The obesity epidemic-Is there a solution?

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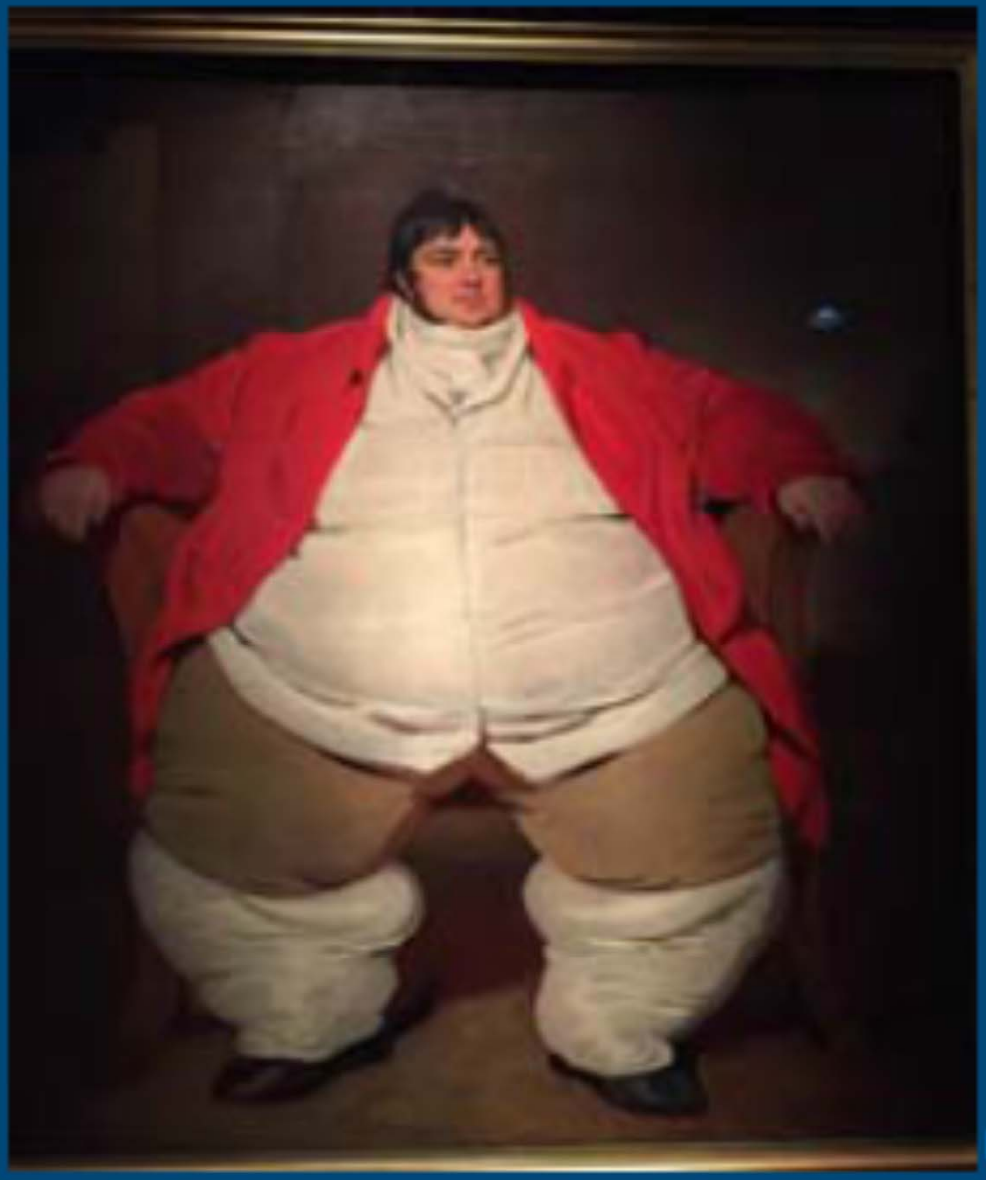
Learning Objectives

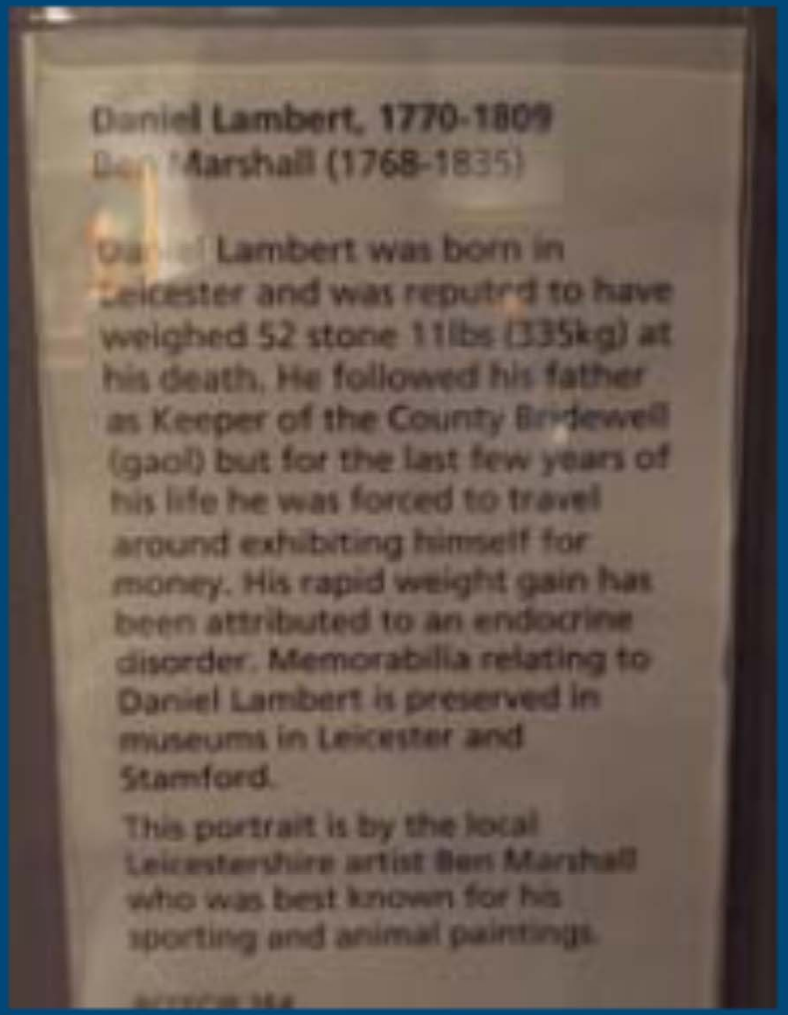
- Articulate the scientific definition of obesity and how to apply the BMI formula.
- Explain that obesity is caused by an interaction of environmental factors and genetic factors (The genetic factors may influence energy expenditure and efficiency as well as appetite control).
- Describe the medical risks and complications associated with obesity.
- Develop treatment goals for clinical management of obesity and design an obesity treatment plan that includes lifestyle modification (healthy nutrition, physical activity and behavior modification), pharmacological management and surgical intervention.

Commonly Asked Questions

- Do I need to know the generic and brand names for the exam?-YES
- Do I need to know the recommended starting dose and dosing ranges for the exam-YES

Morbid Obesity in the 1700's





Hunterian Museum; Royal College of Surgeons. London UK

Etiology of Obesity-Complex and Multifactorial

- **Genetic and epigenetic influences- 70%**
- **Acquired: 30%**
  - **Increased caloric intake**
  - **Biological influences of hormones (leptin, adiponectin etc.)**
  - **Gut microbes**
  - **Imbalance of signals related to energy regulation (gut/adipose vs. hypothalamic)**

What are the latest statistics on adult obesity in the United States?

During the past 20 years, there has been a dramatic increase in obesity in the United States and rates remain high. More than one-third of U.S. adults (35.7%) and approximately 17% (or 12.5 million) of children and adolescents aged 2-19 years are obese.

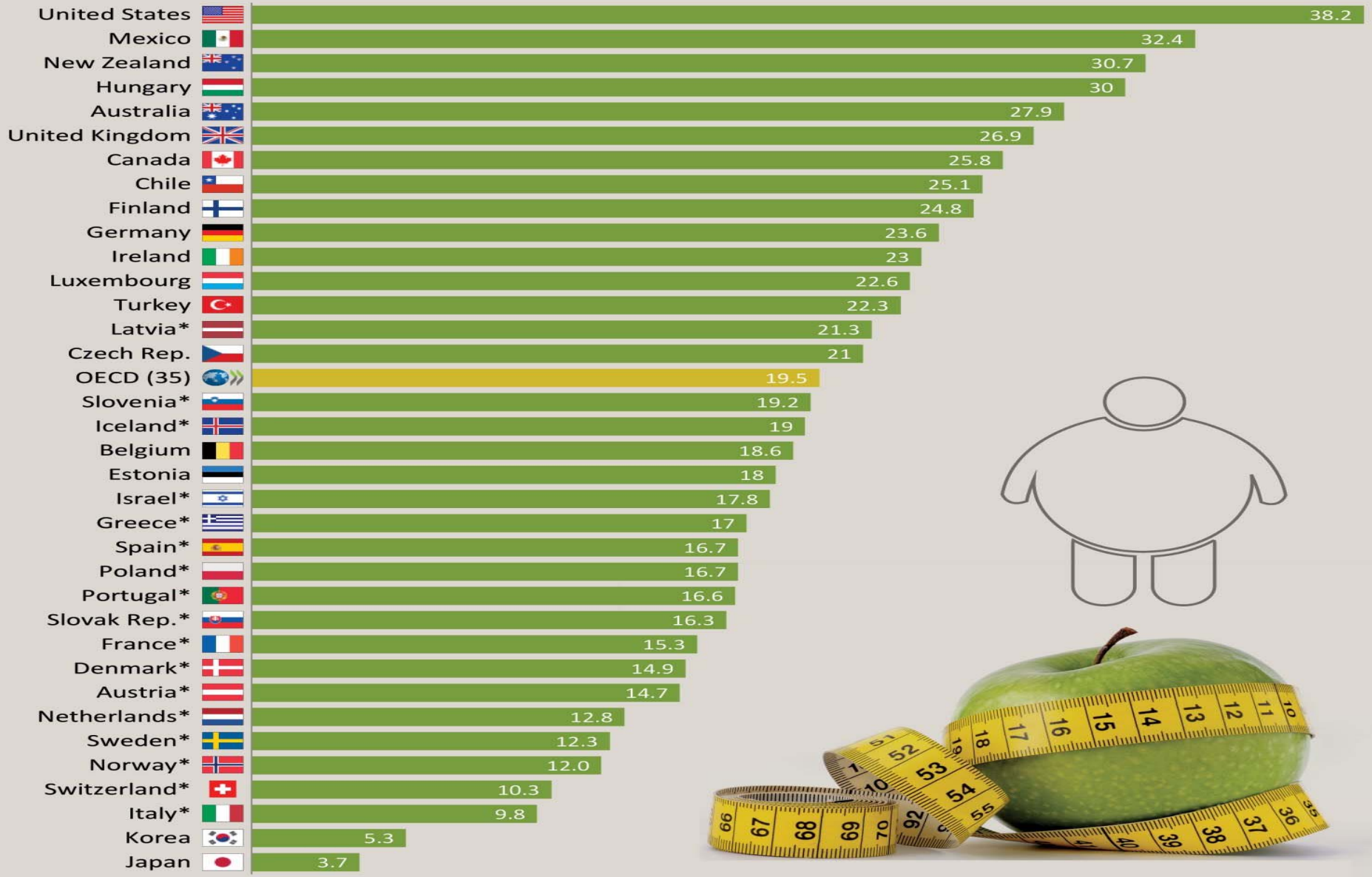
http://www.cdc.gov/obesity/data/facts.html

Obesity in US

- Of all high income countries, the United States has the highest rates of overweight and obesity, with fully a third of the population obese—a rate projected to rise to around 50 percent by 2030.
- As with most health issues, the burden of obesity isn't felt equally across all parts of society. The poor have higher rates than those with higher income. Those with less education have higher rates than those with more education. And certain minority groups—especially African-American and Hispanic women—have much higher rates than other groups.

Obesity rates

As % of total adult population (aged 15 years and over), 2015 or nearest year



Note: * means that self-reported height and weight data are used in these countries, while measured data in other countries.
Source: OECD (2017), OECD Health Statistics 2017 (Forthcoming in June 2017).
www.oecd.org/health/obesity-update.htm

OECD

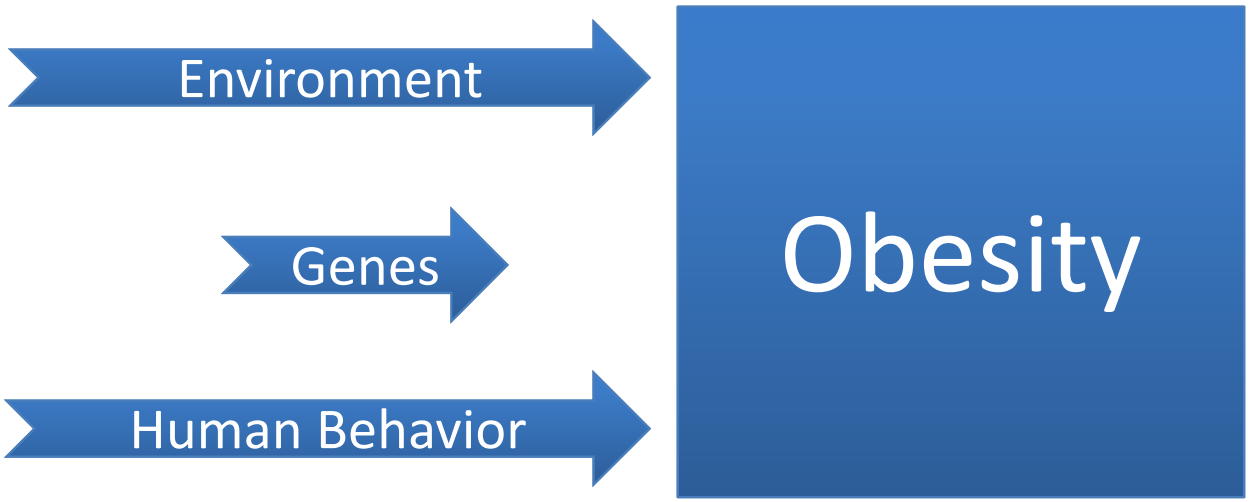
Background

Overweight and obese persons are at increased risk of:

- Hypertension
- Type 2 diabetes
- Coronary heart disease
- Gallbladder disease
- Certain cancers
- Dyslipidemia
- Stroke
- Osteoarthritis
- Sleep apnea

CDC/NCHS NHANES 1999

What factors contribute to obesity?



Genetic Factors

- Changes in genetic makeup of populations may not be fully responsible for the rapid rise in obesity
- Genetic predisposition does play a vital role in the development of obesity

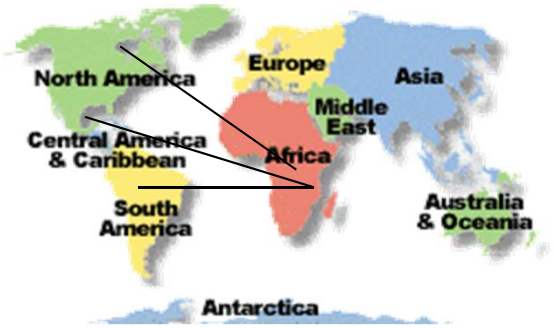
How might genes contribute to obesity?

One of the intriguing explanations for the rapid rise in obesity is the mismatch between today's environment and "energy thrifty genes" that multiplied in the past under different environmental conditions when food sources were rather scarce.

Obesity (2013) 21, 835-846

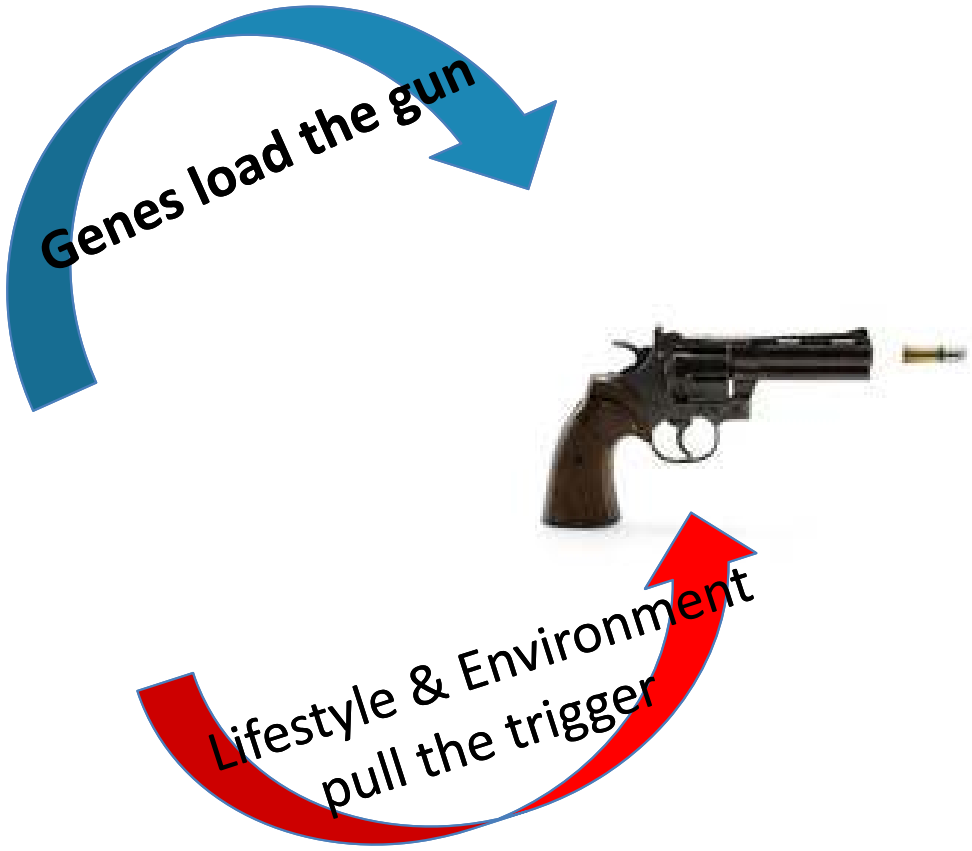
The Thrifty Gene Hypothesis

- Populations exposed to periodic famines, through natural selection increase frequency of ‘protective genes’
- These genes allows efficient energy conservation and fat storage during times of abundance
- In the presence of food abundance, these genes become disadvantageous predisposing to obesity and diabetes



International Journal of Obesity 31; 9 1337-9

Genes: Only Part of the Story



Obesity
Hypertension
Diabetes
Hyperlipidemia

LEPTIN & GHRELIN

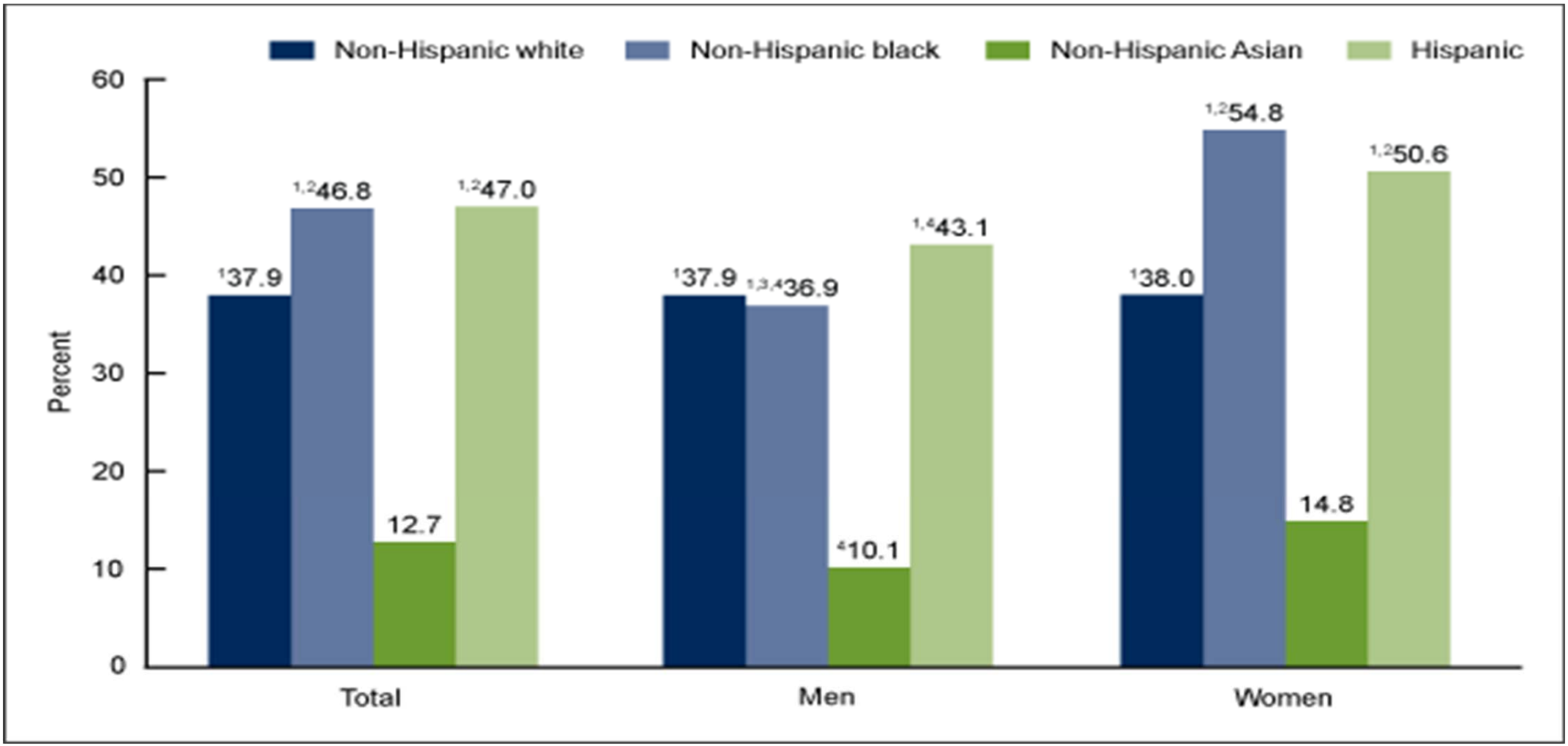
Metabolic adaptations work against weight loss and maintenance of lower body weight: changes in metabolic rate

- Weight loss is associated with a decrease in resting metabolic rate and total energy expenditure independent of body weight and body composition

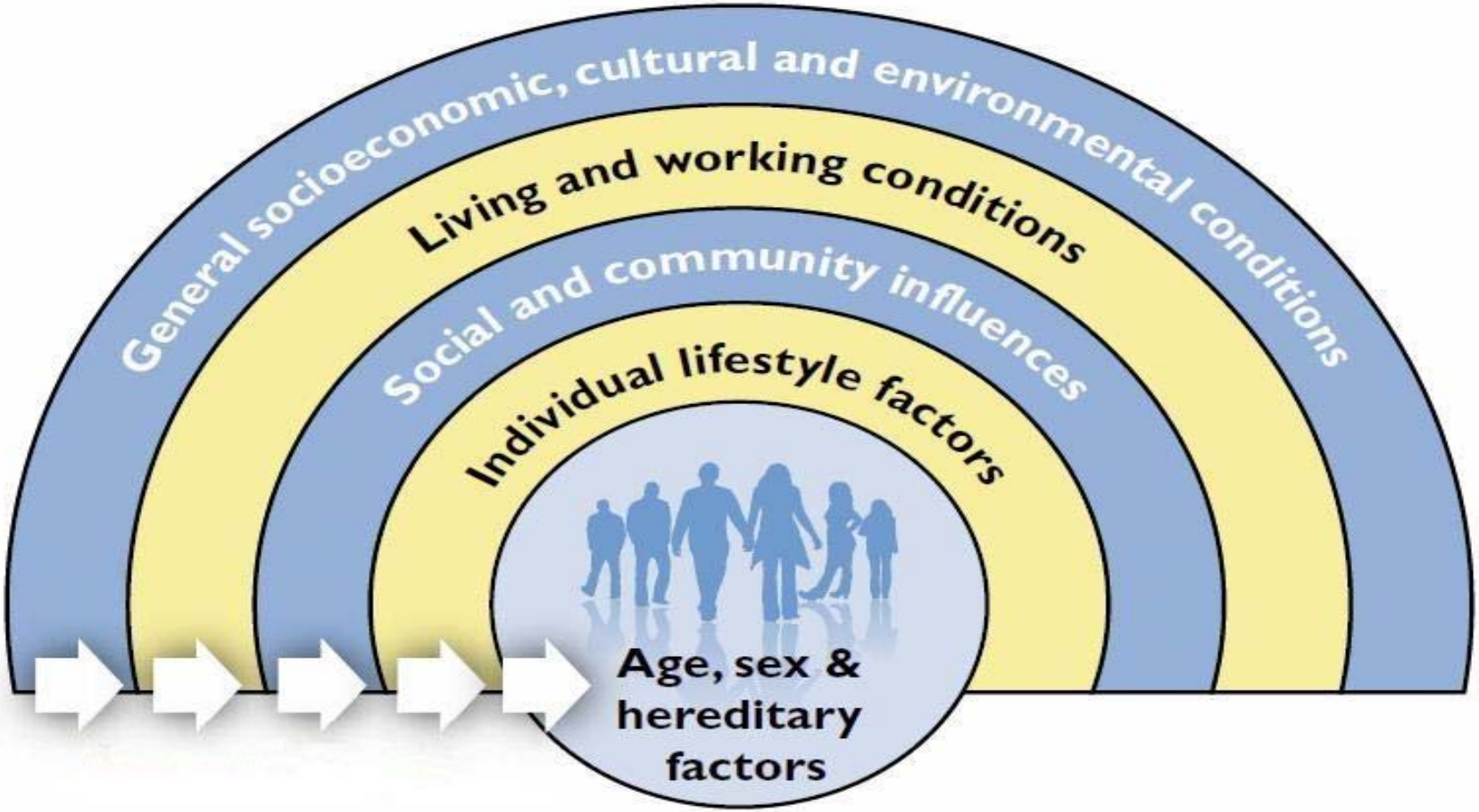
- A formerly obese person requires fewer kcal/day to maintain the same body weight and physical activity level as a never obese person with the same body weight and composition

Almost every sociodemographic group is affected by obesity

Age-adjusted prevalence of obesity among adults aged 20 and over, by sex and race and Hispanic origin: United States 2015-2016



Environmental conditions/Health Determinants



Health Determinants Model

Obesity Prevalence in 2017 by Education and Age

- Obesity decreased by level of education. Adults without a high school degree or equivalent had the highest self-reported obesity (35.6%), followed by high school graduates (32.9%), adults with some college (31.9%) and college graduates (22.7%).
- Young adults were half as likely to have obesity as middle-aged adults. Adults aged 18-24 years had the lowest self-reported obesity (16.5%) compared to adults aged 45-54 years who had the highest prevalence (35.8%).

Obesity and Socioeconomic Status

- Among men, obesity prevalence was lower in the lowest and highest income groups compared with the middle income group. This pattern was seen among non-Hispanic white and Hispanic men. Obesity prevalence was higher in the highest income group than in the lowest income group among non-Hispanic black men.
- Among women, obesity prevalence was lower in the highest income group than in the middle and lowest income groups. This pattern was observed among non-Hispanic white, non-Hispanic Asian, and Hispanic women. Among non-Hispanic black women, there was no difference in obesity prevalence by income. https://www.cdc.gov/obesity/data/adult.html

Number 1 cause of obesity in women of color, particularly Black women

Behavioral Health Issues

- "If there's obesity, there's a good chance, especially if there's morbid obesity, that something tragic happened in that person's history, at one point or another,"
- Sexual abuse is common among morbidly obese women

Precious

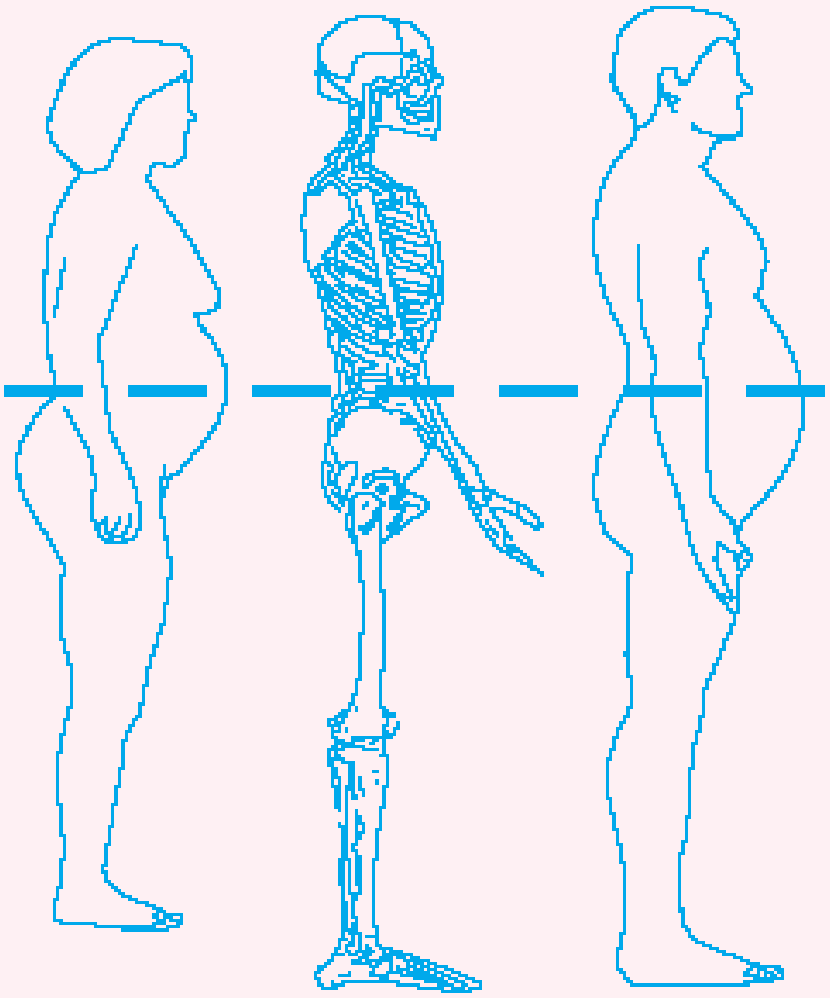
Assessment of Overweight and Obesity***

- Waist Circumference
  - High risk:
    - Men >102 cm (40 in.)
    - Women > 88 cm (35 in.)

- Linked to T2DM, Dyslipidemia, HTN, and CVD

Waist Circumference Measurement

To measure waist circumference, locate the upper hip bone and the top of the right iliac crest. Place a measuring tape in a horizontal plane around the abdomen at the level of the iliac crest. Before reading the tape measure, ensure that the tape is snug, but does not compress the skin, and is parallel to the floor. The measurement is made at the end of a normal expiration.



Measuring-Tape Position for Waist (Abdominal) Circumference in Adults

Classification of Overweight and Obesity by BMI***

Obesity Class		*BMI kg/m²*
• Underweight		< 18.5
• Normal		18.5-24.9
		18.5-23 (Asians)
• Overweight		25—29.9
		23-27.5 (Asians)
• Obese	I	30.0-34.9
		>27.5 (Asians)
	II	35-39.9
	III	40+

Obesity in Children

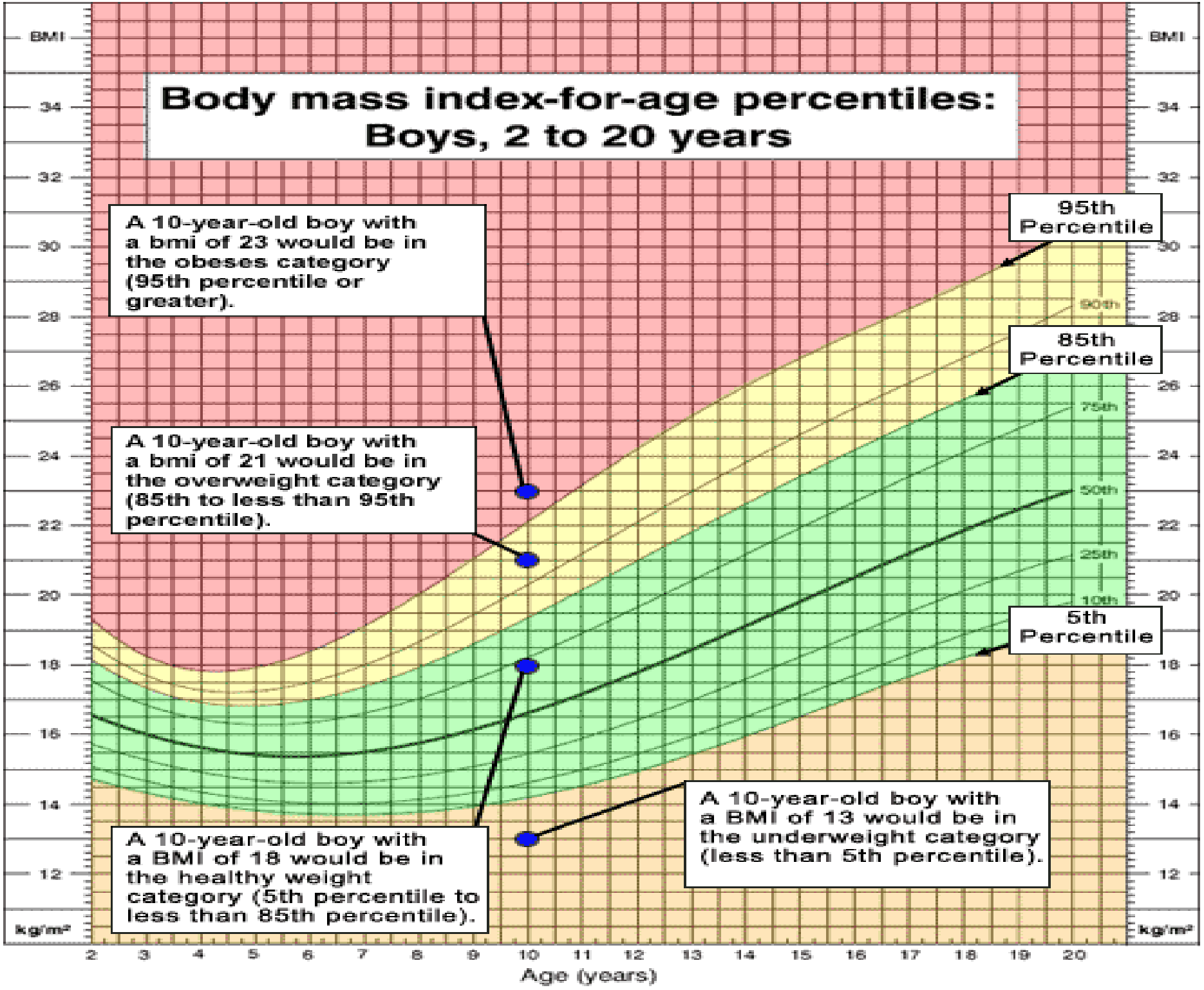
- When defining overweight in children and adolescents, it's important to consider both weight and body composition.
- Among American children ages 2–19, the following are overweight or obese, using the 95th percentile or higher of body mass index (BMI) values on the CDC 2000 growth chart:

Obesity in Children

Overweight children are more likely to be overweight adults.

Successfully preventing or treating overweight in childhood may reduce the risk of adult overweight.

This may help reduce the risk of heart disease and other diseases.


Body mass index-for-age percentiles:
Boys, 2 to 20 years
BMI
kg/m²
Age (years)
95th Percentile
90th
85th Percentile
75th
50th
25th
10th
5th Percentile
A 10-year-old boy with a bmi of 23 would be in the obeses category (95th percentile or greater).
A 10-year-old boy with a bmi of 21 would be in the overweight category (85th to less than 95th percentile).
A 10-year-old boy with a BMI of 18 would be in the healthy weight category (5th percentile to less than 85th percentile).
A 10-year-old boy with a BMI of 13 would be in the underweight category (less than 5th percentile).

- Individuals affected by obesity or excess weight frequently confront stigma and discrimination in the workplace, educational institutions, health care facilities, and many other settings.
- These stigmatizing experiences can impair emotional well-being, leading to depression, anxiety, low self-esteem, and even suicidal behaviors. Unfortunately, weight stigma can also lead to unhealthy behaviors and risk factors that exacerbate obesity
- Thus, weight stigma poses significant consequences for both emotional and physical health.

New Guidelines ***

- **New guidelines say that there is no ideal diet — whatever works to help obese patients lose 5%-10% of their body weight.**
- The most effective diet plans include two to three in-person meetings a month
- People should follow diets that fit their taste and health status
- Doctors should encourage obese patients to lose 5% to 10% of their weight

Medical Nutrition Therapy

- **Personalized plans** for diet management, nutrition education, weight control, exercise and behavior modification are imperative.

Target Weight: Realistic Goals***

- Substitute “healthier weight” for ideal or landmark weight.
- Accept slow, incremental progress to goal.
  - — Short-term goal: 5 to 10 percent loss, **1 to 2 lb per week (4 lb over 4 weeks)**.
  - — Interim goal: Maintenance.
  - — Long-term goal: Additional weight loss, if desired, and long-term weight maintenance.

Weight Loss Goals***

Goal: Decrease body weight by **5-10%** from baseline.

- If goal is achieved, further weight loss can be attempted if indicated.
- Reasonable timeline**: 6 months of therapy**.
  - Moderate caloric deficits
  - Weight loss 1 to 2 lbs./week

Weight Loss Goals

- Start weight maintenance efforts after 6 months.
  - Combined modalities of diet, activity, and behavior therapy
  - May need to be continued indefinitely.
- If unable to lose weight, prevent further weight gain.

Strategies for Weight Loss and Maintenance

- Dietary therapy
- Physical activity
- Behavior therapy
- “Combined” therapy
- Pharmacotherapy
- Weight loss surgery

- *The long and winding road for weight loss drugs*

Pharmacotherapeutic Agents **NOT** for Weight Loss

Noradrenergic agents (*not recommended*)

- Methamphetamine HCL (desoxyephedrine HCL)
- Amphetamine sulfate
- Dextroamphetamine sulfate (Dexedrine)
- Amphetamine/dextroamphetamine mixtures (Adderall)
- Benzphetamine (Didrex)
- Ephedrine (various)

Current FDA Requirements ***

- Drug must produce a statistically significant placebo-subtracted weight loss of greater than 5% of baseline weight at 1 year
- More than 35% of treated patients achieve a > 5% weight loss that must be at least twice that produced by treatment with placebo.
- Drug must improve obesity related metabolic abnormalities, including blood pressure, lipid, and blood glucose levels.
- Circulation 2012;125(17):2156-64

FDA Approved Weight Loss Pills

- Orlistat (Xenical ®)
- Naltrexone SR/Bupropion SR
- Phentermine and Topiramate (Qsymia®)
- Liraglutide (Saxenda ®)

Orlistat (Xenical ®)

Gastrointestinal lipase inhibitor

Orlistat (Xenical)

Hyperlipidemia: 120 mg orally 3 times daily with meals

Obesity: 120 mg orally 3 times daily with meals

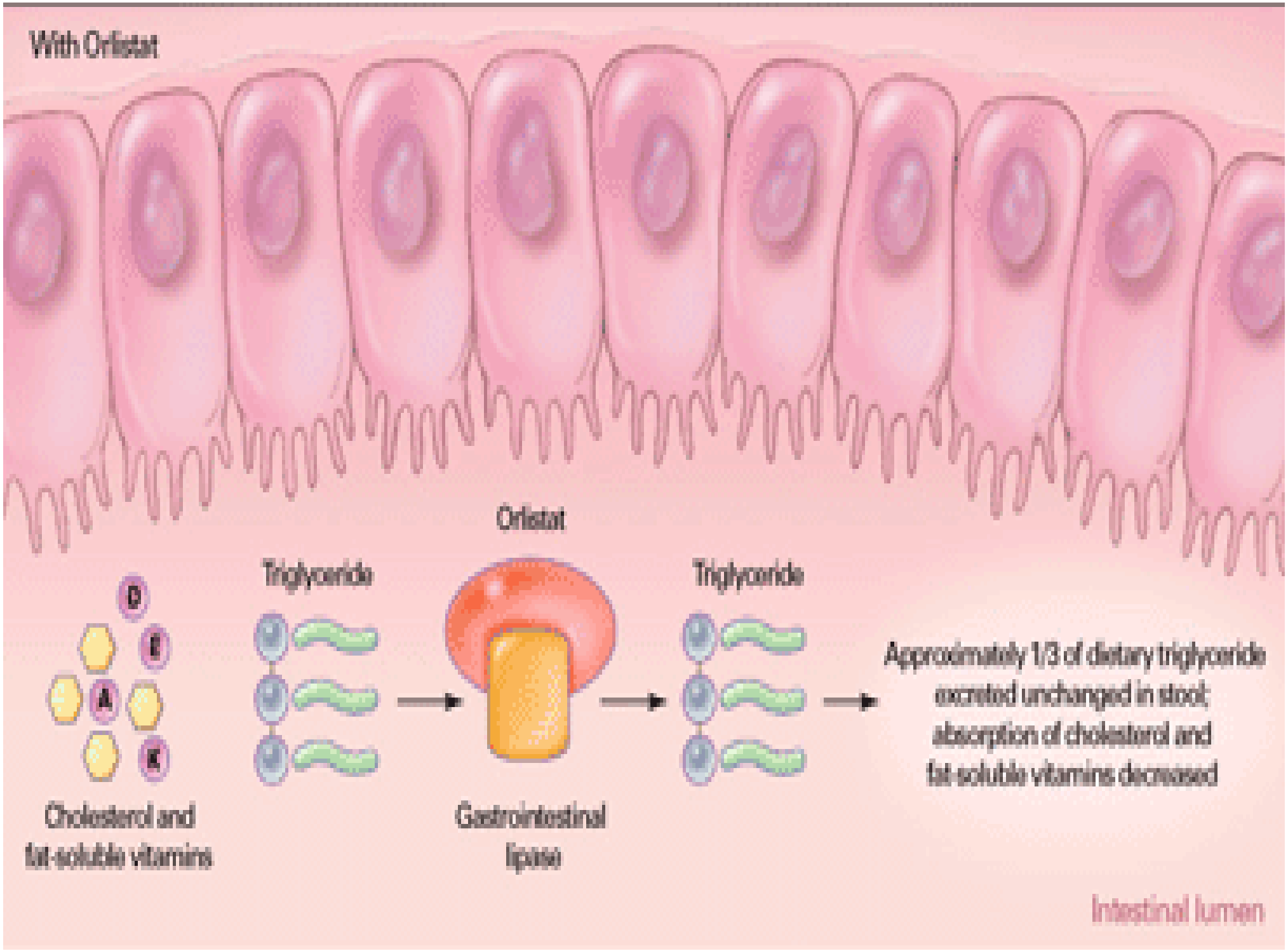
OTC dose 60 mg orally 3 times daily during or within 1 hour of each fat containing meal

Orlistat (Xenical ®) Pediatric Dosing

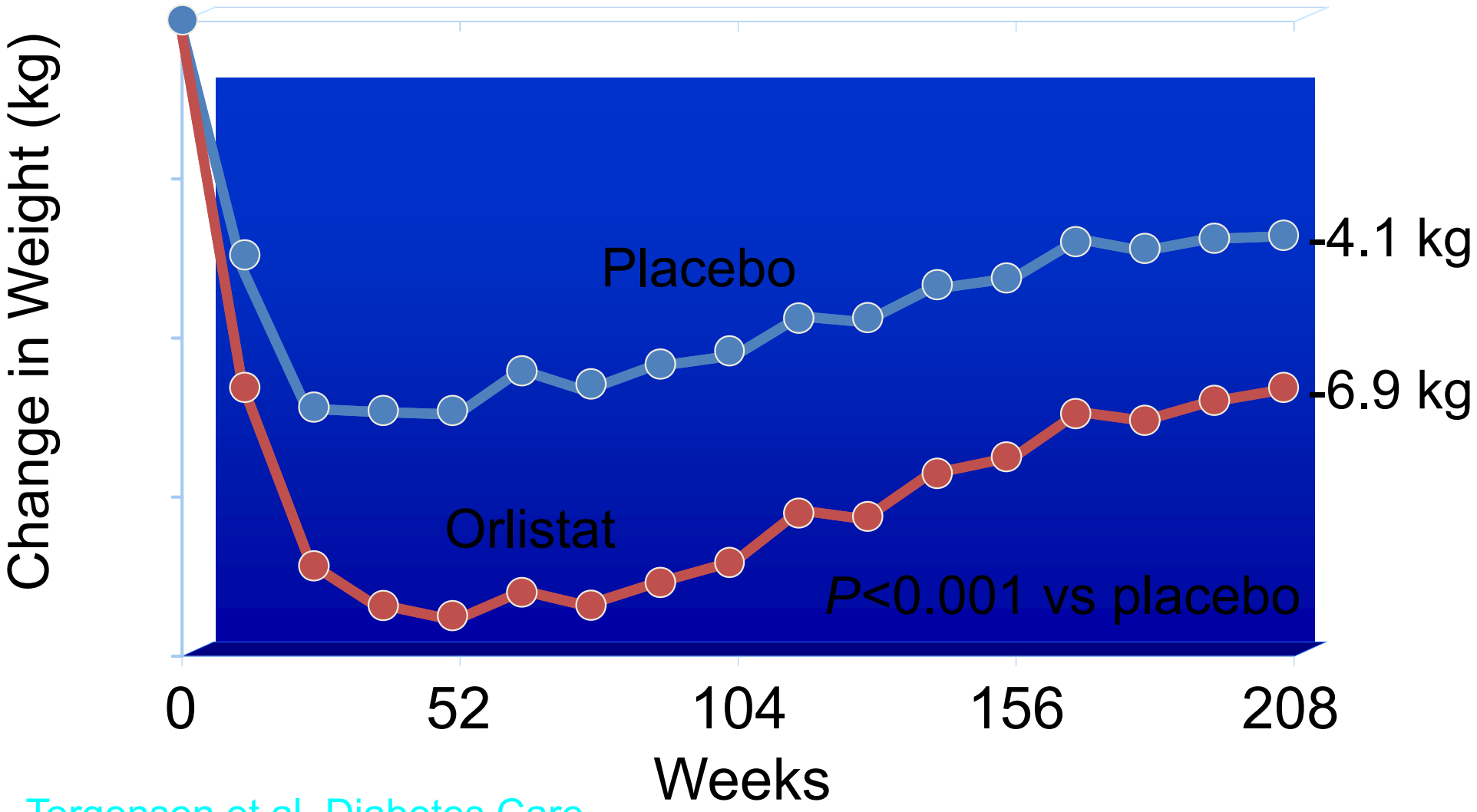
- Pediatric Dosing
- Obesity (12-16 years of age) 120 mg orally 3 times daily during or within 1 hour of each fat containing meal

Lipase Inhibitors (Orlistat-Xenical®) Mechanism of Action

- Gastrointestinal lipases (gastric, pancreatic, carboxylester) are essential for LCT absorption
- Lipase inhibition results in decreased FFA formation from dietary TG
- Orlistat induces weight loss by lowering dietary fat absorption
- Up to 30% decrease in fat absorption occurs with daily doses of 360 mg
- Must be taken with foods that contain fat in order to exert its effect


With Orlistat
Orlistat
Triglyceride
Triglyceride
D
E
A
K
Approximately 1/3 of dietary triglyceride excreted unchanged in stool; absorption of cholesterol and fat-soluble vitamins decreased
Cholesterol and fat-soluble vitamins
Gastrointestinal lipase
Intestinal lumen

Effect of Long-term Orlistat (Xenical ®) on Body Weight



Torgenson et al. Diabetes Care 2004;27:155

Lipase Inhibitors (Orlistat-Xenical®)

Adverse Effects

- Soft stools, abdominal pain/colic, flatulence, fecal urgency, incontinence – at least 1 of these occurs in up to 80% of individuals
- Most common in first 1 – 2 months of therapy
- Malabsorption of fat soluble vitamins may occur – vitamin supplementation should be considered
- Only significant drug interaction is with cyclosporine, where decreases in cyclosporine serum concentrations occur with orlistat use
- Safety and efficacy beyond 4 years is unknown
- OTC status has been approved by FDA

Orlistat (Xenical ®) Clinical Teaching

- Counsel patient to eat a nutritionally balanced diet containing approximately 30% of calories from fat, as taking the drug with a high-fat (greater than 30% total calories from fat) diet or meal may increase gastrointestinal effects.
- This drug may cause abdominal discomfort or pain, oily spotting or evacuation, flatus with discharge, urgency or increased frequency of defecation, nausea, influenza, upper respiratory infection, back pain, headache, menstrual irregularity, or cholelithiasis.
- In order to ensure adequate nutrition, strongly encourage patient to take a multivitamin containing fat-soluble vitamins at least 2 hours before or 2 hours after taking the drug, as the absorption of some fat-soluble vitamins and beta-carotene may be reduced.

Naltrexone SR/Bupropion SR

- Opioid receptor antagonist
- Dopamine/noradrenaline reuptake inhibitor.
- Bupropion's primary mechanism of action is via dopaminergic and noradrenergic stimuli without inhibition of monoamine-oxidase (MAO) or reuptake of serotonin
- Inhibiting reuptake of dopamine and/or norepinephrine decreases the "reward pathway" that various foods can induce.
- Naltrexone, a pure opioid antagonist that blocks an opioid pathway that may slow weight loss

Naltrexone SR/Bupropion SR Dosing

Usual Adult Dose for Weight Loss

- Orally 1 tab (8 mg/90 mg) in am for 1 week;
- 1 tab in am 1 tab in pm for one week;
- 2 tabs in am 1 tab in pm for one week;
- 2 tabs in am 2 tabs in pm
- Stop if <5% loss at 12 weeks

Naltrexone SR/Bupropion SR Side effects

- Nausea, vomiting, headache, dizziness, insomnia
- **Boxed warning:** suicidality; Warning: BP, HR; ↑ seizure risk; glaucoma; hepatotoxicity
- **Contraindications:** seizure disorders; uncontrolled HTN, chronic opioid use; MAOIs; pregnancy

Phentermine and Topiramate (Qsymia ™)

- Qsymia™ is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI)* of:
  - 30 or greater (obese) or
  - 27 or greater (overweight) in the presence of at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia

Qsymia Dosage and Administration

- Recommended dose: Qsymia 3.75 mg/23 mg (phentermine 3.75mg/topiramate 23 mg extended-release) daily for 14 days; then increase to 7.5 mg/46 mg daily.
- Take once daily in morning. Avoid evening dose to prevent insomnia
  - safety and effectiveness in pediatric patients younger than 18 years of age not established

Qsymia Dosage and Administration

- Increase dose (as described) if 3% weight loss is not achieved after 12 weeks on 7.5 mg/46 mg dose
- Discontinue Qsymia if 5% weight loss is not achieved after 12 weeks on maximum daily dose of 15 mg/92 mg.
- Discontinue 15 mg/92 mg dose gradually (as described) to prevent possible seizure.
- Do not exceed 7.5 mg/46mg dose for patients with moderate or severe renal impairment or patients with moderate hepatic impairment.

Qsymia Adverse Effects

- The most common adverse reactions for patients treated with Qsymia included
- tingling sensation of hands and feet,
- dizziness,
- altered taste,
- insomnia,
- constipation and dry mouth.

Qsymia Drug Interactions

- Oral contraceptives: Altered exposure may cause irregular bleeding but not increased risk of pregnancy. Advise patients not to discontinue oral contraceptives if spotting occurs.
- CNS depressants including alcohol: Potentiate CNS depressant effects. Avoid concomitant use of alcohol
- Non-potassium sparing diuretics: May potentiate hypokalemia.
- Measure potassium before/during treatment

Lorcaserin - Belviq®

- The Food and Drug Administration asked Eisai to voluntary withdraw the weight-loss drug lorcaserin (Belviq and Belviq XR) on Feb. 13 after a post-marketing trial with more than 12,000 subjects revealed an increased occurrence of cancer.
- In a Drug Safety Communication, the agency said "health care professionals should stop prescribing and dispensing lorcaserin to patients. Contact patients currently taking lorcaserin, inform them of the increased occurrence of cancer seen in the clinical trial, and ask them to stop taking the medicine. Discuss alternative weight-loss medicines or strategies with your patients."

Liraglutide (Saxenda)

- GLP-1 receptor agonist
- MoA: centrally active to increase satiety and decrease gastric emptying
- Indicated for use in the treatment of obesity for adults with
  - a BMI equal to or greater than 30
  - adults with a BMI of 27 or greater who "have at least one weight-related health condition, such as high blood pressure, type 2 diabetes, or high cholesterol".

Liraglutide (Saxenda)

- Once daily subcutaneous injection
- Initiate at 0.6mg and titrate up weekly by 0.6 mg as tolerated to max of 3.0 mg daily
- Stop if < 5% loss at 12 weeks
- ADE: Nausea 30-40%, Vomiting 10-15%, HA 10%, Diarrhea 20%, Hypoglycemia 10-23%
  - Tolerate out over repeated use

Liraglutide (Saxenda)

- Boxed warning: thyroid c-cell tumors in rodents.
- Warnings: acute pancreatitis, acute gall bladder disease, serious hypoglycemia if used with insulin secretagogue, heart rate increase; use caution in renal impairment; hypersensitivity reactions can occur; monitor for depression or suicidal thoughts.

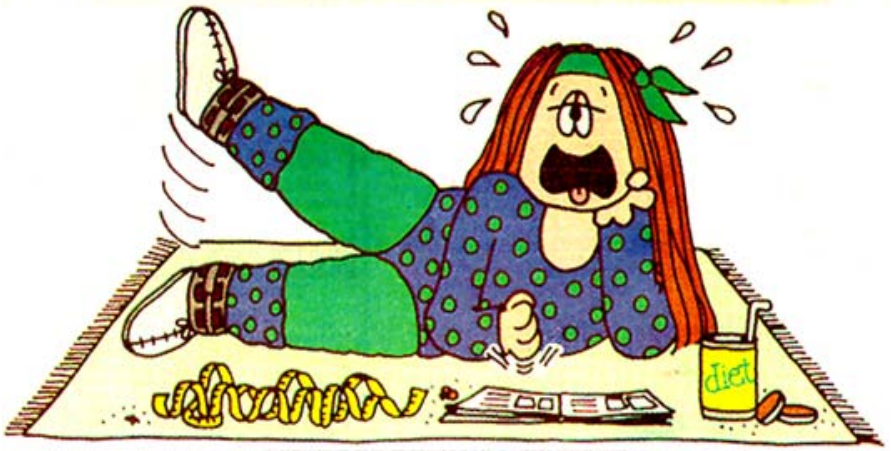
The Washington Post

TUESDAY, MAY 7, 1996

HEALTH

Sorry, Cathy, The New Diet Drug Won't Work All By Itself

(You Still Have to Exercise and Watch What You Eat)

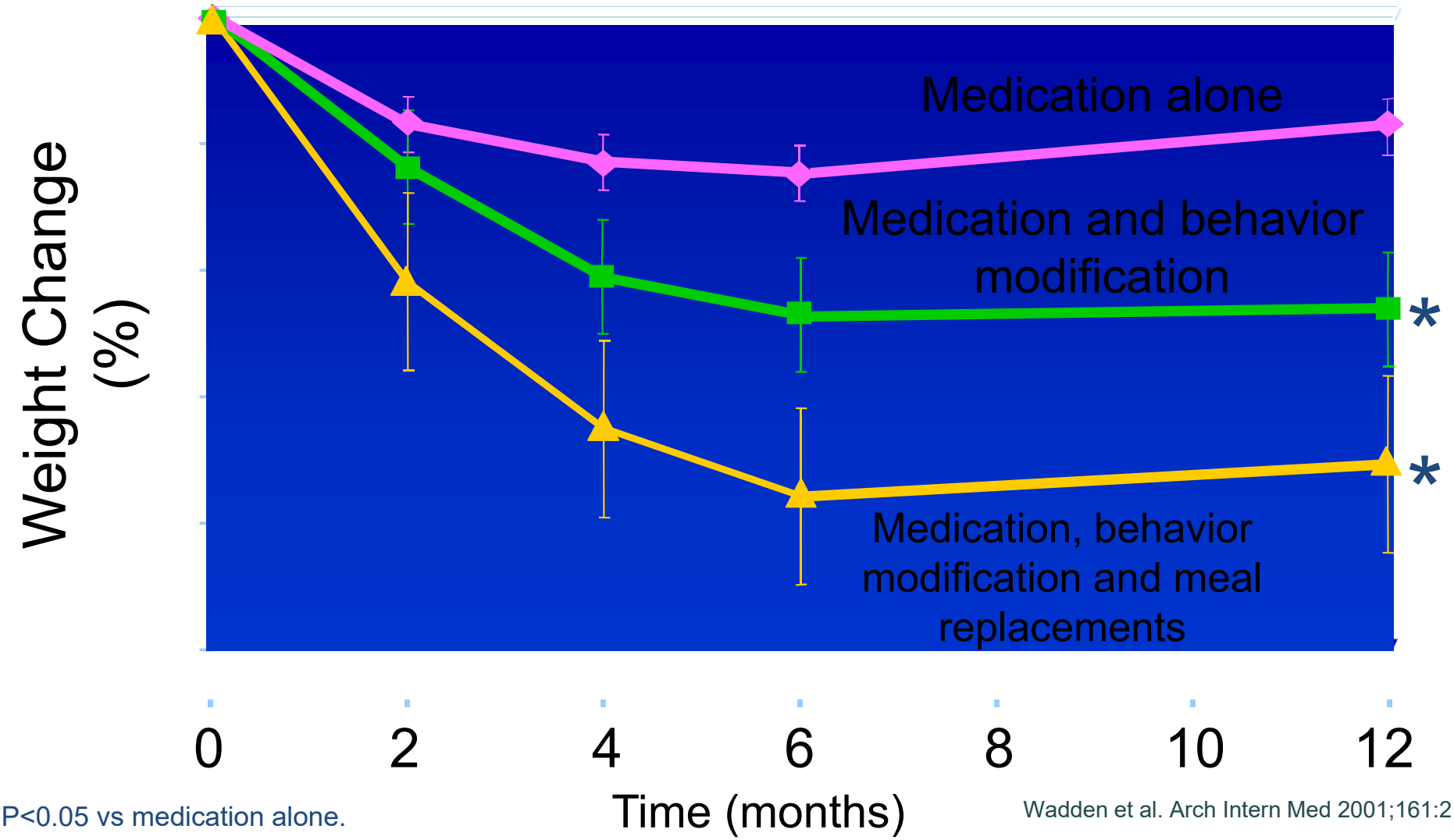


Combined Therapy

- Combined intervention of a calorie-deficit diet, increased physical activity, and behavioral treatment is most successful for weight loss and maintenance.
  Evidence Category A.

- Non-drug interventions should be attempted for at least 6 months before considering treatment.

Additive Effects of Behavior and Diet Therapy with Pharmacotherapy for Obesity



*P<0.05 vs medication alone.

Wadden et al. Arch Intern Med 2001;161:218.

Weight Loss Surgery

Option for limited number of patients with clinically severe obesity. *Evidence Category B.*

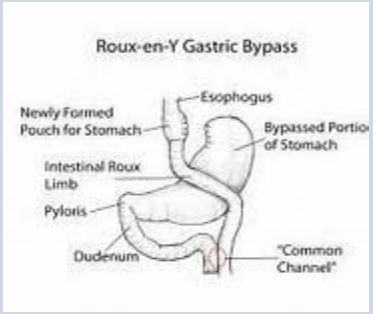
- BMI ≥40 or ≥35 with comorbid conditions
- Reserved for patients in whom medical therapy has failed
- Gastric restriction or gastric bypass

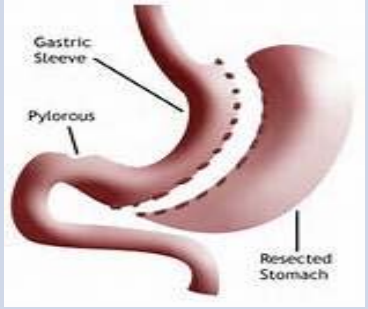
Integrated program must be in place before and after surgery.

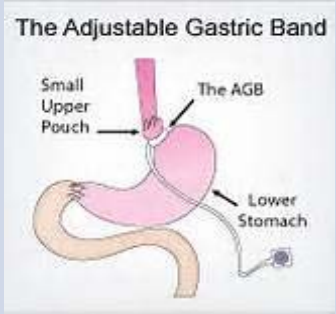
Pharmacotherapy 2013, doi: 10.1002/phar.1277

Surgery and Devices

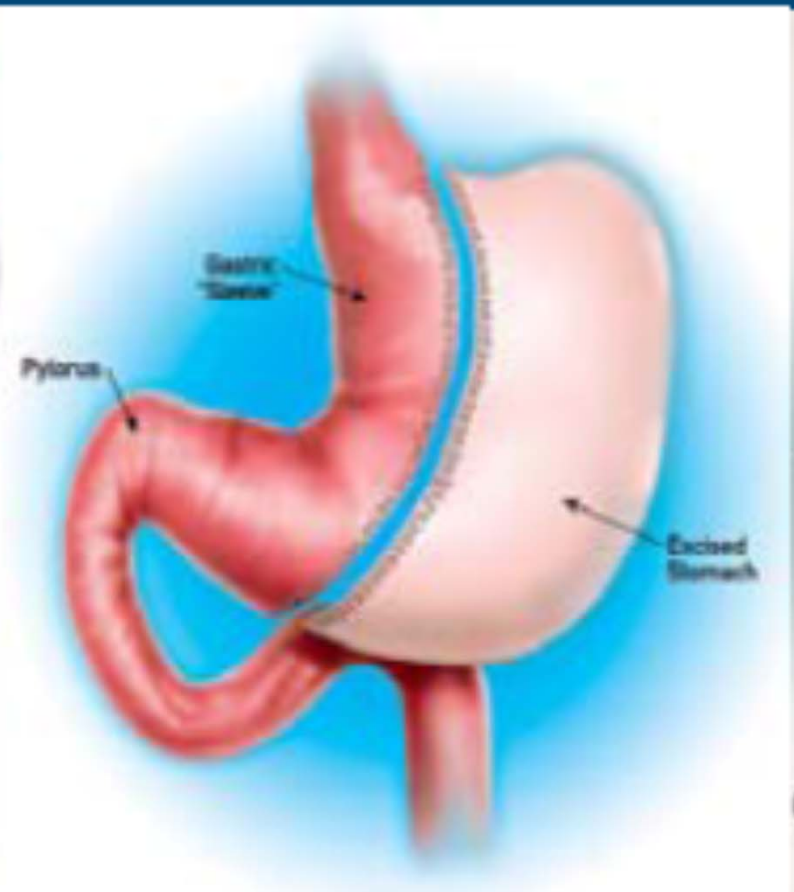
Bypass	Sleeve	Band
Greatest operative risk Alteration of anatomy Irreversible Quickest weight loss Less need for adherence Requires supplements	Less operative risk Alteration of anatomy Irreversible Slower weight loss Less need for adherence No supplements	Least operative risk No alteration of anatomy Reversible Slowest weight loss More need for adherence No supplements

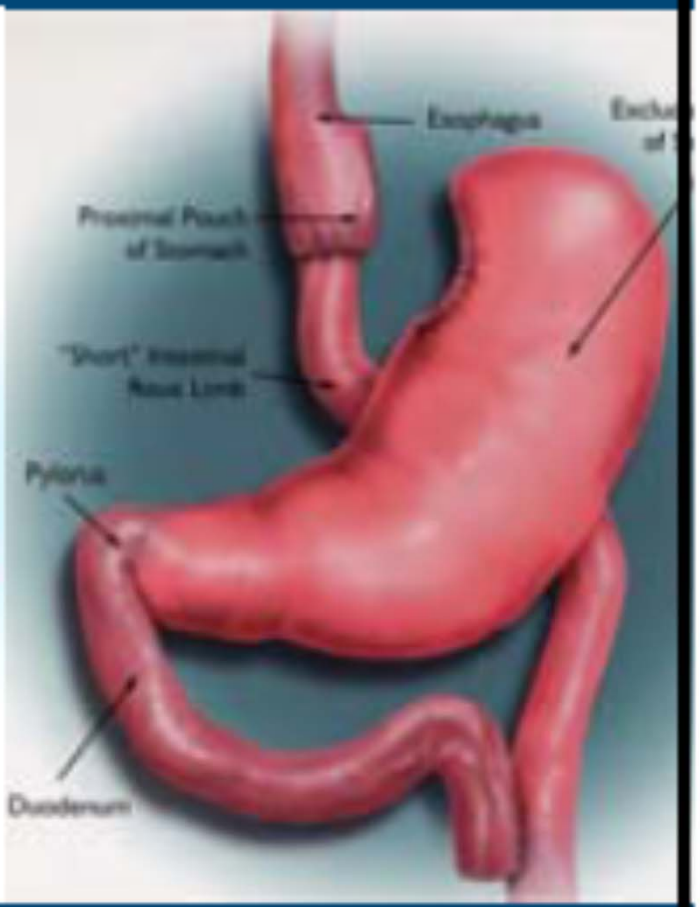






Lap Band Sleeve Gastrectomy **Gastric Bypass**





Low **Effectiveness** High

Risk

Cleveland Clinic

Obesity Treatment in Special Populations

- Smokers
  - All smokers, regardless of weight, should quit smoking.
  - Implement weight gain prevention, treatment efforts as necessary.
- Older adults
  - Evaluate risk-to-benefit ratio.
- Diverse patient populations
  - Tailor treatments to patient needs.

Weight loss – Motivational Interviewing

- Weight loss is a health behavior

- The patient must realize with their own words and thoughts that weight loss is important for them.
  - What is the patient's motivation?
  - What can they do to celebrate

- Changing lifestyle is easy to talk about, but hard to commit to…but there is more

Summary***

- BMI and waist circumference provide a better
  - assessment of total body fat than weight alone
  - are independent predictors of obesity-related disease risk
- Weight loss of as little of 5% can significantly improve BP, lipid levels, and glucose control
- Consider medication therapy ONLY AFTER 6 months of diet, exercise, and behavior modification have failed to stimulate weight loss