Obesity: Pharmacotherapy and Surgical Options

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Disclosures

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OMA Obesity Algorithm eBook, Slides, Authors and Citations

Adult Obesity Algorithm eBook: Detailed overview of Obesity Medicine

Citation: Bays HE, McCarthy W, Christensen S, Wells S, Long J, Shah NN, Primack C. Obesity Algorithm eBook, presented by the Obesity Medicine Association. www.obesityalgorithm.org. 2018-2019. https://obesitymedicine.org/obesity-algorithm/ (Accessed = Insert date)

Adult Obesity Algorithm free downloadable slides: General overview of Obesity Medicine (content omitted in the downloadable slides can be found in the eBook)

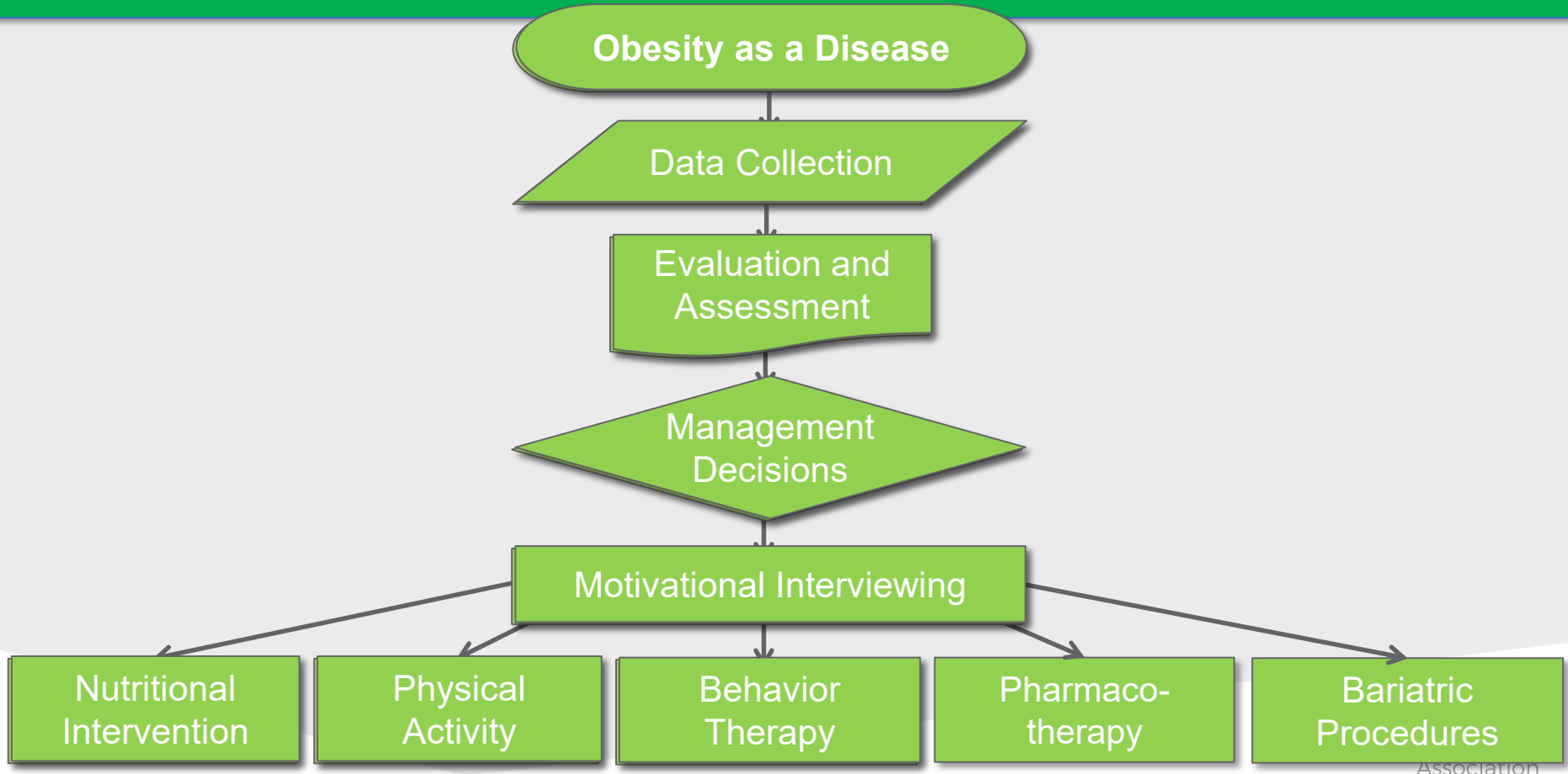
Citation: Bays HE, McCarthy W, Christensen S, Seger J, Wells S, Long J, Shah NN, Primack C. Obesity Algorithm Slides, presented by the Obesity Medicine Association. www.obesityalgorithm.org. 2018-2019. https://obesitymedicine.org/obesity-algorithm-powerpoint/ (Accessed = Insert date)

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. (https://www.abom.org/exam-resources-2/)

Obesity Medicine Association

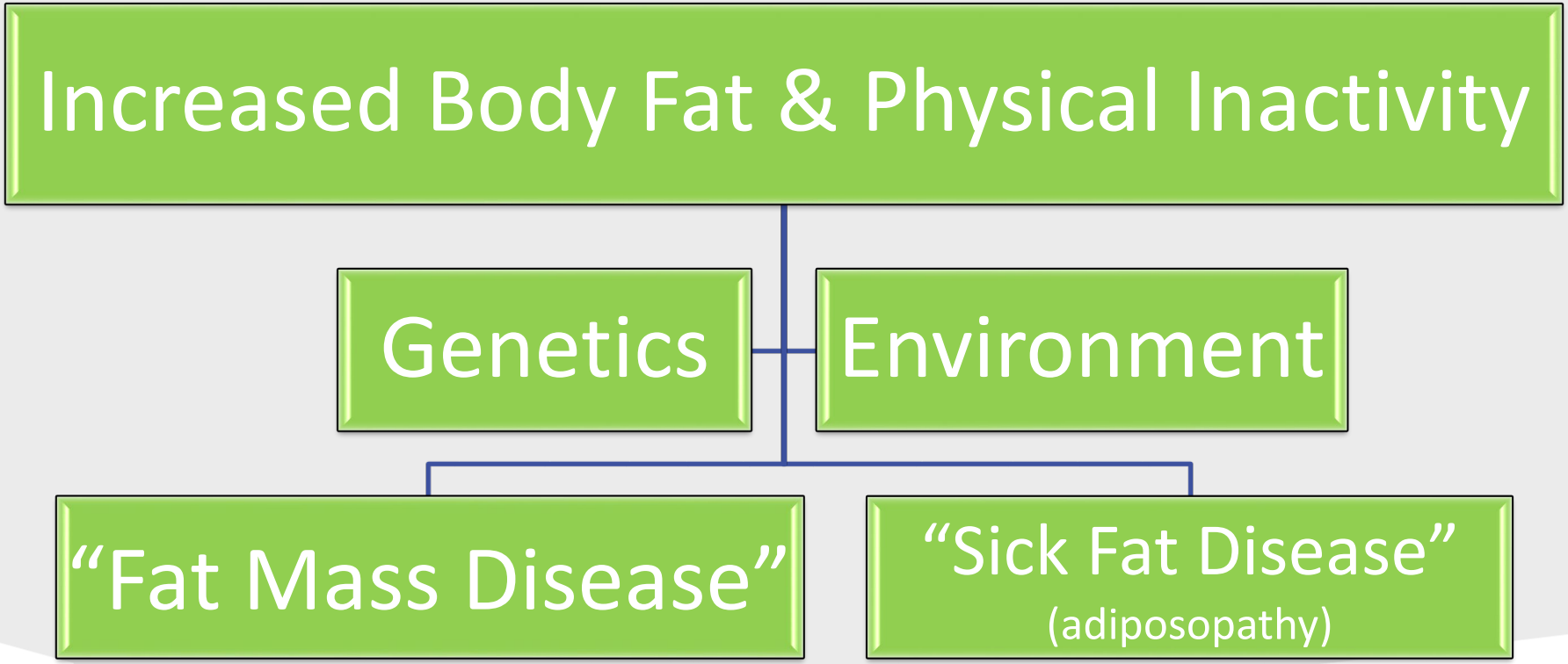
Supporting documents in reference section

The OMA Obesity Algorithm



Supporting documents in reference section

Obesity: Both “Fat Mass Disease” and “Sick Fat Disease” are pathogenic



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Supporting documents in reference section

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.)

Supporting documents in reference section

Obesity Medicine Association

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

Supporting documents in reference section

Obesity Medicine Association

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

Supporting documents in reference section

Obesity Medicine Association

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

Supporting documents in reference section

Obesity Medicine Association

Adiposopathic Immunopathies

- Increased 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)
- Decreased anti-inflammatory adipose tissue factors (e.g., adiponectin)
- Obesity can increase the number of adipose tissue stromal macrophages, and promote a more pro-inflammatory macrophage profile:
- Obesity is often reported to have an increased proportion of M1 macrophages (that produce pro-inflammatory tumor necrosis factor, interleukin IL-6 and monocyte chemoattractant protein-1) relative to M2 macrophages

  (which may produce anti-inflammatory IL-10 and interferons)

Supporting documents in reference section

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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

Supporting documents in reference section

Obesity Medicine Association

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
- Hepatosteatosis (fatty liver)
- Hyperuricemia and gout
- Cholelithiasis
- Acanthosis Nigricans
- Nephrolithiasis
- Glomerulopathy
- Pro-thrombotic predisposition
- Neuropsychiatric diseases (such as worsening depression or loss of gray matter due to adiposopathic immune and endocrine responses)
- Asthma (due to adiposopathic immune and endocrine responses)
- Worsening of other inflammatory diseases (osteoarthritis, atherosclerosis, etc.)

Supporting documents in reference section

Obesity Medicine Association

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.

Supporting documents in reference section

Obesity Medicine Association

Food and Drug Administration (FDA) Principles

FDA-approved Anti-obesity Medication Indications:

- Patients with obesity (e.g., BMI $\geq$ 30kg/m^2)*
- Patients who are overweight (e.g., BMI $\geq$ 27kg/m^2) with presence of increased adiposity complications (e.g., type 2 diabetes mellitus, hypertension, dyslipidemia)*
- Anti-obesity medications are contraindicated in patients hypersensitive to the drugs

Other Principles

- Anti-obesity medications promote variable weight loss over variable duration in patients with overweight or obesity.
- Patients have an average of around 5 – 10% weight loss, with greater weight loss in hyper-responders, and less than 5% weight loss (or even weight gain) in hypo-responders.
- If no clinical improvement (e.g., at least 4 - 5% loss of baseline body weight) after 12-16 weeks with one anti-obesity medication, then 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.

Supporting documents in reference section

Obesity Medicine Association

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 are contraindicated in pregnancy, and should not be administered to, nor taken by women who are pregnant or trying to become pregnant**

Supporting documents in reference section

Obesity Medicine Association

Anti-Obesity Drug Summary

(All have contraindications for hypersensitivity and pregnancy)

Drug	Description	Main Side Effects	Illustrative Drug Interactions
Phentermine	Sympathomimetic amine approved in 1959. It is a DEA Schedule IV stimulant agent approved for short-term use (12 weeks). Some patients may lose about 5% of body weight.	Side effects include headache, high blood pressure, rapid or irregular heart rate, overstimulation, tremor, and insomnia. Should not use with overactive thyroid or uncontrolled high blood pressure or seizure disorder. Contraindicated in patients with history of cardiovascular disease, within 14 days of monoamine oxidase inhibitors, glaucoma, agitated states, drug abuse	During or 14 days following monoamine oxidase (MAO) inhibitors, sympathomimetics, alcohol, adrenergic neuron blocking drugs, and possibly some anesthetic agents
Orlistat	Gastrointestinal lipase inhibitor that impairs digestion of dietary fat. Lower doses are approved over-the-counter. Some patients may lose about 5% of body weight.	Side effects include oily discharge with flatus from the rectum, especially after fatty foods. (May help with constipation.) May promote gallstones and kidney stones. May cause malabsorption of fat soluble vitamins (A, D, E, K). Need to take a multivitamin daily. Contraindicated in chronic malabsorption syndrome and cholestasis. Rare cases of severe liver injury and pancreatitis.	Cyclosporine, hormone contraceptives, seizure medications, thyroid hormones, warfarin
Lorcaserin	Selective, serotonin (5-hydroxytrptamine) 2c receptor agonist that is a DEA Schedule IV agent that improves the sense of fullness. Some patients may lose 5 – 10% of body weight.	Lorcaserin is a generally well-tolerated drug, with headache, dizziness, fatigue, nausea, dry mouth, and constipation occurring more frequently compared to placebo. Warnings and Precautions include serotonin syndrome, neuroleptic malignant syndrome-like reactions, heart failure, psychiatric disorders, and priapism.	Serotonergic (SSRI's, SNRI's, MAO inhibitors) or anti-dopaminergic medications, St John's wort, triptans, bupropion, dextromethorphan, CYP 2D6 substrates

Supporting documents in reference section

Obesity Medicine Association

Anti-Obesity Drug Summary

(All have contraindications for hypersensitivity and pregnancy)

Drug	Description	Main Side Effects	Some Drug Interactions
Liraglutide	Glucagon-like peptide-1 receptor agonist that is an injectable drug. At lower doses (1.8 mg per day), liraglutide is indicated to lower blood sugar among patients with type 2 diabetes mellitus. Liraglutide 3.0 mg per day is approved for treatment of obesity. Some patients may lose 5 – 10% of body weight, especially with the liraglutide higher dose.	Adverse reactions include nausea, hypoglycemia, diarrhea, constipation, vomiting, headache, decreased appetite, dyspepsia, fatigue dizziness, abdominal pain, increase lipase, and renal insufficiency. Contraindicated with personal of family history of medullary thyroid cancer or Type 2 Multiple Endocrine Neoplasia syndrome. Discontinue with suspected pancreatitis, gall bladder disease, or suicidal behavior and ideation. May promote hypoglycemia, particularly in patients with diabetes mellitus treated with insulin or sulfonylureas.	May slow gastric emptying, which may impact absorption of concomitantly administered oral medication.
Naltrexone / bupropion	Combination of naltrexone (opioid antagonist used for addictions) and bupropion (used for depression and smoking cessation). Some patients may lose 5 - 10% of body weight.	Naltrexone / bupropion can cause nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhea, and acute closure glaucoma. The bupropion component is an antidepressant, and antidepressants can increase the risk of suicide thinking in children, adolescents, and young adults; monitor for suicidal thoughts and behaviors. Should not be used in patients with uncontrolled high blood pressure, seizure disorders, or drug/alcohol withdrawal.	Opioid pain medications, anti-seizure medications, MAO inhibitors, and possible drug interactions with other drugs.
Phentermine / topiramate	This is a combination of phentermine (anti-obesity drug) and topiramate (used to treat seizures and migraine headaches). This DEA Schedule IV drug is approved as a weight management pharmacotherapy. Some patients may lose 5 – 10% of body weight.	Phentermine / topiramate can cause paresthesia (tingling or numb feelings to extremities), abnormal taste, insomnia, constipation, dry mouth, and acute angle glaucoma. Should not be used in patients with glaucoma, uncontrolled high blood pressure, heart disease, or hyperthyroidism. Topiramate can cause birth defects. Therefore, phentermine / topiramate should not be started until a pregnancy test is negative, unless the woman is using acceptable contraception, and pregnancy tests should be done monthly during use.	Monoamine oxidase inhibitors. May alter oral contraceptive blood levels.

Functional Foods, Supplements, & Over-the-counter Therapies*

*The Obesity Medicine Association has not endorsed any supplements. This section is intended to provide information the authors believe may be relevant to the clinical management of patients with obesity.

Obesity Medicine Association

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Potential for Publication Bias

Potential publication bias

- Clinicians should be cautious of the published literature regarding supplements or other therapies (including drugs), when the only available evidence is via infrequent, and/or small studies.
- The disproportionate publication of positive or significant results compared to negative or non-significant results potentially compromises the objectivity of literature review and meta-analyses.
- Negative or non-significant study results may not be submitted for publication, are often less likely to be accepted by journals for publication, and potentially less likely to be cited by other journals and the media compared to studies with positive results

Drugs are regulated differently than supplements

- Supplements (do not require a clinical trial development program acceptable to the FDA):
  - Can be marketed without FDA approval
  - Are generally considered safe until proven unsafe
- Drugs (requires a development program acceptable to the FDA):
  - Cannot be marketed until FDA approved
  - Not considered safe until proven saf

Once approved based upon clinical trial efficacy and safety, the FDA assigns an "indicated use" for pharmaceuticals. While not similarly applicable to the health benefits, efficacy or advisability of supplement consumption, independent organizations such as United States Pharmacopeia Dietary Supplement Verification Program (USP verified logo) provide voluntary processes to all for supplement quality indicators (monographs), supporting that what is in the supplement matches what the label says is in the supplement. Independent testing is also performed by companies such as ConsumerLab.com.

Supporting documents in reference section

Obesity Medicine Association

Definitions

	Prescription Drugs	Over-The-Counter Medications (OTC)
Definition	A therapeutic medicine intended for the diagnosis, cure, mitigation, treatment, or prevention of disease	Drugs the FDA considers to be safe and effective, but that do not require a prescription by a health professional (e.g., orlistat)
Approval process	Requires FDA approval before administered and/or prescribed to patients	Requires FDA approval for OTC use via the regulatory process of an OTC drug monograph
Marketing	Regulated by FDA*	Regulated by Federal Trade Commission*

* The FDA Office of Prescription Drug Promotion / OPDP (formerly DDMAC or Division of Drug Marketing, Advertising and Communications). Prescription Drug Advertising: Questions and Answers https://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/ucm076768.htm (accessed April 23, 2018)

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Definitions

	Supplements*	Functional Foods
Definition	Substances taken in addition to dietary intake, such as concentrated form of a nutrient (e.g., vitamins), isolated formulations of a nutrient (e.g., herbs or botanicals), minerals, and amino acids.	Nutrients with potentially favorable effects beyond basic nutrition, such as oatmeal or foods high in substances that may have health benefits (e.g., many phytochemicals)
Approval process	Not applicable. The FDA considers supplements more of a food than drug.	Not applicable
Marketing	Supplements are not permitted to be marketed for the purpose of treating, diagnosing, preventing, or curing diseases. Supplement manufacturers are responsible for ensuring the supplement is safe, claims of benefit are not false or misleading. **	Not applicable

*US Food & Drug Administration. Dietary Supplements. https://www.fda.gov/Food/DietarySupplements/ (accessed April 23, 2018)

**USDA Nutrition.gov. https://www.nutrition.gov/subject/dietary-supplements (accessed April 23, 2018)

Supporting documents in reference section

Obesity Medicine Association

Supplements – Hepatotoxicity

- Increased herbal and dietary supplement (HDS) use is directly proportional to increased HDS-induced liver injury
- HDS-induced liver injury accounts for 20% of cases of hepatotoxicity in the US
- Major implicated agents include anabolic steroids and green tea extract
- Majority of cases of HDS-induced liver injury are from multi-ingredient nutritional supplements

Supporting documents in reference section

Obesity Medicine Association

Over-the-counter Anti-obesity Therapy

Intervention	Mechanism of Action	Effects	Side Effects
Orlistat	Intestinal lipase inhibitor that impairs intestinal fat absorption	Mild weight reduction	Loose, oily stools. Possible deficiency in fat soluble vitamins, liver toxicity, and kidney stones

Supporting documents in reference section

Obesity Medicine Association

Position Statement: Recommendations for Dietary Supplements Sold as Medicinal or Curative for Obesity*

Healthcare providers should:

- Be aware of the lack of credible evidence for efficacy and safety of many supplements promoted for the purpose of weight loss.
- Query patients who desire to accomplish weight loss regarding their use of dietary supplements for this purpose.
- Advise patients who desire to accomplish weight loss of the limited evidence supporting the efficacy and safety of many supplements and the lack of oversight by government agencies regarding the claims made about such supplements
- Be educated on the Dietary Supplement Health and Education Act (DSHEA) and the **roles of FDA and FTC** in safety and claims monitoring of supplements promoted for the purpose of weight loss.
- Healthcare providers are strongly discouraged from engaging in entrepreneurial activities in which they directly profit from the prescribing of non-FDA approved weight-loss remedies where both safety and efficacy have not been proven.

The Obesity Society with co-signatories = Obesity Action Coalition, Obesity Medicine Association, Academy of Nutrition and Dietetics. **www.obesity.org/publications/position-and-policies/medicinal-or-curative** (accessed April 23, 2018)

Supporting documents in reference section

Obesity Medicine Association

Side Effects of Supplements with Insufficient Human Data to Confirm Consistent, Clinically Meaningful, Long-term Weight Loss

Intervention	Side Effects	Description
Chitosan	Indigestion, bloating, constipation	Derived from chitin, a component of crustacean/arthropod exoskeletons (starch similar to cellulose), has both insoluble and soluble properties
Berberine	Nausea, diarrhea, constipation, and abdominal pain	Alkaloid extract from plants such as berberis vulguris (barberry)
Forskolin	Indigestion, hypotension with lightheadedness, syncope, blurred vision, nausea, pale skin, and fatigue	Extract from mint family / Coleus forskohlii
Garcinia Cambogia	Nausea, possible rare cases of liver toxicity	Small green fruit extract containing hydroxycitric acid
Glucomannan	Bloating, flatulence and soft stools	Hemicellulose polysaccharide soluble fiber from roots of the elephant yam
Glucosinolates	High doses may cause goiter and hypothyroidism	Thioesters containing sulfur (mustard family)
Hoodia gordonii (p57)	Increased blood pressure and pulse	Succulent plant consumed by Bushmen in South Africa to reduce appetite
Irvingia gabonensis	Flatulence, headache, sleep disturbances	Seeds from African mango / soluble fiber
Raspberry ketones	Raspberry eructation (burps)	Extracted from raspberries.

Dangers of Weight Loss Supplements Banned by the FDA

Many banned weight loss supplements are illegally available via the Internet. Clinicians and patients should be aware of these products and their associated risks.

Intervention	Side Effects	Mechanism of Action
1,3-dimethylamylamine methylhexanamine- DMAA (geranium or pelargonium graveolens extract)	Adverse adrenergic side effects (e.g., high blood pressure, myocardial infarction, psychiatric disorders, nervous system disorders, and sudden death)	Stimulant, often illegally combined with caffeine
Ephedra (ma huang)	Adverse adrenergic side effects (e.g., high blood pressure, palpitations, myocardial infarction, stroke, seizure, and sudden death)	Ephedrine and pseudoephedrine may reduce appetite
Bitter orange/ synephrine	Adverse adrenergic side effects	Synephrine may reduce appetite

Supporting documents in reference section

Obesity Medicine Association

Dangers of Weight Loss Supplements Banned by the FDA

Many banned weight loss supplements are illegally available via the Internet. Clinicians and patients should be aware of these products and their associated risks.

Intervention	Side Effects	Mechanism of action
2,4 Dinitrophenol (2,4 DNP or DNP)	Hyperthermia, tachycardia, diaphoresis, tachypnea, cardiac arrest, and death	Uncoupling of mitochondrial oxidative phosphorylation and increased fat metabolism
Phenylpropanolamine (PPA)	Headache, tremor, insomnia, agitation, palpitations, high blood pressure, cerebral vasculitis, myocardial infarction, and hemorrhagic strokes	Synthetic sympathomimetic amine, functionally similar to amphetamine and ephedrine, with appetite suppressant effects
Sibutramine	Headache, anxiety, dry mouth, insomnia, myocardial infarction and stroke	Monoamine reuptake inhibitor, increasing norepinephrine, serotonin and dopamine concentrations in the synaptic clefts and suppressing appetite

Supporting documents in reference section

Obesity Medicine Association

Weight Loss Therapies with Mandated Disclaimer by the FDA

Intervention	Proposed mechanism of action	Effects	Warnings
Human chorionic gonadotropin (HCG)	Marketed as reducing appetite and preserving muscle mass during administration of very low-fat diets	Meta-analyses do not support clinically significant weight loss. Since 1976, the FDA has mandated a disclaimer for those who administer HCG*	In 2016, the American Medical Association passed policy that *"The use of HCG for weight loss is inappropriate."*

*1976 FDA disclaimer for HCG: *"There is no substantial evidence that HCG increases weight loss beyond that resulting from caloric restriction, that it causes a more attractive or normal distribution of fat, or that it decreases the hunger and discomfort associated with calorie restrictive diets."*

Supporting documents in reference section

Obesity Medicine Association

Bariatric Surgery

Physiology, Procedures, Micronutrients, Microbiome, Complications

Obesity Medicine Association

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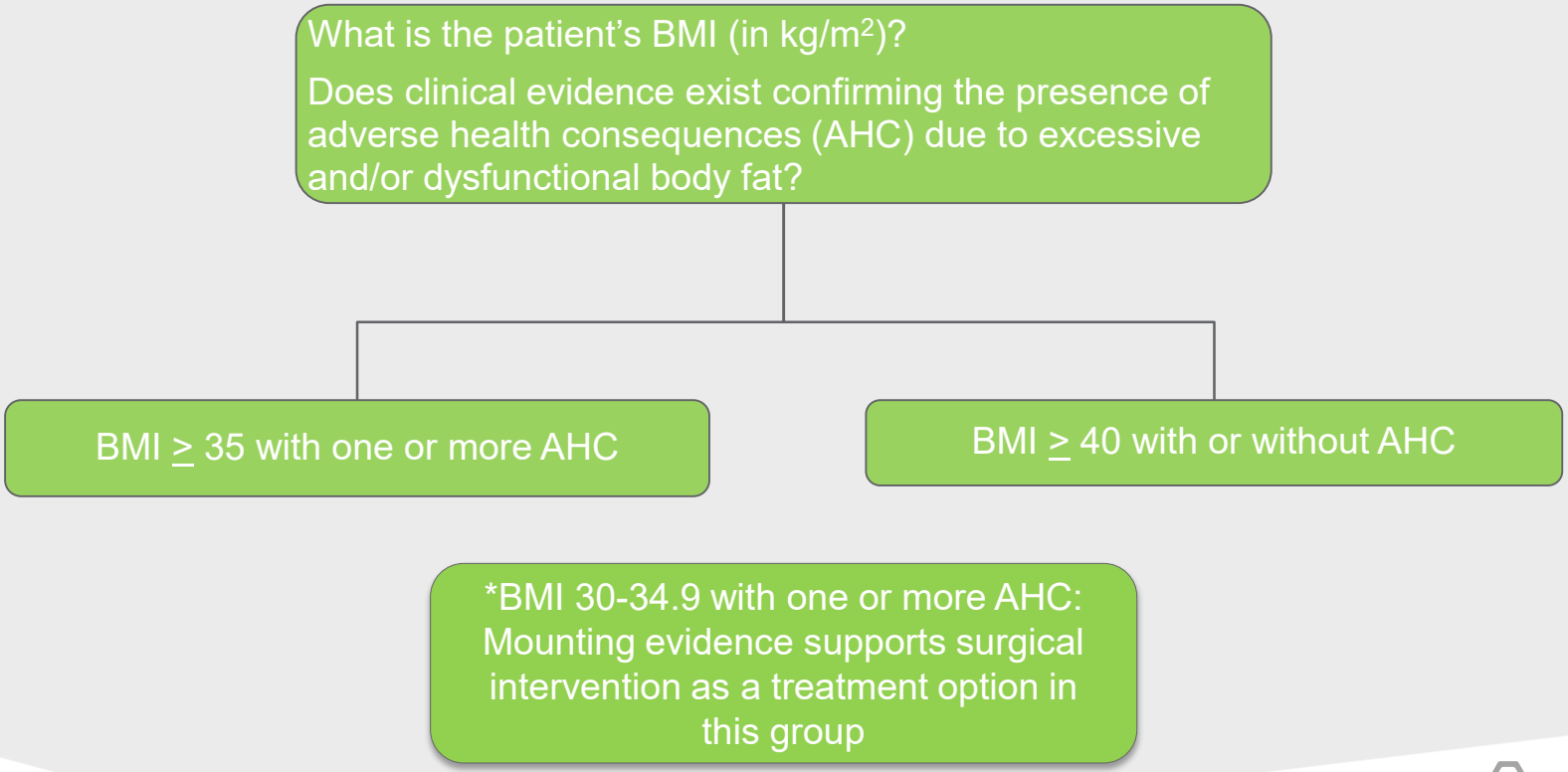
Potential Bariatric Surgery Candidate



Supporting documents in reference section

Obesity Medicine Association

Bariatric Surgery Pre-operative Evaluation

- Medical evaluation by a clinician 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)

Supporting documents in reference section

Obesity Medicine Association

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”

Supporting documents in reference section

Obesity Medicine Association

Bariatric Surgical Procedures

	Pros	Cons	Expected loss in percent excess body weight* at two years	Optimally suited for patients with:	Other comments
Roux-en-Y Gastric Bypass	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
Vertical Sleeve Gastrectomy	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
Laparoscopic Adjustable Gastric Banding	Least invasive; removable	25-40% 5 year removal rate internationally	30-50%	Lower BMI; no metabolic disease	Any metabolic benefits achieved are *dependent* on weight loss
Biliopancreatic Diversion *with* Duodenal Switch	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

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

Supporting documents in reference section

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

Supporting documents in reference section

Obesity Medicine Association

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

Supporting documents in reference section

Obesity Medicine Association

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 doudenal 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

Supporting documents in reference section

Obesity Medicine Association

Vertical Sleeve Gastrectomy (VSG)

Most Common Chronic Complications

- Weight regain or lack of long-term weight loss
- Sleeve dilation
- Worsening GERD or de novo GERD
- Luminal stenosis/strictures
- Alkaline reflux gastritis
- Staple line ulcers and 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

Supporting documents in reference section

Obesity Medicine Association

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

Supporting documents in reference section

Obesity Medicine Association

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

Supporting documents in reference section

Obesity Medicine Association

Biliopancreatic Diversion with Duodenal Switch (BPD/DS)

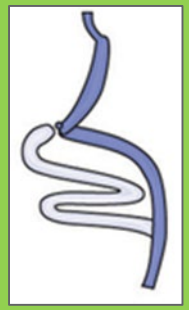
Procedure in which a partial gastrectomy (much like a sleeve) is performed, removing 70-80% greater curvature of the stomach sparing the pylorus and a small portion of the duodenum and the creation of a Roux-en-Y duodenoenterostomy bypassing a large portion of the intestine.

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
  - Irritable bowel syndrome
- Patient demonstrates an unwillingness or an inability to follow / afford long-term recommendations (e.g., blood testing and post-operative vitamins) 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



Supporting documents in reference section

Obesity Medicine Association

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.

Supporting documents in reference section

Obesity Medicine Association

Other FDA-approved Bariatric Technologies

Aspiration Therapy via Modified Percutaneous Endoscopic Gastrostomy (PEG)

- Mechanism: Drains 30% of ingested meal
- Indication: Body mass index 35-55 kg/m^2
- 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^2 or > 35 kg/m^2 among those with adverse consequences of obesity
- Efficacy: 8.5% excess weight loss
- Safety: Potential gastroparesis (vagal trunk injury or entrapment)

Supporting documents in reference section

Obesity Medicine Association

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^2; approved for up to 6 months
- Types: Intragastric fluid-filled and swallowable gas filled balloons
- 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

Supporting documents in reference section

Obesity Medicine Association

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.asmbs.org.

Supporting documents in reference section

Obesity Medicine Association

Micronutrient Deficiency Replacement after Bariatric Surgery: Vitamins/Minerals

Vitamin/ Mineral	Assessment	Replacement of Deficiency & Maintenance
Vitamin A	Retinol	• If deficiency with corneal keratinization, ulceration or necrosis: 50-100,000 IU IM for 3 days, followed by IU IM for 2 weeks; if no corneal changes: 10,000 - 25,000 IU orally for 1-2 weeks • Further treatment depends on persistent malabsorptive effects, as may most be a concern with biliopancreatic diversion/duodenal switch, which may require maintenance oral vitamin A at least 5000 IU per day
Vitamin B1 (Thiamine)	Thiamine	• If hyperemesis, then 100mg IV for 7 days, then 50 mg/d until thiamine in normal range, and then maintenance oral vitamin B1 of at least 3 mg per day.
Vitamin B9 (Folate)	Red blood cell (RBC) folate	• 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 500 ug/d of folic acid
B12 (Cobalamin)	Vitamin B12	• 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. Maintenance dose may include 500 – 1000 ug oral vitamin B12 per day.
Calcium	Calcium	• In addition to ensuring adequate vitamin D, calcium deficiency is typically treated with calcium citrate 1200-1500 mg/d. Calcium citrate may be better absorbed than calcium carbonate • Calcium should be taken at least 1 hour apart from other supplements, especially iron (which competes for absorption)
Iron	Ferritin, iron, total iron binding capacity	• For moderate deficiency, menstruating women, or patients at risk for iron deficiency anemia, total elemental iron oral intake (including in a multivitamin) is often 150 - 200 mg/d • Iron supplementation may be more effective with vitamin C supplementation 500 mg/d • For severe deficiency, IV iron is sometimes required, which is provided in multiple different formulations, some of which require test doses.

Supporting documents in reference section

Obesity Medicine Association

Micronutrient Deficiency Replacement after Bariatric Surgery: Vitamins/Minerals

Vitamin/Mineral	Assessment	Replacement of Deficiency & Maintenance
Vitamin D	25-hydroxyl-(OH)-vitamin D	• A typical oral dose for mild deficiency of vit. D3 is 3000 IU/d, followed by at least 1000 IU/d after gastric bypass and 2000 IU/d after biliopancreatic diversion/duodenal switch once normal range vitamin D levels are achieved • For severe deficiency (e.g., biliopancreatic diversion), IM 100,000 IU vitamin D3 once per month, or otherwise, vitamin D2 50,000 IU/wk orally until vit. D levels in normal range, then D3 3000 IU if still with substantial malabsorptive signs and symptoms, or if stable with vitamin D values in the normal range, then at least D3 1000 IU/d after gastric bypass and D3 2000 IU/d after biliopancreatic diversion/duodenal switch. • 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)
Vitamin E	A-Tocopherol	• A typical dose to treat vitamin E deficiency is 400 to 800 IU/d orally, with oral vitamin E 400 IU/d especially for biliopancreatic diversion.
Vitamin K	Prothrombin time	• 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 4 mg or 300 ug/d. Continued treatment depends on persistent malabsorptive effects, as may most be a concern with biliopancreatic diversion/duodenal switch.
Zinc	Zinc	• 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. If malabsorption less of a risk, then a common dose of zinc is 8 – 15 mg per day.

Supporting documents in reference section

Obesity Medicine Association

Investigational Anti-obesity Pharmacotherapy

Obesity Medicine Association

CLINICAL LEADERS IN OBESITY MEDICINE®

Priorities of Anti-Obesity Drug Development: Functional principles

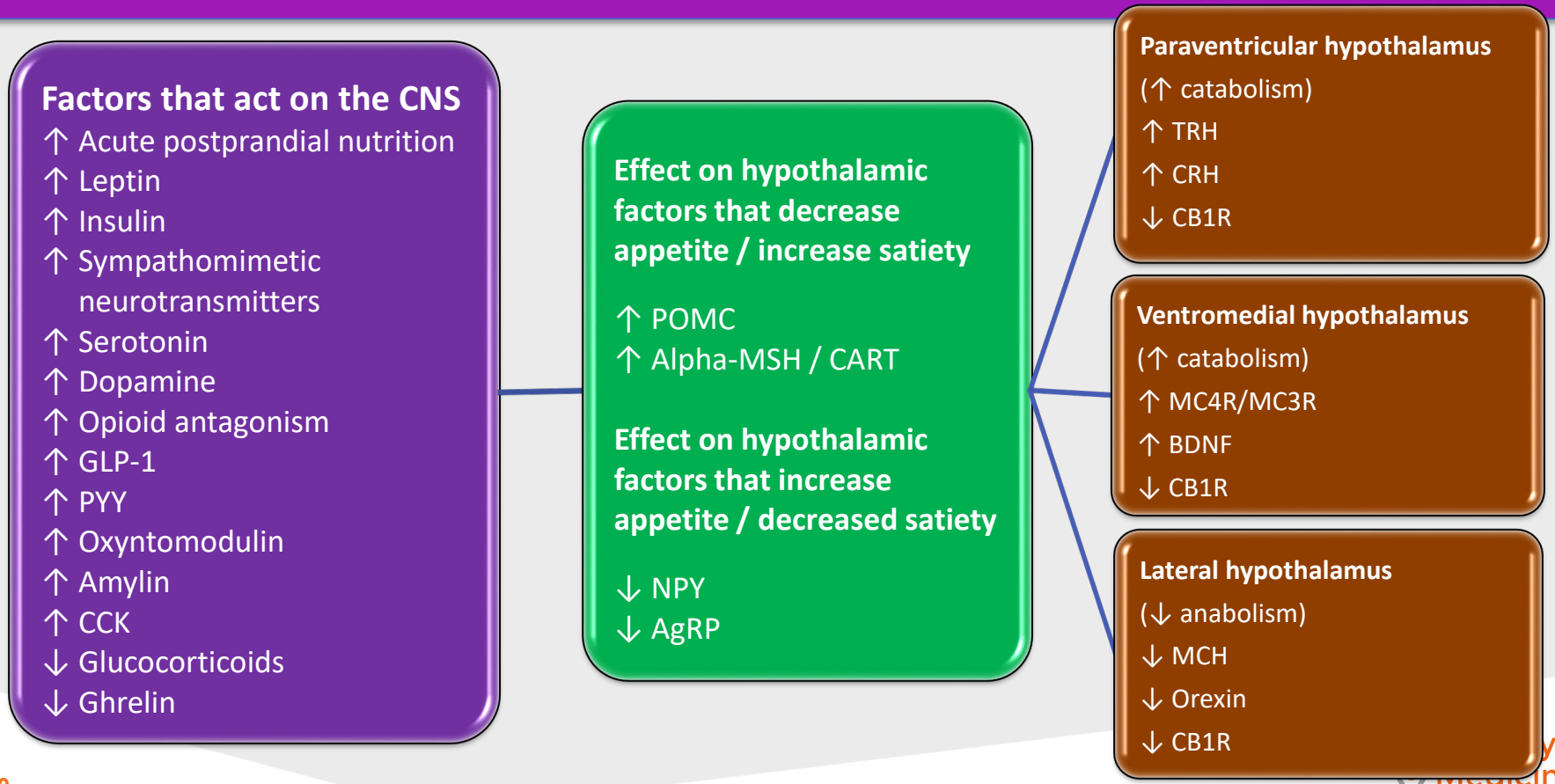
- A meta-analysis of 157 microarray datasets from five independent studies and identified a meta-signature of 1,511 genes ***"endorses the development of effective bioinformatics workflow and further grants an indication for the acceptance of adiposopathy as the root mechanistic pathology that poses risk for development of type 2 diabetes; concept of adiposopathy in place of metabolic syndrome will open the possibility to design drugs, those will ameliorate adipose functions and hence proved to be more effective against type 2 diabetes."***

- *"An emerging concept is that the development of anti-obesity agents must not only reduce fat mass (adiposity) but must also correct fat dysfunction (adiposopathy)."*

Supporting documents in reference section

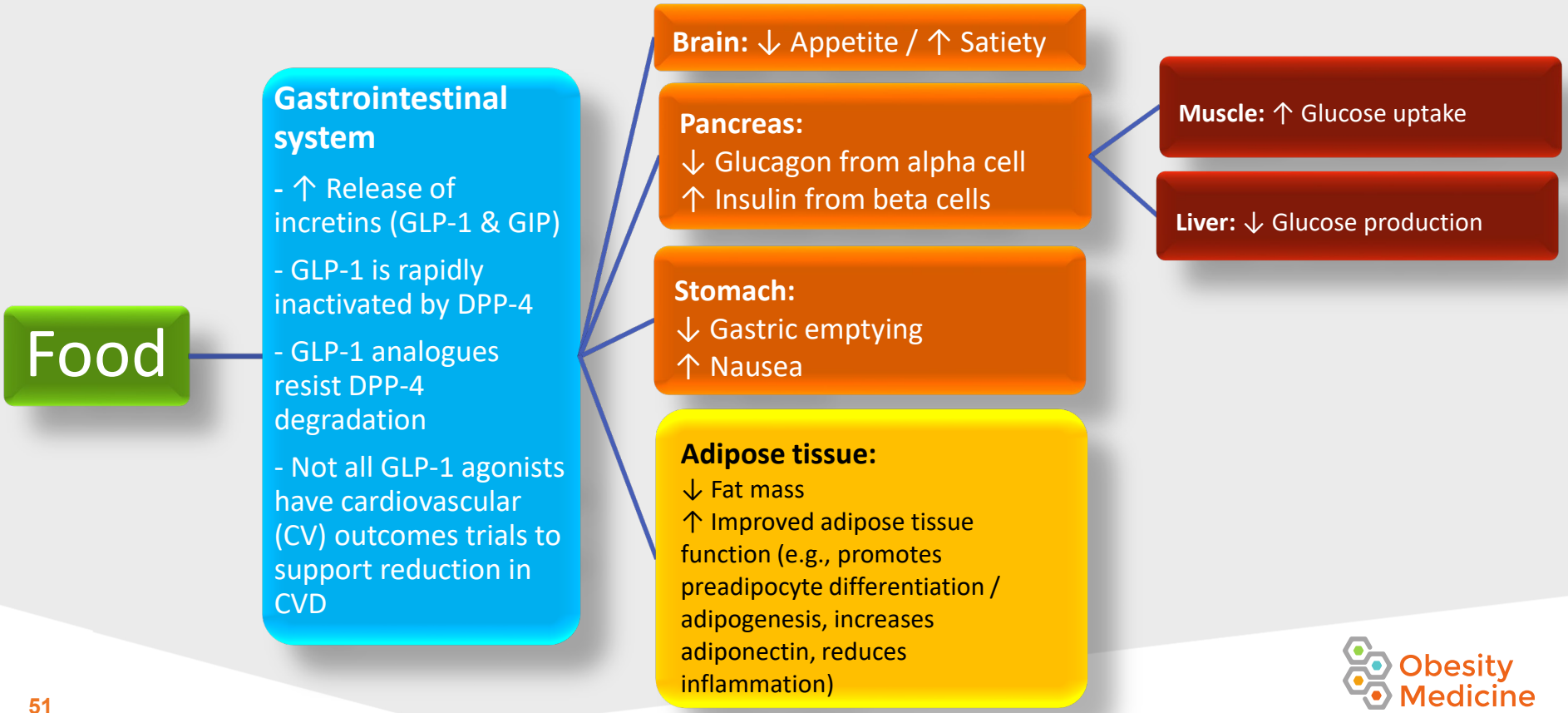
Obesity Medicine Association

Illustrative Targets of Anti-Obesity Therapy



Supporting documents in reference section

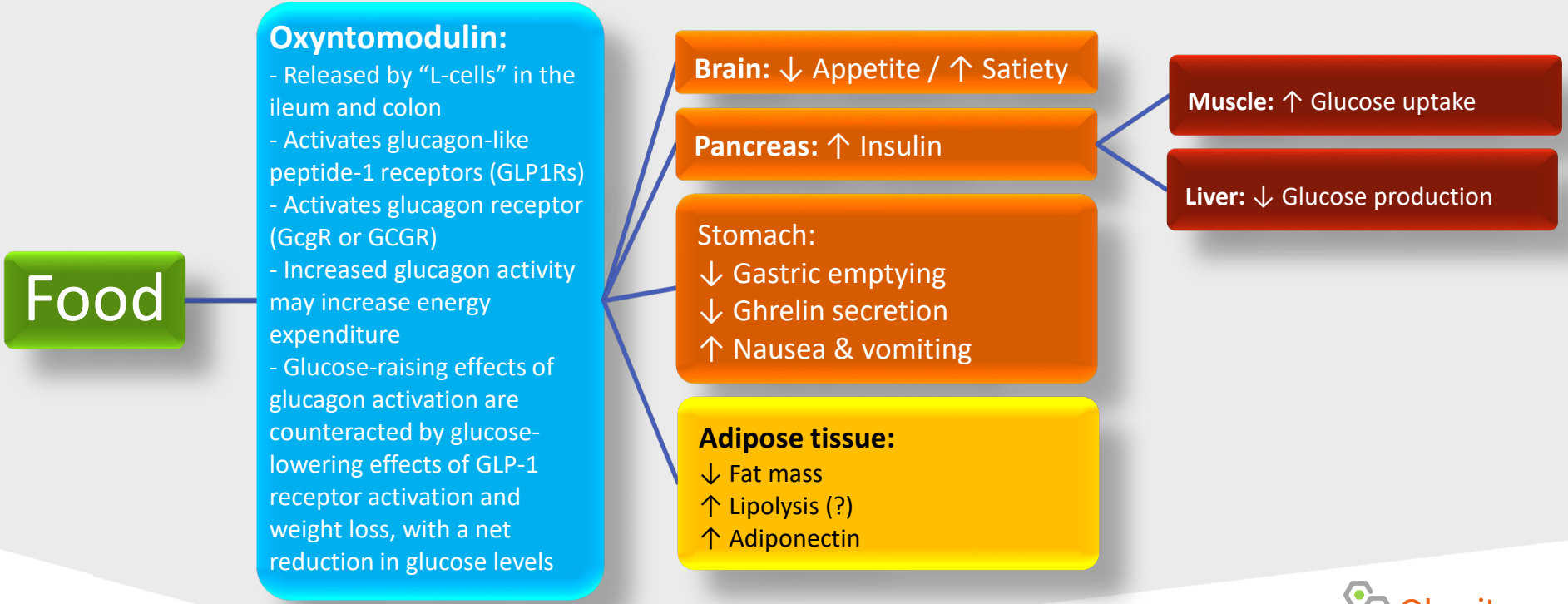
Glucagon-like peptide-1 (GLP-1) agonists



Supporting documents in reference section

Obesity Medicine Association

Oxyntomodulin anti-obesity agents



Supporting documents in reference section

Obesity Medicine Association

Development of anti-obesity pharmacotherapy is following path of drug development of other metabolic diseases

Bias against the use of pharmacotherapy to treat metabolic diseases thought to be caused by unhealthy diet and physical inactivity

Early Days:

Skepticism, if not bias existed against medications to agressively treat diabetes mellitus, hypertension, and dyslipidemia – often thought to be diseases of unhealthy lifestyle

Today:

- Medications to treat diabetes mellitus, hypertension and dyslipidemia are accepted and recommended adjuncts to healthy nutrition and appropriate physical activity
- Use of medications to treat metabolic diseases have proven outcomes benefits, represent standards of care, and often a metric to assess quality of medical care

Supporting documents in reference section

Obesity Medicine Association

Development of anti-obesity pharmacotherapy is following path of drug development of other metabolic diseases

Treatment of the disease of obesity

Past anti-obesity treatments

- May not always achieve sufficient weight loss to achieve patient expectations
- May not always be well tolerated
- May not always have proven health benefits (e.g., improved cardiovascular outcomes)
- May not have mortality benefits

Potential for current and future anti-obesity agents

- Efficacious
- Well tolerated
- Proven health benefits (e.g., improved cardiovascular outcomes)
- Proven mortality benefits

Supporting documents in reference section

Obesity Medicine Association

Obesity: Pharmacotherapy and Surgical Options

Harold Edward Bays MD, FOMA, FTOS, FACC, FACE, FNLA
Medical Director / President
Louisville Metabolic and Atherosclerosis Research Center
Your Body Goal
Louisville KY USA

Tucson Osteopathic Medical Foundation
28th Annual Southwestern Conference
May 2, 2019

45 minute presentation
7:30 – 9:30 AM Session