends, etc.) engaged in physical activity
  - Safe environment
  - Parks or other areas for leisure activity
  - Accessible gym
  - Workplace exercise equipment
- Inadequate maintenance of increased physical activity, once started
- Insufficient education on physical activity
  - Benefits
  - Risks
  - Techniques
  - Recommendations

# Why Do People Regain Body Weight?

## Physiologic Priority Imbalance

- Neuro-biologic processes strongly resist starvation
- Neuro-biologic processes weakly resist over-nutrition
- Analogous example:
  - Hypoglycemia can be profoundly symptomatic and may promote physiologic and behavioral priority for immediate caloric intake
  - Hyperglycemia is often asymptomatic and rarely promotes physiologic and behavioral priority for immediate reduced caloric intake

## Neurobiology

- Weight loss may decrease neuroendocrine factors, which in turn may increase appetite
  - Leptin
  - Insulin
  - Cholecystokinin
  - Peptide YY
- Weight loss may increase ghrelin, which in turn may increase appetite
- Poor restorative sleep

# Why Do People Regain Body Weight?

## Energy Expenditure

- Decrease in resting energy expenditure with weight loss
- Greater muscle efficiency with weight loss, resulting in less energy expenditure with physical activity

## Behavior

- Lack of maintaining accountability logs
- Intervening stress
- Changing life circumstances
- Changing health status
- Resorting to previous nutritional and/or physical activity habits after achieving initial weight-loss success

# Behavior Therapy Techniques: Elements for Optimal Success

## Doable

- Practical
- Accessible
  - Frequency
  - Consistency

## Efficacious

- Evidence-based

## Measurable

- Feedback
- Trackable
- Verifiable

## Self-ownership

- Autonomous stakeholder
- Personal stakeholder
  - Positive reinforcement
  - Negative reinforcement

# Behavior Therapy: Encounters and Education

## Frequent Encounters with Medical Professional or Other Resources Free from Provider Bias

- Physician
- Dietitian
- Nurse educator
- Advanced practitioners
- Physical activity professional trainer (i.e., trainer, physiologist, etc.)
- Mental-health professional
- Certified health coach
- Web-based programs
- Mobile access (i.e., text messages, applications, etc.)
- Multidisciplinary approach
  - Clinicians with professional expertise
  - Patient with self expertise

## Education

- Medical health
- Mental health
- Nutrition
- Physical activity
- Establish healthy sleep habits
- Establish healthy eating habits (i.e., reduce speed of eating, drink water between meals, choose and have available healthy snacks, etc.)
- Recognize and anticipate inevitable weight-loss plateaus

# Behavior Therapy: Stimulus Control and Cognitive Restructuring

## Stimulus Control

- Avoid eating for reasons other than hunger
- Avoid frequent snacking
- Avoid binge eating
- Utilize portion control
- Environmental removal of foods identified as especially tempting for the individual patient
- Being habitually mindful of eating stimuli may allow best chance for stimulus control

## Cognitive Restructuring

- Address matters of body image
- Identify and establish a plan to counteract unhelpful or dysfunctional thinking leading to unhealthy behaviors and actions
- Emphasize rationale of aggressive yet realistic weight-loss expectations through an emphasis on weight loss as a matter of medical and mental health
- Encourage patient to:
  - Acknowledge he/she is capable of positive thoughts and behaviors
  - Replace unhelpful thoughts and behaviors with more productive ones
  - Practice behavior therapy skills between clinician encounters

# Behavior Therapy: Goal Setting and Self-Monitoring

## Goal Setting

- Patients are given step-by-step instructions to accomplish goals (i.e., nutrition and physical activity prescriptions)
- SMART
  - **S**pecific
  - **M**easurable
  - **A**ssignable
  - **R**ealistic
  - **T**ime-related
- Goals beyond body weight alone may include overall improvement in physical and mental health

## Self Monitoring

- Daily or weekly body weights
- Other routine self-anthropometric measurements (i.e., calipers for percent body fat, tape measure for waist circumference, myotape for muscle mass, etc.)
- Food diaries (including online services or mobile applications)
- Physical activity logs
- Pedometer/accelerometer measures
- Changes in clothing size
- Photo journaling



# Behavior Therapy: Behavioral Contracting and Problem Solving

## Behavioral Contracting

- Tokens of reward
- Financial incentives

## Problem Solving, Social Support, and Other Reinforcement Contingencies

- Stress management
- Establish alternative back-up procedures to engage during times that challenge adherence to agreed upon plans (e.g., stressful periods, life changes, etc.)
- Health care team support
- Mental-health professional
- Other group or social support
- Commercial weight loss/maintenance programs
- Encourage interactions with others that may provide positive recognitions for successes

# Technologies for Weight Management

# Technologies and Social Media

## Applications

- Record and assess nutritional and physical activity metrics
- May be assessed and reviewed by clinicians between face-to-face evaluations

## Interactive Technology

- Body-weight scales that provide interactive feedback via email or text messaging
- Wearable technologies
  - Tracks active minutes, steps, floors climbed, distance, and caloric consumption
  - Monitors heart rate and sleep patterns
  - Provides daily exercise statistics
  - Wirelessly syncs with smartphones and computers, providing interactive information to user

## Websites

- Websites can provide educational information regarding:
  - Nutrition
  - Caloric content of foods
  - Physical activity
  - Expected energy expenditure with certain physical activities
  - Meal plans
  - Recipes

## Social Media

- Post daily meals and snacks to followers to enhance accountability (Twitter, Facebook, etc.)
- Obtain nutritional and physical activity advice from others (Twitter, Facebook, blogs, forums, etc.)

# Anti-obesity Medications

# Anti-obesity Medications

Adjunct to nutritional, physical activity, and behavioral therapies.

## Objectives:

- Treat disease
  - Adiposopathy or sick fat disease (SFD)
  - Fat mass disease (FMD)
- Facilitate management of eating behavior
- Slow progression of weight gain/regain
- Improve the health, quality of life, and body weight of the patient with overweight or obesity

5-10 percent weight loss may improve both metabolic and fat mass disease.

# Food and Drug Administration (FDA) Principles

## FDA-approved Anti-obesity Medication Indications:

- Patients with obesity (e.g., BMI  $\geq$  30kg/m<sup>2</sup>)\*
- Patients who are overweight (e.g., BMI  $\geq$  27kg/m<sup>2</sup>) with presence of increased adiposity complications (e.g., type 2 diabetes mellitus, hypertension, dyslipidemia)\*

If no clinical improvement after 12-16 weeks with one anti-obesity medication, consider alternative anti-obesity medication or increasing anti-obesity medication dose (if applicable).

\*While body mass index (BMI) is the only measure listed in the prescribing information for anti-obesity medications, BMI has limitations. Especially in muscular individuals or those with sarcopenia, overweight and obesity are more accurately assessed by other measures.

# Pregnancy and Lactation Categorization

## Update to FDA Pregnancy and Lactation Labeling

- In December 2014, the FDA issued its “Pregnancy and Lactation Labeling Final Rule” (PLLR), which went into effect on June 30, 2015.
- The PLLR removed letter pregnancy categories - A, B, C, D, and X.
- Due to the fact that the prescribing information materials for most anti-obesity medications have yet to be updated to reflect the new rules, the Obesity Algorithm continues to include pregnancy and lactation categories.
- In general, anti-obesity drugs should not be administered to, nor taken by women who are pregnant or trying to become pregnant.

## Examples of Anti-obesity Medications Approved in 1999 or Before

- Phentermine
- Diethylpropion
- Phendimetrazine
- Benzphetamine
- Orlistat

## Examples of Anti-obesity Medications Approved in 2012 and Beyond

- Lorcaserin
- Phentermine HCL/topiramate extended release
- Naltrexone HCL/bupropion HCL extended release
- Liraglutide



# Sympathomimetic Amines

- Examples: Phentermine, diethylpropion, phendimetrazine, benzphetamine
- Increases satiety
- Drug Enforcement Agency (DEA) Schedule weight-management agents
  - DEA IV for phentermine and diethylpropion
  - DEA III for phendimetrazine and benzphetamine
- Potential adverse experiences include:
  - Palpitation
  - Tachycardia
  - Increased blood pressure
  - Overstimulation
  - Tremor
  - Dizziness
  - Insomnia
  - Dysphoria
  - Headache
  - Dryness of mouth
  - Dysgeusia
  - Diarrhea
  - Constipation
  - Pregnancy category X

# Gastrointestinal Lipase Inhibitors

- Example: Orlistat
- Impairs gastrointestinal energy absorption
- Potential adverse experiences include:
  - Oily discharge from the rectum
  - Flatus with discharge
  - Increased defecation
  - Fecal incontinence
  - May increase risk of cholelithiasis
  - May increase risk of urinary oxalate
  - Rare post-marketing reports of severe liver injury
  - May decrease fast-soluble vitamin absorption (e.g., vitamins A, D, E, K, and beta carotene)
  - Pregnancy category X

# Lorcaserin

## Indications and Use

- Serotonin (5-hydroxytryptamine) 2c receptor agonist anti-obesity medication
- Drug Enforcement Agency Schedule IV drug
- Dose = 10 milligrams (mg) twice per day for immediate release formulation;  
20 mg once per day for extended release formulation

## Potential Drug Interactions

- The safety of lorcaserin co-administration with other serotonergic or anti-dopaminergic agents is not yet established, which includes selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, monoamine oxidase inhibitors, triptans, bupropion, dextromethorphan, St. John's Wort: use with extreme caution due to the risk of serotonin syndrome or neuroleptic malignant syndrome. Similarly, other listed potential drug interaction include tricyclic antidepressants, lithium, tramadol, and dopamine antagonists.

## Pharmacokinetics

- Lorcaserin is metabolized in the liver with metabolites excreted in the urine

# Lorcaserin

## Most Common Adverse Reactions\*

- Headache
  - Dizziness
  - Fatigue
  - Nausea
  - Constipation
  - Cough
  - Dry Mouth
- \*May increase prolactin levels

## Contra-indications

- Pregnancy (Category X)

## Warnings and Precautions

- The safety of coadministration with other serotonergic or antidopaminergic agents has not been established. If Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS) – like Reactions occur, lorcaserin should be immediately discontinued and the patient provided supportive treatment.
- If signs or symptoms of valvular heart disease develop, then consider lorcaserin discontinuation and evaluate the patient for possible valvulopathy.
- May cause disturbances in attention or memory; use with caution in patients working with hazardous machinery when starting lorcaserin treatment
- Due to potential euphoria and dissociation, do not exceed recommended dose of lorcaserin 10 mg twice daily, or 20 mg extended-release formulation once a day.
- Discontinue lorcaserin if depression or suicidal thoughts develop.
- Among patients treated with diabetes mellitus medications, weight loss may cause hypoglycemia.
- Patients experiencing priapism should seek emergency treatment if an erection lasts >4 hours, and lorcaserin should be used with caution in patients predisposed to priapism.

# Phentermine HCL/Topiramate Extended Release

Completion of Risk Evaluation and Mitigation Strategy (REMS) program to inform prescribers and female patients about the increased risk of congenital malformations (especially orofacial clefts) in infants exposed to phentermine HCL/topiramate extended release during the first trimester of pregnancy\*

## Indications and Use

- Drug Enforcement Agency Schedule IV drug
- Phentermine is a shorter-acting sympathomimetic amine approved as monotherapy as a weight-management drug
- Topiramate is a longer-acting neurostabilizer approved as monotherapy for seizure disorders and migraine headache prevention
- Doses = Once daily in the morning with or without food
  - Starting dose = 3.75 mg/23 mg (phentermine/topiramate extended release)
  - After 14-day intervals, and as clinically indicated, escalate doses to:
    - Recommended dose = 7.5 mg/46 mg
    - Titration dose = 11.25 mg/69 mg
    - Top dose = 15 mg/92 mg

\*Completion of the FDA-mandated REMS program is optional and not required prior to prescribing phentermine HCL/topiramate extended release. Implementation of a REMS program by clinicians and pharmacies is intended to provide appropriate safety information to females of reproductive potential.

# Phentermine HCL/Topiramate Extended Release

## Potential Drug Interactions

- May alter the exposure to oral contraceptives, causing irregular menstrual bleeding but not an increased risk of pregnancy
  - Oral contraceptives should not be discontinued if spotting occurs
- May potentiate central nervous system depressants such as alcohol
  - Patients should avoid concomitant alcohol
- May potentiate hypokalemia of non-potassium-sparing diuretics

## Pharmacokinetics

- Phentermine is metabolized by the liver, with most excreted by the kidney
- Topiramate is excreted mainly by the kidney

# Phentermine HCL/Topiramate Extended Release

## Most Common Adverse Reactions

- In clinical trials, adverse reactions occurring more than or equal to 5 percent of the time include:
  - Paresthesia
  - Dizziness
  - Dysgeusia (taste distortion/perversion)
  - Insomnia
  - Constipation
  - Dry mouth

## Laboratory Abnormalities May Include

- Metabolic acidosis
- Elevated creatinine
- Lowering of glucose levels

# Phentermine HCL/Topiramate Extended Release

## Contra-indications

- Contra-indicated:
  - Glaucoma
  - Hyperthyroidism
  - During or within 14 days of taking monoamine oxidase inhibitors
  - Women of reproductive potential should have a negative pregnancy test before treatment and monthly thereafter and should use effective contraception while on phentermine HCL/topiramate extended release
  - Pregnancy or nursing (Pregnancy category X)
- Should be discontinued in patients with:
  - Unacceptable increases in adrenergic responses, such as increase in heart rate, especially in those with cardiac and/or cerebrovascular disease
  - Suicidal behavior and ideation
  - Acute myopia and secondary angle-closure glaucoma
  - Unacceptable mood and sleep disorders
  - Cognitive impairment
  - Pregnancy or nursing



# Naltrexone HCL/Bupropion HCL Extended Release

## Indications and Use

- Naltrexone is an opioid antagonist
- Bupropion is an aminoketone antidepressant with relatively weak inhibition of neuronal reuptake of norepinephrine and dopamine
- Drug Enforcement Agency Schedule: Not a scheduled drug
- Tablets = 8 mg/90 mg (naltrexone HCL/bupropion HCL extended release)
- Dosing:
  - Week 1 = 1 tablet in AM, no tablets in PM
  - Week 2 = 1 tablet in AM, 1 tablet in PM
  - Week 3 = 2 tablets in AM, 1 tablet in PM
  - Week 4 and beyond = 2 tablets in AM, 2 tablets in PM

# Naltrexone HCL/Bupropion HCL Extended Release

## Potential Drug Interactions

- Monoamine oxidase inhibitors: Increased risk of hypertensive reactions
- Drugs Metabolized by CYP2D6: Bupropion inhibits CYP2D6 and can increase concentrations 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)
- CYP2B6 inhibitors (e.g., ticlopidine or clopidogrel) can increase bupropion exposure. Do not exceed one tablet twice daily when taken with CYP2B6 inhibitors.
- CYP2B6 inducers (e.g., ritonavir, lopinavir, efavirenz, carbamazepine, phenobarbital, and phenytoin) may reduce efficacy by reducing bupropion exposure. Avoid concomitant use.
- Should be dosed with caution with drugs that lower seizure threshold
- CNS toxicity can occur when used concomitantly with dopaminergic drugs (e.g., levodopa and amantadine)
- Drug laboratory test interactions:
  - Can cause false positive urine test results for amphetamines

# Naltrexone HCL/Bupropion HCL Extended Release

## Pharmacokinetics

- Both parent and the 6-beta-naltrexol metabolite are active
- Naltrexone and 6-beta-naltrexol are not metabolized by cytochrome P450 enzymes
- Naltrexone and its metabolites are excreted primarily by the kidney
- Bupropion is extensively metabolized
- CYP2B6 is the principal isozyme involved in the formation of hydroxybupropion, whereas cytochrome P450 isozymes are not involved in the formation of the other active metabolites
- Bupropion and its metabolites inhibit CYP2D6
- Following oral administration of 200 mg of <sup>14</sup>C-bupropion in humans, 87 percent and 10 percent of the radioactive dose were recovered in the urine and feces, respectively

# Naltrexone HCL/Bupropion HCL Extended Release

## Most common adverse reactions

- Nausea
- Constipation
- Headache
- Vomiting
- Dizziness
- Insomnia
- Dry mouth
- Diarrhea

## Contra-indications

- Uncontrolled hypertension
- Seizure disorders, anorexia nervosa or bulimia, or undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs
- Use of other products containing bupropion
- Chronic opioid use
- During or within 14 days of taking monoamine oxidase inhibitors
- Known allergy to any of its ingredients
- Contra-indicated during pregnancy or nursing mothers (pregnancy category X)

# Naltrexone HCL/Bupropion HCL Extended Release

## Warnings

- Monitor for depression or suicidal thoughts and discontinue if these symptoms develop
- Risk of seizure may be minimized by adhering to the recommended dosing schedule and avoiding co-administration with high-fat meals
- Monitor blood pressure and heart rate in all patients, especially those with cardiac or cerebrovascular disease
- Hepatotoxicity: Cases of hepatitis and clinically significant liver dysfunction observed with naltrexone exposure
- Angle-closure glaucoma has occurred in patients with untreated anatomically narrow angles treated with antidepressants
- Weight loss may cause hypoglycemia in patients treated with anti-diabetes mellitus medications. Glucose levels should be monitored.

## Indications and Use

- Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist
- Drug Enforcement Agency Schedule: Not a scheduled drug
- Solution for subcutaneous injection, pre-filled, multi-dose pen that delivers doses of 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg, or 3 mg
- Inject subcutaneously in the abdomen, thigh, or upper arm; the injection site and timing can be changed without dose adjustment
- Recommended dose of liraglutide for treatment of obesity is 3 mg daily, any time of day, without regard to the timing of meals
- Dosing:
  - Week 1 = 0.6 mg per day
  - Week 2 = 1.2 mg per day
  - Week 3 = 1.8 mg per day
  - Week 4 = 2.4 mg per day
  - Week 5 and onward = 3.0 mg per day

\*Liraglutide for obesity was approved by the Food and Drug Administration (FDA) with a Risk Evaluation and Mitigation Strategy (REMS) program. While optional and not required prior to prescribing Liraglutide for obesity, the manufacturer provides a communication plan, implemented towards healthcare providers likely to prescribe Liraglutide for obesity. The goal is to inform healthcare providers about the potential risk of medullary thyroid carcinoma and the risk of acute pancreatitis (including necrotizing pancreatitis) associated with Liraglutide for obesity.

\*Evaluate the change in body weight after 16 weeks and discontinue Liraglutide for obesity if the patient has not lost at least 4% of baseline body weight since it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.

# Liraglutide

## Potential Drug Interactions

- Liraglutide delays gastric emptying. This may impact absorption of concomitantly administered oral medications.
- Liraglutide has low potential for pharmacokinetic drug-to-drug interactions related to cytochrome P450 and plasma-protein binding

## Pharmacokinetics

- Unlike native GLP-1, liraglutide is stable against metabolic degradation by both peptidases and has a plasma half-life of 13 hours after subcutaneous administration
- Liraglutide exposures are similar among three subcutaneous injection sites (upper arm, abdomen, and thigh); absolute bioavailability of liraglutide following subcutaneous administration is approximately 55 percent
- Liraglutide is endogenously metabolized similar to large proteins without a specific organ as a major route of elimination
- Following a [3H]-liraglutide dose, intact liraglutide is not detected in urine or feces, with only a minor part excreted as liraglutide-related metabolites in urine or feces (6 percent and 5 percent, respectively)

# Liraglutide

## Most common adverse reactions

- Nausea
- Hypoglycemia
- Diarrhea
- Constipation
- Vomiting
- Headache
- Decreased appetite
- Dyspepsia
- Fatigue
- Dizziness
- Abdominal pain
- Increased lipase

## Contra-indications

- Personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia syndrome type 2
- Hypersensitivity to liraglutide or any product components
- Pregnancy



## Warnings

- Counsel patients regarding the risk of medullary thyroid carcinoma (thyroid C-cell tumors) and the symptoms of thyroid tumors
- Discontinue promptly if pancreatitis is suspected; do not restart if pancreatitis is confirmed
- If cholelithiasis or cholecystitis are suspected, gallbladder studies are indicated
- Serious hypoglycemia can occur when liraglutide is used with an insulin secretagogue (i.e., a sulfonylurea)
  - Consider lowering the dose of anti-diabetes drugs to reduce the risk of hypoglycemia
- Monitor heart rate at regular intervals to evaluate for possible heart rate increase
- Renal impairment has been reported post-marketing, usually in association with nausea, vomiting, diarrhea, or dehydration, which may sometimes require hemodialysis
  - Use caution when initiating or escalating doses of liraglutide in patients with renal impairment
- Post-marketing reports exist regarding serious hypersensitivity reactions (e.g., anaphylactic reactions and angioedema)
  - If these occur, then liraglutide and other suspect medications should be discontinued, and the patient instructed to promptly seek medical advice
- Monitor for depression or suicidal thoughts and discontinue liraglutide if symptoms develop

# Early versus Late Weight- Management Intervention: Illustrative Consequences

# Early Treatment/Prevention

## 44-year-old woman with overweight/obesity

- Pre-diabetes mellitus
- Pre-hypertension
- Mild dyslipidemia
- Discomfort to weight-bearing joints
- Mild snoring
- Low self-esteem due to increased body weight

### Optimal Treatment Strategy

Decide to engage in early, proactive interventions intended to *prevent* onset of adverse health consequences from sick fat disease (diabetes mellitus, dyslipidemia, and hypertension) and fat mass disease (osteoarthritis):

- Optimize nutritional therapy and physical activity
- Initiate behavioral therapy
- Consider anti-obesity medications
- Consider bariatric surgery

Prevent onset of metabolic disease:

- Diabetes mellitus
- Dyslipidemia
- Hypertension

Prevent fat mass diseases:

- Osteoarthritis
- Sleep apnea
- Depression

# Delayed Treatment

## 44-year-old woman with overweight/obesity

- Pre-diabetes mellitus
- Pre-hypertension
- Mild dyslipidemia
- Discomfort to weight-bearing joints
- Mild snoring
- Low self-esteem due to increased body weight

### Sub-optimal Treatment Strategy

Simply tell the patient to diet and exercise and otherwise wait for the onset of diabetes mellitus, dyslipidemia, hypertension, osteoarthritis, sleep apnea, and depression. Once adverse health consequences are blatantly apparent:

- Optimize nutritional therapy and physical activity
- Initiate behavioral therapy
- Consider anti-obesity medications
- Consider bariatric surgery

*Continued...*

# Delayed Treatment

## If optimal intervention for obesity treatment and prevention is delayed, and the patient develops adverse consequences:

- Follow diabetes mellitus evaluation and treatment guidelines
  - American Diabetes Association Clinical Practice Recommendations
  - American Association of Clinical Endocrinology Comprehensive Diabetes Management Algorithm
- Follow lipid evaluation and treatment recommendations and guidelines
  - National Lipid Association Dyslipidemia Summary and Recommendations
  - American College of Cardiology/American Heart Association Cholesterol Guidelines
- Follow blood pressure guidelines
  - Report of the Joint National Committee for Management of High Blood Pressure in Adults
- Follow other disease-specific guidelines
- Utilize diabetes mellitus therapies most likely to improve adipose tissue function
- In patients with fat mass disease, utilize diabetes mellitus therapies having neutral or body weight loss effects, such as metformin, glucagon-like peptide-1 (GLP-1) agonists, sodium glucose cotransporter-2 (SGLT2) inhibitors, etc.
- Utilize lipid therapies most likely to reduce atherosclerotic coronary heart disease risk and least likely to increase body weight
- Utilize blood pressure therapy most likely to reduce cardiovascular disease risk, which may also provide other health benefits (e.g. diuretics, angiotensin converting enzyme inhibitors, etc.)
- Utilize non-steroidal anti-inflammatory agents to treat osteoarthritis
- Treat sleep apnea
- Utilize anti-depressant medications least likely to promote further weight gain
- Administer additional pharmaceuticals and/or treatment modalities as indicated

# Bariatric Surgery

Before eating (during fasting): GI hormones may increase hunger



- Ghrelin
- Neuropeptide Y

After eating: GI hormones may decrease hunger/promote satiety



- Somatostatin
- Cholecystinin
- Motilin
- Insulin
- Glucagon
- Pancreatic polypeptide

- Amylin
- Fibroblast growth factor19
- Glucagon like peptide-1
- Oxyntomodulin
- Peptide YY



After eating: GI hormones may help manage digestion through slowed gastric motility/emptying



- Cholecystokinin
- Amylin
- Glucagon like peptide-1
- Oxyntomodulin
- Peptide YY

After eating: GI hormones may stimulate the release of digestive enzymes



- Gastrin
- Cholecystokinin
- Secretin

After eating: GI hormones may have counter-regulatory functions impairing digestive enzyme release



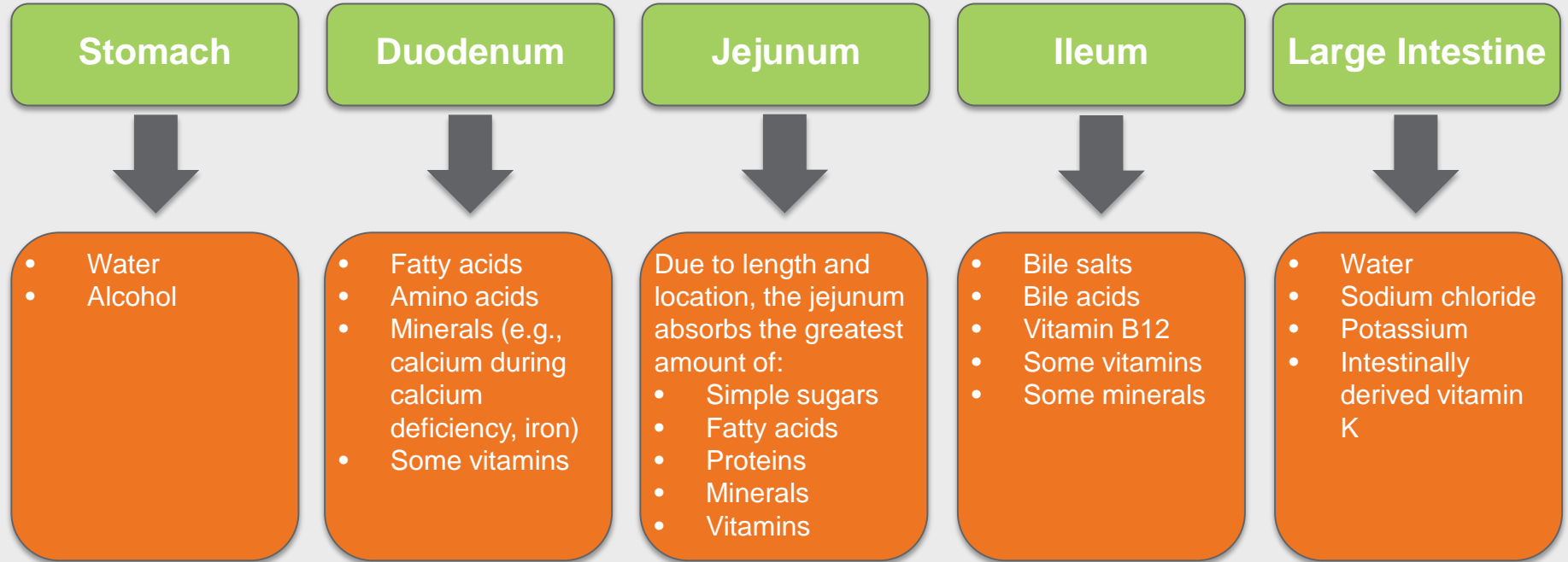
- Somatostatin
- Secretin
- Pancreatic polypeptide
- Glucagon like peptide-2
- Oxyntomodulin
- Peptide YY

After eating: GI hormones may assist with post-absorptive nutrient management



- Somatostatin
- Insulin
- Glucagon
- Fibroblast growth factor19

# Nutrient Absorption



# Potential Bariatric Surgery Patient

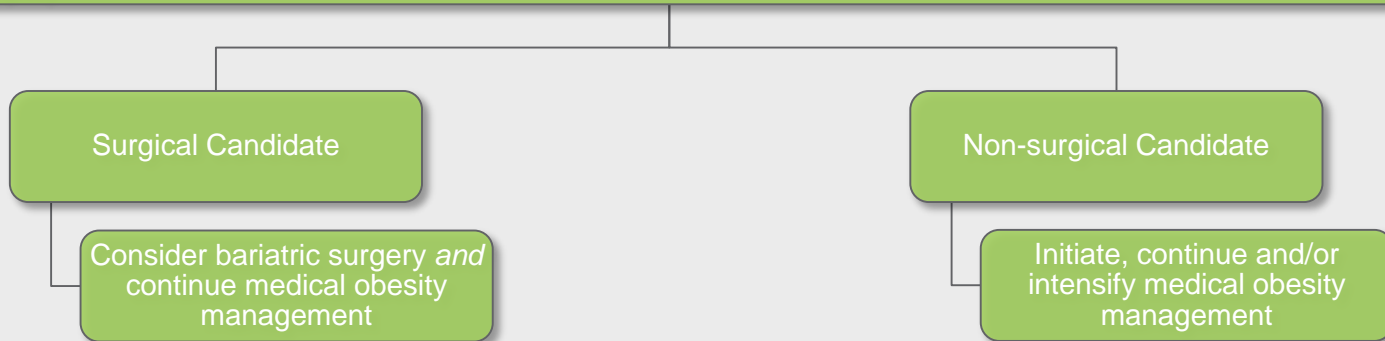
Does clinical evidence exist that the increase in body fat is pathogenic?

Did the patient make reasonable attempts to reduce body weight and improve health?

Was the patient evaluated by a physician trained in comprehensive management of overweight and obesity (e.g., certified by the American Board of Obesity Medicine)?

Does the patient demonstrate a commitment to follow post-operative recommendations, maintain necessary lifestyle changes and agree to life-long post-operative medical surveillance?

What are the specific insurance criteria that need to be met (e.g., documentation of prior unsuccessful weight loss attempts)?



# Bariatric Surgery

Regardless of the bariatric surgical procedure chosen, the surgery is best performed by an appropriately trained surgeon at an accredited surgery center.

The accreditation of a bariatric surgery center is determined by the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP).

# Potential Bariatric Surgery Candidate

What is the patient's BMI (in kg/m<sup>2</sup>)?

Does clinical evidence exist confirming the presence of adverse health consequences (AHC) due to excessive and/or dysfunctional body fat?

BMI  $\geq$  35 with one or more AHC

BMI  $\geq$  40 with or without AHC

\*BMI 30-34.9 with one or more AHC:  
Mounting evidence supports surgical  
intervention as a treatment option in  
this group



# Bariatric Surgery Pre-operative Evaluation

- Medical evaluation by physician specializing in the care of patients with overweight or obesity
- Surgical consultation by bariatric surgery specialist
- Cardiology, pulmonary, gastroenterology, and/or other specialty consultation as indicated
- Mental health assessment: underlying eating disorders; mood disorders; substance abuse; history of physical or emotional trauma; education regarding potential for increased suicide risk and transfer addictions post op; evaluation of existing coping mechanisms
- Nutritional assessment (e.g., dietitian)
- Educational support (e.g., pre-operative seminar)

# Excess Weight Loss

- “Excess weight loss” is a term, mainly used in the surgical literature, to describe the percent amount of weight lost in excess of ideal body weight
- May have variances based upon how ideal body weight is determined
- It is challenging to directly compare “excess weight loss” often described in the surgical literature to the “weight loss” described in the medical literature, which is simply the percent of weight loss from baseline
- For the same amount of actual weight loss, the percent “excess weight loss” is often a higher reported value compared to “weight loss”

# Bariatric Surgical Procedures

	Pros	Cons	Expected loss in percent excess body weight* at two years	Optimally suited for patients with:	Other comments
<b>Roux-en-Y Gastric Bypass</b>	Greater improvement in metabolic disease	Increased risk of malabsorptive complications over sleeve	60-75%	Higher BMI, GERD, Type 2 DM	Largest data set, more technically challenging than LAGB, VSG
<b>Vertical Sleeve Gastrectomy</b>	Improves metabolic disease; maintains small intestinal anatomy; micronutrient deficiencies infrequent	No long term data	50-70% (*3-year data)	Metabolic disease	Can be used as the first step of staged approach; most common based on 2014 data
<b>Laparoscopic Adjustable Gastric Banding</b>	Least invasive; removable	25-40% 5 year removal rate internationally	30-50%	Lower BMI; no metabolic disease	Any metabolic benefits achieved are <i>dependent</i> on weight loss
<b>Biliopancreatic Diversion with Duodenal Switch</b>	Greatest amount of weight loss and resolution of metabolic disease	Increased risk macro- and micronutrient deficiencies over bypass	70-80%	Higher BMI, Type 2 DM	Most technically challenging

251 \*Excess body weight (EBW) = (total body weight) - (lean body weight)

# Roux-en-Y Gastric Bypass (RNY)

A surgical procedure wherein the stomach is completely divided into a small proximal gastric pouch leaving a large “bypassed” gastric remnant in situ. The proximal gastric pouch is attached to a “roux” limb of small bowel, bypassing the large gastric remnant, all of the duodenum, and a portion of the proximal small intestine.

## General

- Hospital stay = 1-4 days
- Recovery = 1-2 weeks
- Contra-indications:
  - Poor surgical candidate
  - Severe psychiatric disorder
  - Intolerance to general anesthesia
  - Pregnancy
  - Drug or alcohol addiction
  - Untreated gastric ulcer
  - Crohn’s disease
- Patient demonstrates an unwillingness or an inability to follow long term recommendations which can lead to life threatening micronutrient deficiencies

## Most Common Acute Complications

- Nausea/Vomiting
- Dehydration
- Gastrointestinal obstruction
- Gastrointestinal bleeding
- Acute gout exacerbation
- Anastomotic leaks
- Infection
- Cardiac dysrhythmias
- Atelectasis and pneumonia
- Deep vein thrombosis
- Pulmonary emboli
- Death



# Roux-en-Y Gastric Bypass (RNY)

## Common Chronic Complications

- Weight regain
- Pouch/Anastomotic dilation
- Anastomotic/Marginal ulcers
- Esophageal dilation
- Dumping syndrome with reactive hypoglycemia
- Small bowel obstruction caused by internal hernias or adhesions
- Anastomotic stenosis/stricture
- Gallstones
- Calcium deficiency
- Secondary hyperparathyroidism
- Bacterial overgrowth
- Kidney stones (oxalosis)
- Metabolic acidosis
- Iron deficiency
- Protein malnutrition
- Other nutritional and mineral deficiencies (i.e., deficiencies of vitamins A, C, D, E, B, and K, folate, zinc, magnesium, thiamine)
- Anemia (often related to mineral and nutrition deficiencies)
- Neuropathies (resulting from nutritional deficiencies)
- Gout exacerbation
- Osteoporosis (often caused by calcium deficiency and chronically elevated parathyroid hormone levels)
- Depression
- Potential need for revision or conversion to another procedure

# Vertical Sleeve Gastrectomy (VSG)

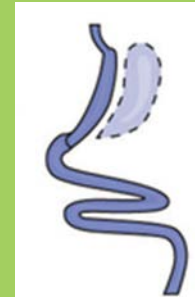
A surgical procedure wherein the stomach is reduced to about 25 percent of its original size by the surgical removal of a large portion of the stomach along the greater curvature, resulting in a narrower sleeve or tube-like structure.

## General

- Hospital stay = 1-2 days
- Recovery = 1-2 weeks
- Contra-indications:
  - Poor surgical candidate
  - Severe psychiatric disorder
  - Intolerance to general anesthesia
  - Pregnancy
  - Drug or alcohol addiction
  - Untreated gastric ulcer
  - Barrett's esophagus
  - Achalasia
  - Previous gastrectomy
  - Previous gastric bypass
- Sometimes used as a staged approach to gastric bypass or duodenal switch

## Most Common Acute Complications

- Nausea/Vomiting
- Dehydration
- Gastrointestinal obstruction
- Gastrointestinal bleeding
- Staple line leaks
- Infection
- GERD
- Cardiac dysrhythmias
- Atelectasis and pneumonia
- Deep vein thrombosis
- Pulmonary emboli
- Death



# Vertical Sleeve Gastrectomy (VSG)

## Most Common Chronic Complications

- Weight regain or lack of long-term weight loss
- Sleeve dilation
- Gastric ulcers
- Worsening GERD or de novo GERD
- Luminal stenosis/strictures
- Alkaline reflux gastritis
- Staple line leaks
- Fistula formation
- Gallstones
- Calcium deficiency
- Secondary hyperparathyroidism
- Iron deficiency
- Anemia (related to mineral and nutrition deficiencies)
- B12 & B1 deficiency(IF)
- Protein malnutrition uncommon
- Vitamin deficiencies uncommon
- Kidney stones (oxalosis)
- Depression
- Potential need for revision or conversion to another procedure

# Laparoscopic Adjustable Gastric Banding (LAGB)

A surgical procedure where an adjustable band is placed around the upper stomach creating a small pouch. The band diameter is adjustable through the percutaneous introduction of saline via a subcutaneous port which is accessed in the upper abdomen.

*\*Performance of LAGB has declined due to limited long-term efficacy and international removal rate of at least 25 percent at five years.*

## General

- Outpatient procedure
- Recovery usually one week
- Food bolus obstruction (dry meat; starches)
- Contra-indications:
  - Poor surgical candidate
  - Severe psychiatric disorder
  - Intolerance to general anesthesia
  - Pregnancy
  - Drug or alcohol addiction
  - Untreated gastric ulcer, severe GERD, Barrett's disease
  - Autoimmune disease





# Laparoscopic Adjustable Gastric Banding (LAGB)

## Most Common Acute Complications

- Nausea/vomiting
- Dehydration
- Band too tight with gastrointestinal obstructive symptoms (i.e., dysphagia)
- Hemorrhage
- Gastrointestinal bleeding
- Infection
- Cardiac dysrhythmias
- Atelectasis and pneumonia
- Deep vein thrombosis

## Most Common Chronic Complications

- No weight loss or weight regain
- Band slippage, erosion, ulceration, port infection, disconnection, and displacement
- Esophageal dilation
- Rare nutrient deficiencies if persistent vomiting or marked and sustained decrease in nutritional intake
- Depression
- Potential need for removal, revision or conversion to another procedure

# Biliopancreatic Diversion with Duodenal Switch (BPD/DS)

Procedure in which a partial gastrectomy (much like a sleeve) is performed, removing 70-80% greater curvature of the stomach sparing the pylorus and a small portion of the duodenum and the creation of a Roux-en-Y duodenenterostomy bypassing a large portion of the intestine.

## General

- Hospital stay = 2-4 days
- Recovery = 2-4 weeks
- Contra-indications:
  - Poor surgical candidate
  - Severe psychiatric disorder
  - Intolerance to general anesthesia
  - Pregnancy
  - Drug or alcohol addiction
  - Untreated gastric ulcer
  - Crohn's disease
- Patient demonstrates an unwillingness or an inability to follow long term recommendations which can lead to life threatening micronutrient deficiencies

## Most Common Acute Complications

- Nausea/Vomiting
- Dehydration
- Gastrointestinal obstruction
- Gastrointestinal bleeding
- Acute gout exacerbation
- Anastomotic leaks
- Infection
- Cardiac dysrhythmias
- Atelectasis and pneumonia
- Deep vein thrombosis
- Pulmonary emboli
- Death



# Biliopancreatic Diversion with Duodenal Switch (BPD/DS)

## Most Common Chronic Complications

- Weight regain
- Pouch dilation
- Anastomotic/Marginal ulcers
- Small bowel obstruction caused by internal hernias or adhesions
- Anastomotic stenosis/stricture
- Gallstones
- Calcium deficiency
- Secondary hyperparathyroidism
- Bacterial overgrowth
- Kidney stones (oxalosis)
- Metabolic acidosis
- Iron deficiency
- Protein malnutrition\*
- Other nutritional and mineral deficiencies (i.e., deficiencies of vitamins A, C, D, E, B, and K, folate, zinc, magnesium, thiamine)\*
- Anemia (often related to mineral and nutrition deficiencies)
- Neuropathies\* (resulting from nutritional deficiencies)
- Gout exacerbation
- Osteoporosis (often caused by calcium deficiency and chronically elevated parathyroid hormone levels)
- Depression
- Potential need for revision

\*The BPD/DS has a much higher incidence of both macro- and micronutrient deficiencies compared to other bariatric surgeries.

# Other FDA-approved Bariatric Technologies

## Modified Percutaneous Endoscopic Gastrostomy (PEG)

- Mechanism: Drains 30% of ingested meal
- Indication: Body mass index 35-55 kg/m<sup>2</sup>
- Efficacy: 12% excess weight loss at one year
- Safety: Potential tube site inflammation/infection

## Electrical Vagal Blocking System

- Mechanism: Pacemaker-like implantable device surgically placed under skin, with lead wires placed around the vagus nerve just above the stomach; blocks vagal impulses to brain resulting in decreased hunger and increased satiety
- Indication: Body mass index > 40 kg/m<sup>2</sup> or > 35 kg/m<sup>2</sup> among those with adverse consequences of obesity
- Efficacy: 8.5% excess weight loss
- Safety: Potential gastroparesis (vagal trunk injury or entrapment)



# Other FDA-approved Bariatric Technologies

## Intragastric Balloons

- Mechanism: Balloon is inserted into stomach and filled
- Indication: Body mass index  $\geq 30$  and  $\leq 40$  kg/m<sup>2</sup>; approved for up to 6 months
- Efficacy: 12-31% excess weight loss over 6 months
- Safety: Stomach blockage with uncomfortable fullness, vomiting, stomach ulcer, gastric hypertrophy

## Endoscopic Plication Devices

- Mechanism: Endoscopic suturing of the stomach reduces gastric volume
- Indication: Investigational
- Efficacy: 30-50% excess weight loss for up to 1-2 years
- Safety: Stitch failure with weight regain

# Bariatric Surgery: Early Complications (First 30 Days)

The complications listed here are unique to bariatric surgery and not inclusive of more general post-operative complications that can occur (e.g., pneumonia, PE).

## Leak or Perforation (Typically after RNY, BPD/DS, VSG):

- Can lead to acute peritonitis
- Technical failure within the first 72 hours (with ischemia can occur up to 14 days post-op)
- Can also occur at any time due to ulcer perforation (avoid NSAIDS, steroids, nicotine, caffeine, alcohol)
- Often with acute and severe abdominal pain (may *NOT* have peritonitis symptoms if on steroids)
- Fever, tachycardia, abdominal or back pain, and leukocytosis
- Urgent surgical exploration may be required but can sometimes be managed with endoscopic stent and drain (in selected cases)
- Imaging not always diagnostic but when performed, water soluble contrast preferred (abdominal CT or Upper GI)
- *Immediate surgical consultation is critical for suspected leak or perforation EVEN if imaging is negative*

# Bariatric Surgery: Early Complications (First 30 Days)

The complications listed here are unique to bariatric surgery and not inclusive of more general post-operative complications that can occur (e.g., pneumonia, PE).

## **Bleeding at the Surgical Site or Rarely Intraluminal/Gastrointestinal (More Likely with RNY, BPD/DS, and VSG):**

- Usually within 72 hours post-op, may require early intervention or reoperation
- Symptoms: tachycardia, hypotension, drop in hemoglobin/hematocrit, oliguria
- From three to seven days out, cause is more likely due to erosions and ulcerations at the anastomoses or along staple lines

## **Wound Infection (Possible after All Procedures):**

- Abdominal pain, excessive drainage, fever/chills, decreased appetite, leukocytosis, change in bowel pattern
- Presence of intra-abdominal infection/abscess may require drainage percutaneously or by re-operation

# Bariatric Surgery: Late Complications (Beyond 30 Days)

The complications listed here are unique to bariatric surgery and not inclusive of more general post-operative complications that can occur (e.g., pneumonia, PE).

## Gastro-gastric Fistula (RNY):

- Results in increased capacity to ingest food, and/or increased passing of food into the gastric remnant (where it is more completely digested and absorbed)
- Possible contributing factor to suboptimal weight loss/weight regain and recurrence of metabolic disease
- A non-healing ulcer should raise concern for a gastro-gastric fistula

## Band Erosion through Gastric Wall into the Lumen (LAGB):

- Suspect if band is full but patient perceives no restriction or obstructive symptoms with empty or minimally filled band
- Can also present as infection with pain, fevers, leukocytosis
- Pain/infection may or may not be present
- Diagnose with EGD, surgical consult for removal is required for eroded band



# Bariatric Surgery: Late Complications (Beyond 30 Days)

The complications listed here are unique to bariatric surgery and not inclusive of more general post-operative complications that can occur (e.g., pneumonia, PE).

## Incisional Hernias (More Common with Open Procedures):

- Pain at one of the incisional sites
- Maybe be palpable defect but due to body habitus this may be difficult to ascertain on exam and CT or US is needed to confirm
- Repair usually postponed until significant weight loss unless signs of bowel incarceration/strangulation (bowel obstruction)

## Internal Hernias (RNY/BPD-DS):

- Usually accompanied by intermittent, post prandial pain and emesis, sometimes only pain
- Herniation through defect in the mesentery created during the surgical procedure
- Challenging to diagnose both clinically and radiographically- if suspected, diagnostic laparoscopy often needed
- *Surgical emergency if sudden/acute onset*

# Bariatric Surgery: Early or Late Complications

The complications listed here are unique to bariatric surgery and not inclusive of more general post-operative complications that can occur (e.g., pneumonia, PE).

## **Intestinal (Small Bowel) Obstruction (RNY, BPD-DS, or Open Procedure):**

- Abdominal pain, nausea/vomiting, (constipation/obstipation not present if partial)
- Usually six months or longer out from surgery but can be anytime
- May be associated with an internal hernia, narrowing of the roux limb due to scarring, intussusception, and/or adhesions
- Evaluation: CT scan abdomen most common but can also be seen on plain flat/upright abdominal x-rays

## **Stricture (Stomal Stenosis) (RNY or BPD-DS):**

- Post-prandial, epigastric abdominal pain and vomiting (often with frothy emesis)
- Usually 4-6 weeks following RNY
- May result from narrowing of the anastomosis or angulation of the intestinal limbs
- May be associated with anastomotic ulcer (RNY and BPD-DS)
- EGD +/- balloon dilation. Surgery only after multiple failed dilations

## **Band Obstruction: Band Too Tight, Band Slip/Prolapse (LAGB):**

- Abdominal pain, reflux, and regurgitation of undigested food which occurs post-prandially
- Weight gain can occur due to dependence on liquid calories
- Diagnostic testing: Can be clinical diagnosis, or upper GI imaging/EGD
- Surgery indicated for a slip which is not relieved after the complete removal of all band fluid

# Bariatric Surgery: Early or Late Complications

The complications listed here are unique to bariatric surgery and not inclusive of more general post-operative complications that can occur (e.g., pneumonia, PE).

## **Dumping Syndrome (RNY):**

- Unique complication of RNY (due to bypass of the pyloric emptying mechanism), which is common in the first 18 months postoperatively
- Occurs in approximately 70-85 percent of patients with RNY
- Symptoms: facial flushing, lightheadedness, fatigue, reactive hypoglycemia, and postprandial diarrhea
- Treatment: often includes avoidance of foods with high glycemic index/load, avoidance of drinking fluid with meals

## **Gallbladder or Gallstone Disease:**

- Right upper quadrant or epigastric post-prandial or nocturnal pain (classically radiating to back or right shoulder)
- Diagnostic testing includes labs (if elevated white blood cell count, alkaline phosphatase, bilirubin, liver transaminases, or amylase lipase send to Emergency Room for urgent surgical consult)
- Imaging: Abdominal ultrasound (abdominal CT if abdominal wall thickness impairs ultrasound), consider HIDA scan if ultrasound is negative

## **Marginal Ulcer (at an anastomotic site-most common with RNY)**

- Abdominal pain +/- vomiting
- Must stop NSAIDs, steroids, nicotine, caffeine, alcohol, and/or illicit drugs to heal
- Proton pump inhibitor 3 times/day plus Carafate 4 times/day; optimize protein intake; surgery for failed refractory ulcer
- Diagnose with upper endoscopy, consider surgery for refractory disease

# Bariatric Surgery: Common Micronutrient Deficiencies

	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.asmb.org](http://www.asmb.org).

# Micronutrients: Vitamins

Derived from plant and animal foods, and necessary for metabolic processes, such as serving as a non-protein facilitator (coenzyme) for protein enzymes.

# Vitamin A Deficiency

## Background

- Vitamin A is an essential fat-soluble nutrient important for vision
- Vitamin A deficiency may lead to night blindness
- Vitamin A is also involved with adipocyte function, as well as lipid and possibly glucose metabolism

## Bariatric Surgery

- Vitamin A deficiency is rarely reported after laparoscopic adjustable gastric banding, gastric sleeve, or Roux-en-Y gastric bypass
- Vitamin A deficiency is reasonably common with biliopancreatic diversion/duodenal switch
- Retinol levels are often routinely monitored after biliopancreatic diversion/duodenal switch

# Vitamin B1 (Thiamine) Deficiency

## Background

- Vitamin B1/thiamine is an essential water-soluble nutrient involved in cellular processes such as mitochondrial function (fatty acid oxidation)
- Vitamin B1 deficiency is known as beriberi, which may present as weakness
- “Dry” beriberi includes Wernicke-Korsakoff encephalopathy (e.g., ophthalmoplegia, dementia, ataxia, amnesia)
- “Wet” beriberi includes congestive heart failure
- Patients with alcoholism are at risk for Vitamin B1 deficiency

## Bariatric Surgery

- Preoperative thiamine deficiency is more common in African-American and Hispanic patients
- Vitamin B1 deficiency is sometimes reported after laparoscopic adjustable gastric banding, gastric sleeve, Roux-en-Y gastric bypass, or biliopancreatic diversion/duodenal switch
- The risk of thiamine deficiency is increased with post-operative vomiting, which sometimes requires monitoring post-operative thiamine levels

# Vitamin B2 (Riboflavin) Deficiency

## Background

- Vitamin B2/riboflavin is an essential water-soluble nutrient involved with many cellular processes
- Its deficiency may cause a distinctive bright pink tongue, cracked lips, throat swelling, scleral erythema, lowered blood cell count, coma, and death

## Bariatric Surgery

- Vitamin B2 deficiency is rarely reported after laparoscopic adjustable gastric banding, sleeve gastrectomy, Roux-en-Y gastric bypass, or biliopancreatic diversion / duodenal switch
- Vitamin B2 deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Post-operative riboflavin levels are usually monitored only with signs and symptoms of deficiency



# Vitamin B3 (Niacin) Deficiency

## Background

- Vitamin B3/niacin is an essential water-soluble nutrient highly expressed in adipose tissue
- Niacin deficiency is known as pellagra
- Presentation includes the “4 Ds” of diarrhea, dermatitis, dementia, and death
- Mainly located in sun-exposed areas, the dermatologic manifestations include erythema, desquamation, scaling, and keratosis

## Bariatric Surgery

- Vitamin B3 deficiency is rarely reported with laparoscopic adjustable gastric banding, sleeve gastrectomy, Roux-en-Y gastric bypass, or biliopancreatic diversion/duodenal switch
- Vitamin B3 deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Post-operative niacin levels are usually monitored only if signs and symptoms of deficiency

# Vitamin B5 (Pantothenic Acid) Deficiency

## Background

- Vitamin B5/pantothenic acid is an essential water-soluble nutrient used to synthesize coenzyme-A, as well as proteins, carbohydrates, and fats
- Pantothenic acid is derived from a Greek word meaning “from everywhere,” is found in most foods, and its deficiency may cause numerous, wide-ranging adverse effects, such as paresthesias and other signs and symptoms

## Bariatric Surgery

- Vitamin B5 deficiency is rarely reported with laparoscopic adjustable gastric banding, sleeve gastrectomy, Roux-en-Y gastric bypass, or biliopancreatic diversion / duodenal switch
- Vitamin B5 deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Post-operative pantothenic acid levels are usually monitored only if signs and symptoms of deficiency

# Vitamin B6 (Pyridoxine) Deficiency

## Background

- Vitamin B6/pyridoxine is an essential water-soluble nutrient important for nutrient metabolism and neurologic function
- Pyridoxine deficiency can cause skin eruptions resembling seborrheic dermatitis, intertrigo, atrophic glossitis, angular cheilitis, conjunctivitis, sideroblastic anemia, and neurologic symptoms (e.g., somnolence, confusion, and peripheral neuropathy)

## Bariatric Surgery

- Vitamin B6 deficiency is rarely reported with either laparoscopic adjustable gastric banding, sleeve gastrectomy, Roux-en-Y gastric bypass, or biliopancreatic diversion / duodenal switch
- Vitamin B6 deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Post-operative pyridoxine levels are usually monitored only if signs and symptoms of deficiency

# Vitamin B7 (Biotin) Deficiency

## Background

- Vitamin B7/biotin is an essential water-soluble nutrient important in fatty acid synthesis, amino acid catabolism, and gluconeogenesis
- Biotin is usually produced in more than adequate amounts by intestinal bacteria
- Biotin deficiency causes hair loss, conjunctivitis, scaly/erythematous rash (around eyes, nose, mouth, and genital area), anemia, and central/peripheral nervous system disorders
- Biotin deficiency can be exacerbated by consumption of raw eggs, which bind vitamin B7, making it relatively inactive

## Bariatric Surgery

- Vitamin B7 deficiency is rarely reported with laparoscopic adjustable gastric banding, sleeve gastrectomy, Roux-en-Y gastric bypass, or biliopancreatic diversion / duodenal switch
- Vitamin B7 deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Post-operative pyridoxine levels are usually monitored only if signs and symptoms of deficiency

# Vitamin B9 (Folate) Deficiency

## Background

- Vitamin B9/folic acid is an essential water-soluble nutrient absorbed in the duodenum and proximal jejunum
- Folic acid deficiency may cause megaloblastic anemia, as well as loss of appetite and weight loss
- Preconception folate deficiency is associated with fetal neural tube defects

## Bariatric Surgery

- Vitamin B9 deficiency is sometimes reported with laparoscopic adjustable gastric banding, sleeve gastrectomy, Roux- en-Y gastric bypass, or biliopancreatic diversion / duodenal switch
- Vitamin B9 deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Post-operative folic acid levels (red blood cell folate) are often routinely monitored
- Folic acid supplements are often administered after bariatric surgeries, especially in premenopausal, menstruating women of childbearing potential

# Vitamin B12 (Cyanocobalamin) Deficiency

## Background

- Vitamin B12/cyanocobalamin is an essential water-soluble nutrient cleaved from its protein by the hydrochloric acid in the stomach, then combined with a protein called intrinsic factor, and then absorbed in the terminal ileum
- Vitamin B12 deficiency may induce sterol regulatory element binding, protein-mediated cholesterol biosynthesis, and impaired metabolism of odd-chain fatty acids
- Vitamin B12 deficiency may also cause megaloblastic anemia and contribute to central nervous system disorders

## Bariatric Surgery

- Vitamin B12 deficiency is commonly reported with laparoscopic adjustable gastric banding, sleeve gastrectomy, Roux-en-Y gastric bypass, or biliopancreatic diversion / duodenal switch
- Vitamin B12 deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Post-operative vitamin B12 levels are often routinely monitored
- Vitamin B12 supplements are often administered after bariatric surgeries

# Vitamin C Deficiency

## Background

- Vitamin C is an essential water-soluble nutrient and cofactor for many enzymatic processes
- Vitamin deficiency is known as scurvy
- Signs and symptoms include lethargy, weight loss, dry hair and skin, bruising, bleeding gums, loss of teeth, fever, and death

## Bariatric Surgery

- Vitamin C deficiency is rarely reported with laparoscopic adjustable gastric banding, sleeve gastrectomy, Roux-en-Y gastric bypass, or biliopancreatic diversion / duodenal switch
- Vitamin C deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Post-operative vitamin C levels are usually monitored only if signs and symptoms of deficiency

# Vitamin D Deficiency

## Background

- Vitamin D is an essential fat-soluble nutrient important for calcium metabolism (and other minerals), bone health, and adipocyte function
- Vitamin D deficiency may result in decreased bone mineralization, osteopenia, secondary hyperparathyroidism, and hypocalcemia

## Bariatric Surgery

- Vitamin D deficiency is common among pre-operative patients with overweight or obesity
- Vitamin D deficiency is rarely reported to worsen with laparoscopic adjustable gastric banding
- Vitamin D deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Vitamin D deficiency sometimes occurs with sleeve gastrectomy and Roux-en-Y gastric bypass and commonly occurs with biliopancreatic diversion/duodenal switch
- After bariatric procedures, 25-hydroxy- (OH)-vitamin D, calcium, phosphorous, and parathyroid hormone are often monitored post-operatively
- Calcium and vitamin supplements are commonly administered after bariatric surgeries



# Vitamin E Deficiency

## Background

- Vitamin E is an essential fat-soluble nutrient important for antioxidant and enzymatic activities, and gene expressions, as well as neurologic function and adipocyte function
- Vitamin E deficiency may cause neuropathy and ataxia

## Bariatric Surgery

- Vitamin E deficiency is rarely reported with laparoscopic adjustable gastric banding, sleeve gastrectomy, or Roux-en-Y gastric bypass.
- Vitamin E deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Vitamin E deficiency may more often occur in patients undergoing biliopancreatic diversion/duodenal switch
- Alpha-tocopherol levels are often routinely monitored after biliopancreatic diversion/duodenal switch.

# Vitamin K Deficiency

## Background

- Vitamin K is an essential fat-soluble nutrient important for blood coagulation
- Vitamin K deficiency may cause bruising and increased risk for bleeding

## Bariatric Surgery

- Vitamin K deficiency is rarely reported with laparoscopic adjustable gastric banding, sleeve gastrectomy, or Roux-en-Y gastric bypass
- Vitamin K deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Vitamin K deficiency is reasonably common with biliopancreatic diversion/duodenal switch
- Prothrombin time is often routinely measured after biliopancreatic diversion/duodenal switch

# Micronutrients: Minerals and Trace Elements

## Minerals

- Non-organic substances necessary for important biological processes (e.g., vital part of an enzyme)
- Calcium, phosphorous, magnesium, potassium, and sodium

## Trace Elements

- Non-organic substances required by the body for biological functions (e.g., vital part of an enzyme), but only in minute amounts
- Iron, cobalt, zinc, selenium, molybdenum, and iodine

# Calcium Deficiency

## Background

- Calcium is an essential mineral necessary for proper nerve transmission, muscle contraction, bone structure, and cellular function
- Concurrent magnesium deficiency may worsen hypocalcemia by impairing parathyroid hormone secretion (hypomagnesemia may also promote hypokalemia)
- Calcium deficiency may result in decreased bone mineralization, osteopenia, and secondary hyperparathyroidism
- Severe hypocalcemia can lead to tetany (e.g., muscle contractions, spasms, paresthesias)

## Bariatric Surgery

- Calcium deficiency is rarely reported with laparoscopic adjustable gastric banding
- Relative calcium deficiency is sometimes reported with gastric sleeve or Roux-en-Y gastric bypass, when assessed by elevated parathyroid levels (even if calcium levels are within normal limits)
- Calcium deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Calcium deficiency commonly occurs with biliopancreatic diversion/duodenal switch
- Although calcium levels may not be decreased in all patients with overweight or obesity, vitamin D deficiency may be present
- 25-hydroxy-(OH)-vitamin D, calcium, phosphorous, and parathyroid hormone are often monitored post-operatively
- Calcium and vitamin D supplements are commonly administered after bariatric surgeries

# Copper Deficiency

## Background

- Copper is a trace element absorbed from the small intestine
- Copper deficiency (which may accompany iron deficiency) may clinically manifest by anemia, neuropathies, difficulty walking, increased muscle tone or spasticity, and cardiomegaly

## Bariatric Surgery

- Copper deficiency is rarely reported with laparoscopic adjustable gastric banding, gastric sleeve, Roux-en-Y gastric bypass, or biliopancreatic diversion/duodenal switch
- Copper deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Post-operative copper levels are usually monitored only if signs and symptoms of deficiency

# Iron Deficiency

## Background

- Iron is a trace element and is normally absorbed in the duodenum and jejunum of the intestine
- Iron deficiency can result in microcytic anemia (possibly manifested clinically by pica), with low iron levels, low ferritin levels, and increased transferrin or total iron-binding capacity

## Bariatric Surgery

- Iron deficiency is rarely reported with laparoscopic adjustable gastric banding
- Iron deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Iron deficiency commonly occurs with gastric sleeve, Roux-en-Y gastric bypass and biliopancreatic diversion/duodenal switch
- After bariatric procedures, iron, ferritin, transferrin, and total iron binding capacity are often monitored
- Iron supplements are often administered after bariatric surgeries, especially among premenopausal, menstruating women of childbearing potential

# Selenium Deficiency

## Background

- Selenium is a trace element that helps protect cells from free radical damage
- Selenium deficiency may cause cardiomyopathy (Keshan disease)

## Bariatric Surgery

- Selenium deficiency is rarely reported after laparoscopic adjustable gastric banding, gastric sleeve, Roux-en-Y gastric bypass, or biliopancreatic diversion/duodenal switch
- Selenium deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Post-operative selenium levels are usually monitored only if signs and symptoms of deficiency

# Zinc Deficiency

## Background

- Zinc is a trace element and is important for intestinal mucosal function
- Zinc deficiency can cause poor wound healing, hair loss, acrodermatitis enteropathica-like rash, taste alterations, glossitis, and impaired folate absorption (potentially contributing to folic acid deficiency)

## Bariatric Surgery

- Zinc deficiency is rarely reported after laparoscopic adjustable gastric banding
- Zinc deficiency can be mitigated with appropriate nutrition and a high-quality multivitamin supplement
- Zinc deficiency sometimes occurs with sleeve gastrectomy, Roux-en-Y gastric bypass and is common with biliopancreatic diversion/duodenal switch
- Post-operative zinc levels are usually monitored only if signs and symptoms of deficiency



# Nutritional Principles Following Bariatric Surgery

- Nutritional advice will depend upon type of bariatric procedure
- Three to five small meals a day
- Chew small bites of food thoroughly
- Avoid consuming liquids during meals, delay for at least 30 minutes after meals
- Protein: At least 60 grams/day, optimally 1.2 to 1.5 grams/kg/day
- Avoid concentrated sweets to minimize dumping and to reduce caloric intake
- High-quality multivitamins are routinely recommended after bariatric procedures, irrespective of deficiencies, which are often recommended to be chewable or liquid
- Other routine supplements often include:
  - Vitamin B12 500 µg/d tablet or sublingual, or 1000 µg/mo IM
  - Iron at least 27 mg of elemental iron daily, with at least 500 mg vitamin C
  - Calcium citrate 1200 mg/d, preferably with vitamin D

# Micronutrient Deficiency Replacement after Bariatric Surgery: Vitamins/Minerals

Vitamin/Mineral	Assessment	Replacement of Deficiency
Vitamin A	Retinol	<ul style="list-style-type: none"> <li>If corneal keratinization, ulceration or necrosis: 50-100,000 IU IM for 3 days, followed by IU IM for 2 weeks</li> <li>If no corneal changes: 10-25,000 IU orally for 1-2 weeks</li> <li>Further treatment depends on persistent malabsorptive effects, as may most be a concern with biliopancreatic diversion/duodenal switch</li> </ul>
Vitamin B1 (Thiamine)	Thiamine	<ul style="list-style-type: none"> <li>If hyperemesis, then 100mg IV for 7 days, then 50 mg/d until thiamine in normal range</li> </ul>
Vitamin B9 (Folate)	Red blood cell (RBC) folate	<ul style="list-style-type: none"> <li>If daily multivitamin has 400ug of folic acid, then replacement dose for deficiency is an additional 800 ug/d orally (total of 1200 ug/d of folic acid until RBC folate in normal range, and then a multivitamin with at least 400 ug/d of folic acid</li> </ul>
B12 (Cobalamin)	Vitamin B12	<ul style="list-style-type: none"> <li>A typical dose to treat B12 deficiency 1000 ug/mo IM, 1000 ug/wk sublingually, or 350-500 ug/d orally until B12 in normal range</li> </ul>
Calcium	Calcium	<ul style="list-style-type: none"> <li>In addition to ensuring adequate vitamin D, calcium deficiency is typically treated with calcium citrate 1200-1800 mg/d. Calcium citrate may be better absorbed than calcium carbonate</li> <li>Calcium should be taken at least 1 hour apart from other supplements, especially iron</li> </ul>
Iron	Ferritin, iron, total iron binding capacity	<ul style="list-style-type: none"> <li>For moderate deficiency, menstruating women, or patients at risk for iron deficiency anemia, total elemental iron intake (including in a multivitamin) should be 50-100 mg/d</li> <li>Minimum iron supplementation should be 18 mg/d, which may be more effective with vitamin C supplementation 500 mg/d</li> <li>For severe deficiency, IV iron is sometimes required, which is provided in multiple different formulations, some of which require test doses.</li> </ul>

# Micronutrient Deficiency Replacement after Bariatric Surgery: Vitamins/Minerals

Vitamin/Mineral	Assessment	Replacement of Deficiency
Vitamin D	25-hydroxyl-(OH)-vitamin D	<ul style="list-style-type: none"> <li>• A typical dose for mild deficiency of vit. D is 1000 IU/d after gastric bypass and 2000 IU/d after biliopancreatic diversion/duodenal switch</li> <li>• For severe deficiency, a single dose of vit. D 50,000 IU/wk orally can be given until vit. D levels in normal range, then 3000 IU if still with substantial malabsorptive signs and symptoms, of if stable, 1000 IU/d after gastric bypass and 2000 IU/d after biliopancreatic diversion/duodenal switch</li> <li>• Regarding formulation, vit. D2 (ergocalciferol) is a form of dietary vit. D found in plants. Vit.D3 (cholecalciferol) is found in foods of animal origin and is similar to the vit. D3 generated when 7-dehydrocholesterol in the skin is converted by ultraviolet radiation from sunlight. Both D2 and D3 are reported as 25-hydroxyvitamin D, which is then converted by the kidneys into the more active 1,25 dihydroxyvitamin D (calcitriol). Vit. D3 may be preferred (longer half-life and potentially more potent) than vit. D2. Although the most potent, calcitriol is more rarely used (.25 or .50 mcg/d orally)</li> </ul>
Vitamin E	A-Tocopherol	<ul style="list-style-type: none"> <li>• A typical dose to treat vitamin E deficiency is 400 to 800 IU/d orally.</li> </ul>
Vitamin K	Prothrombin time	<ul style="list-style-type: none"> <li>• If vitamin K deficiency occurs during substantial gastrointestinal malabsorption, then vitamin K can be replaced 10 mg by slow IV. Otherwise, typical oral replacement dose is 300 ug/d. Continued treatment depends on persistent malabsorptive effects, as may most be a concern with biliopancreatic diversion/duodenal switch.</li> </ul>
Zinc	Zinc	<ul style="list-style-type: none"> <li>• A typical replacement dose for zinc deficiency is 60 mg of elemental zinc twice daily. Zinc consumption may impair copper absorption, thus 1 mg of copper should be given per each 10 mg of zinc administered. Once zinc is in normal range, if malabsorption remains a risk, a typical supplemental dose is zinc 30 mg/d.</li> </ul>

# Microbiome: Gut Flora Basics

Microbiome = Collection of micro-organisms

Microbiota = Organisms themselves

# Microbiome: Gut Flora Basics

- Humans organism has ~10 trillion human cells
- Human gut is colonized by 100 trillion cells (bacteria, fungi and viruses)
- Unless due to a pathogenic infection, the gut microbiome is usually neither healthy or unhealthy; the clinical implications are dependent upon the individual
  - Individuals who are underweight may benefit from microbiota that promote more efficient absorption of nutrients
  - Individuals who are overweight or with obesity may not benefit from microbiota that promote more efficient absorption of nutrients

# Microbiome: Gut Flora Bacteria

- Over 1,000 bacterial species, with over 90% anaerobic
- Substrates: Sloughed intestinal cells, plant polysaccharides, starch cellulose, and bile components
- Functions include:
  - Metabolizing essential nutrients
  - Synthesizing vitamin K
  - Fermentation of sugars to acids, gasses, or alcohol
  - Digesting cellulose
  - Promoting angiogenesis
  - Enhancing enteric nerve function

# Microbiome: Gut Flora Bacteria

- Stomach and proximal small intestine = limited amounts of bacteria (e.g., acid-tolerant lactobacilli and streptococci bacteria)
- Ileum and colon = trillions of bacteria
- Major phyla of intestinal microbiome
  - Gram Negative Bacteroidetes: May assist with epithelial cell maturation and function
  - Gram Positive Firmicutes: May more efficiently extract calories from carbohydrates through fermentation of indigestible foods into short-chain fatty acids
- Obesity = Firmicutes proportionally increases compared to Bacteroidetes

## Increased Nutrient Absorption

- Enhanced monosaccharide intestinal uptake through enriched carbohydrate enzymes in the gut (e.g., microbial glycoside hydrolases, polysaccharide lyases, and carbohydrate esterases)
- Increased fermentation of nutrients to short-chain fatty acids, which are absorbed and utilized for gluconeogenesis, lipogenesis, and which may increase the permeability of the intestinal epithelium, increasing absorption of macromolecules from the intestine
- Increased density of small intestinal villi capillaries allowing for greater nutrient absorption



# Microbiome: Gut Microbiota Promotion of Increased Body Fat

## Increased Lipogenesis

- Increased Sterol Regulatory Element Binding Protein-1 (SREBP-1) activity, promoting lipogenesis
- Reduced hepatic and muscle fatty acid oxidation

# Microbiome: Gut Microbiota Promotion of Increased Body Fat

## Increased Inflammation

- Pro-inflammatory signaling, such as that generated in response to lipopolysaccharide component of bacterial outer membranes, may affect neurobehavioral brain centers, and adversely affect adipocyte function leading to adiposopathy and increased risk for metabolic disease

## Alterations in Bile Acid Metabolism

- Relationship between microbiota and bile acids are interdependent, with the types of bile acids delivered by the liver affecting the microbiome, and the microbiome affecting bile acid structure once in the gut, and thus affecting the types of bile acids composing the bile-acid pool
- Gut microbiota promotes bile acid deconjugation, dehydrogenation, and dehydroxylation, increasing the chemical diversity of intestinal and systemic bile acids
- Bile acids affect glucose and lipid metabolism via interactions with bile acid receptors such as farnesoid X receptor (FXR), takeda G protein coupled receptor 5 (TGR5), and fibroblast growth factor 19 (FGF19)

## Alterations in Gut Hormones

- Suppressed secretion of fasting-induced adipose factor (angiopoietin-like protein), which may reduce adipose tissue fatty-acid oxidation, reduce uncoupling of the process of mitochondrial adipose tissue adenosine triphosphate generation, and reduce thermogenesis
- Decreased glucagon-like peptide 1, which may impair increased satiety after meals

## Bariatric Surgery May:

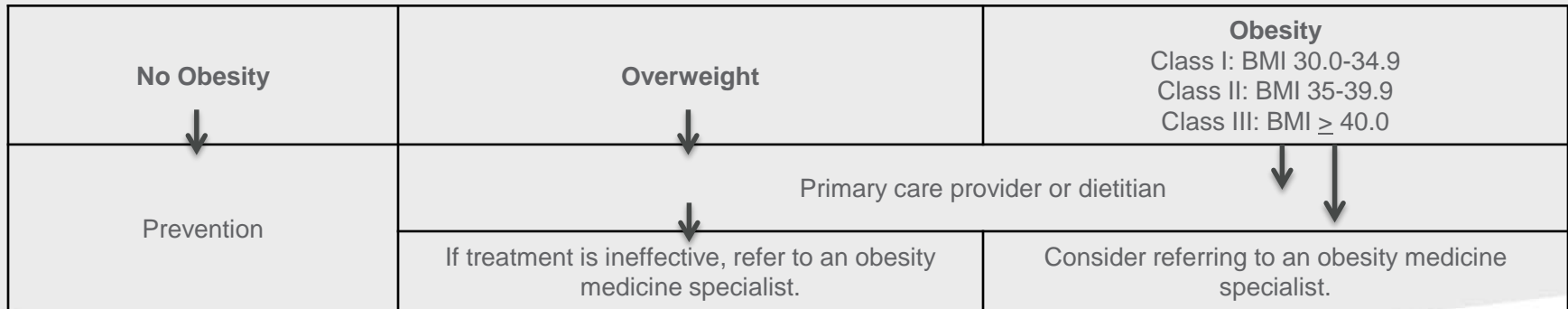
- Reduce availability of nutrients delivered to the gut
- Reduce lipogenic signaling (gut and systemic)
- Reduce inflammation (gut and systemic)
- Alter bile-acid metabolism and increase bile-acid pool favoring metabolic processes involving glucose and lipids
- Alter gut hormones favoring metabolic processes involving glucose and lipids
- Decrease the Firmicutes:Bacteroidetes ratio, potentially reducing the efficiency of extracting calories from gut carbohydrates

# Executive Summary

# Assess for the Presence of Obesity, Adiposopathy, Fat Mass Disease

Obesity may be assessed using several criteria (thresholds vary based on gender and ethnic differences):

Body Mass Index (BMI)	18.5-24.9 kg/m <sup>2</sup>	25.0-29.9 kg/m <sup>2</sup>	≥30 kg/m <sup>2</sup>
Percent Body Fat	Male: <25% Female: <32%		Male: >25% Female: >32%
Waist Circumference	Male: <40 in. Female: <35 in.		Male: >40 in. Female: >35 in.
Edmonton Obesity Staging System	Stage 0, 1, 2, 3, 4		



# Assess for the Presence of Obesity, Adiposopathy, Fat Mass Disease

<b>Body Mass Index</b>	BMI = (weight in kg)/(height in m) <sup>2</sup> OR 703 x (weight in pounds)/(height in inches) <sup>2</sup>
<b>Percent Body Fat</b>	Can be calculated using bio-impedance, near infrared reactance, DEXA scan or whole body air-displacement plethysmography.
<b>Waist Circumference</b>	Can be measured by tape measure around the abdomen at the level of the anterior superior iliac crests, parallel to the floor. Tape should be snug against skin without compressing.
<b>Edmonton Obesity Staging System</b>	<p>STAGE 0: No apparent risk factors, no physical symptoms, functional limitations, and/or impairment of well-being</p> <p>STAGE 1: Presence of obesity-related subclinical risk factors, mild physical symptoms, mild psychopathology, mild functional limitations, and/or mild impairment of well-being</p> <p>STAGE 2: Presence of established obesity-related chronic disease, moderate psychopathology, moderate functional limitations, and/or impairment of well-being</p> <p>STAGE 3: Established end-organ damage, significant psychopathology, significant functional limitations, and/or impairment of well-being</p> <p>STAGE 4: Severe (potentially end-stage) disabilities from obesity-related chronic diseases, severe disabling psychopathology, severe functional limitations, and/or severe impairment of well-being</p>

Obesity medicine specialists, certified by the American Board of Obesity Medicine, dedicate a portion or all of their practice to the treatment of obesity. They perform a medical evaluation (history, physical, laboratory, body composition) and provide medical supervision for lifestyle change (nutrition, activity, behavior change), medications, or very low-calorie diets. Obesity is a chronic medical disease and often requires lifelong treatment.



# Evaluation and Treatment Summary

## Comprehensive Evaluation of the Patient with Overweight/Obesity

<b>History</b>	Weight history, past medical history, family history, social history, screening for weight-promoting medications, food intake, activity, review of systems
<b>Physical Examination</b>	Height, weight, blood pressure, body composition analysis, waist measurement, complete physical examination
<b>Laboratory Tests*</b>	Complete blood count, electrolytes, liver function, kidney function, fasting lipid profile, thyroid tests, hemoglobin A1c, uric acid, vitamin D
<b>Diagnostic Testing*</b>	EKG, echocardiogram, exercise stress test, sleep study, barium swallow or esophago-duodenoscopy

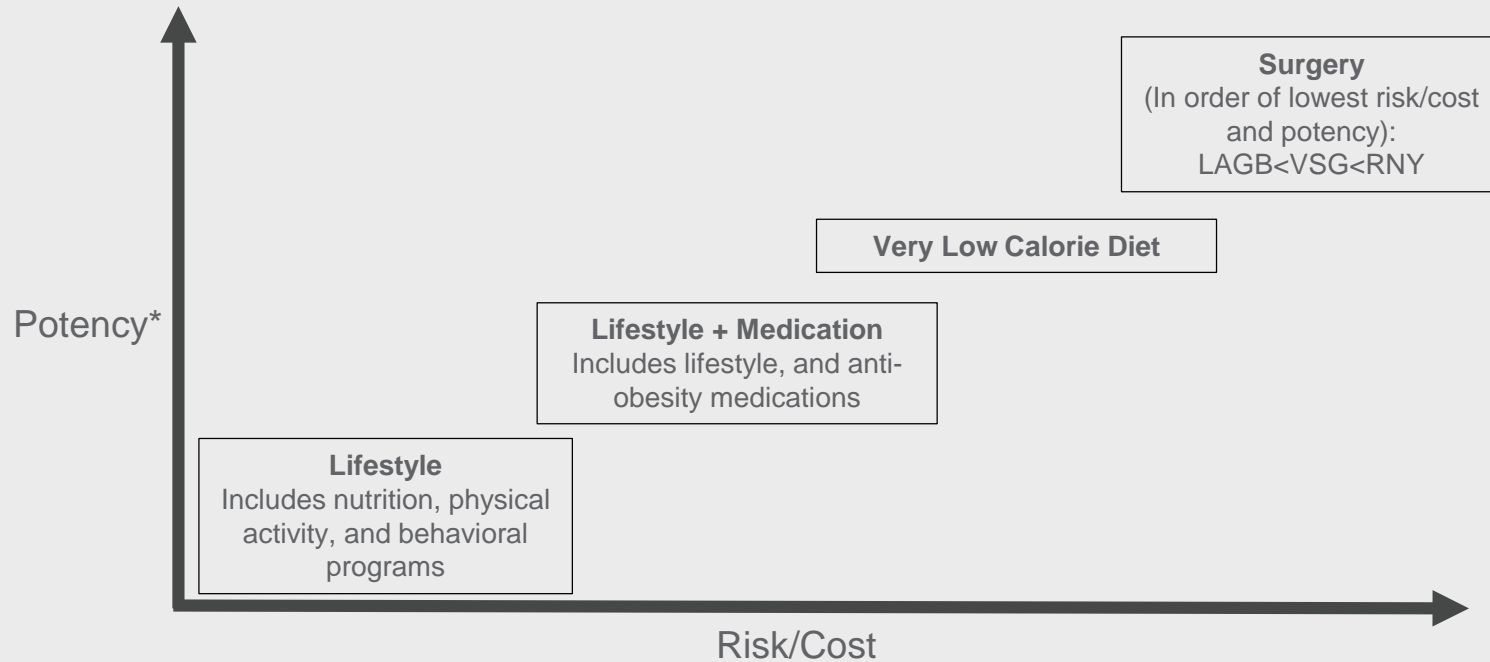
\*lab and diagnostic testing should be individualized

## Individualized Treatment Plans\*

<b>Diet</b>	Use calorie restriction, carbohydrate restriction, food journaling, very low-calorie diet programs
<b>Activity</b>	Give exercise prescription, use pedometers, limit TV and computer time, decrease sedentary time, initial goal of 150 minutes per week of moderate-intensity physical activity
<b>Counseling</b>	Eliminate provider bias and stigma, identify self-sabotage, develop strong support, address stress management, sleep optimization, other psychological support as needed
<b>Pharmacotherapy</b>	Use pharmacotherapy as part of a comprehensive program
<b>Referral</b>	Consider referral to an obesity medicine specialist

\*If ineffective, consider referral to a metabolic and bariatric surgeon. Optimal pre- and post-operative care includes an obesity medicine specialist.

# Current Treatment Options for Obesity



\*Potency includes many factors, such as the amount, rate, and sustainability of weight loss, and the long-term resolution of adiposopathy and fat mass disease. Potency varies greatly for each individual (i.e., long-term adherence to a lifestyle program can be as potent as gastric bypass surgery).

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# Disclosures

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