Metabolic Syndrome Across the Life Cycle-After Reproduction Age

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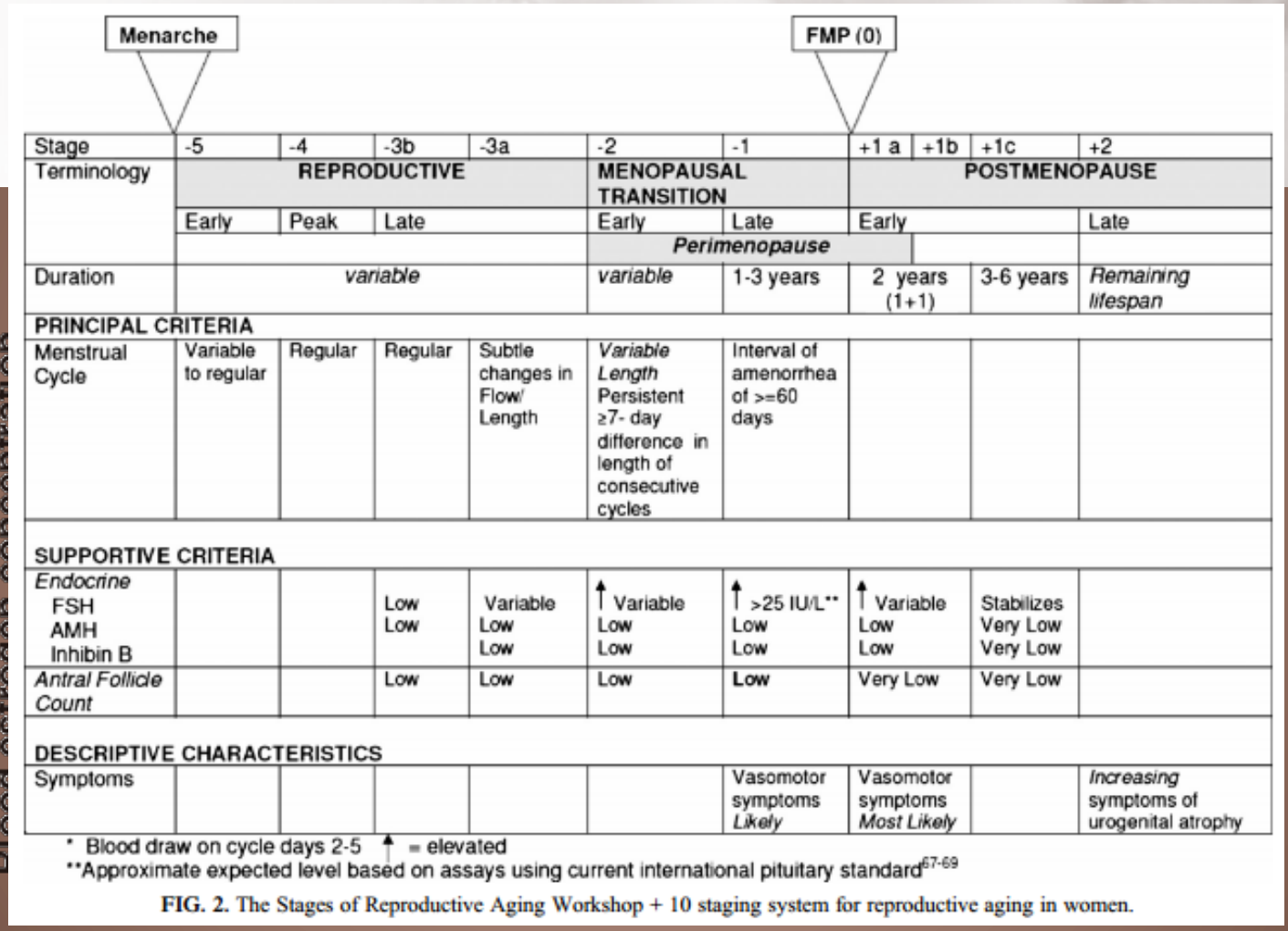
Disclosure:

- No financial disclosure.
- Worked as a consultant health coach for Take Shape for Life. Ended in 2017.
- No off brand medication use.

Objectives

- Brief review Physiology of peri-menopausal and menopausal transition period.
- Discuss physiology of obesity and functionality of adipose cell.
- Discuss Obesity and how it relates to Metabolic Syndrome.
- Outline Treatment overview of Obesity and Metabolic Syndrome.



Menarche						FMP (0)				
Stage	-5	-4	-3b	-3a	-2	-1	+1 a	+1b	+1c	+2
Terminology	REPRODUCTIVE				MENOPAUSAL TRANSITION		POSTMENOPAUSE			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	*variable*				*variable*	1-3 years	2 years (1+1)		3-6 years	*Remaining lifespan*
PRINCIPAL CRITERIA										
Menstrual Cycle	Variable to regular	Regular	Regular	Subtle changes in Flow/ Length	*Variable Length* Persistent ≥7- day difference in length of consecutive cycles	Interval of amenorrhea of >=60 days				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Low Low	Variable Low Low	↑ Variable Low Low	↑ >25 IU/L** Low Low	↑ Variable Low Low		Stabilizes Very Low Very Low	
Antral Follicle Count			Low	Low	Low	Low	Very Low		Very Low	
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms *Likely*	Vasomotor symptoms *Most Likely*			*Increasing* symptoms of urogenital atrophy

* Blood draw on cycle days 2-5 ↑ = elevated

**Approximate expected level based on assays using current international pituitary standard[67-69]

FIG. 2. The Stages of Reproductive Aging Workshop + 10 staging system for reproductive aging in women.

Blood estrogen concentration

https://www.otsuka.co.jp/en/health_illness/menopause/chenge.html

Key hormonal changes in Menopausal Transition (MT)

- During MT, follicles become more resistant to gonadotropins stimulation → FSH and LH levels will increase → leading to stromal stimulation of the ovary → increase in estrone levels and decrease in estradiol levels.
- Granulosa cells producing inhibin in the ovary will decease in production as a result of negative feedback of elevated FSH levels.
- The most significant decrease is noted in the levels of estradiol, spanning from 2 years before final menstrual period (FMP) till 4 years after FMP.
- Total serum testosterone does not change with MT
- DHEAS decline with age
- No specific changes in thyroid function related to menopause have been found.
- A trend in rising total cholesterol, LDL and apolipoprotein B levels in conjunction of loss of protective effect of HDL is noted.

Buttler L, Santoro N. The reproductive endocrinology of menopausal transition. Steroids 2011 June.
Santoro N,; Obstetrics Gynecol Clin North America. 2011 Sep. 38(3):455-66. [Medline]
Smith KE,; Current Obstetric and Gynecologic Diagnosis and Treatment. 8th ed. New York; Lange Medical books; 1994. 1030-1050

Physiologic Changes and Symptoms during MT:

- Hot flashes of flushes (Most common)
- Insomnia
- Weight gain and bloating
- Mood changes
- Irregular menses
- Mastodynia
- Depression
- Headache

Buttler L, Santoro N. The reproductive endocrinology of menopausal transition. Steroids 2011 June.

Menopause and Development of Comorbidities

- Menopause is associated with increase risk and development of:
  - Cardiovascular problems/Coronary artery disease
  - Breast cancer
  - Osteoporosis
  - Gynecological cancers
  - Central nervous system diseases
  - Obesity and metabolic syndrome

Buttler L, Santoro N. The reproductive endocrinology of menopausal transition. Steroids 2011 June.

The National Health and Nutrition and Examination Survey

- The National Health and Nutrition Examination Survey (NHANES) data found that:
  - 51.7 percent of women ages 20-39 were classified as “overweight” or “affected by obesity”
  - 68.1 percent of women ages 40-59 were classified as “overweight” or “affected by obesity”
- During the time of perimenopausal and MT time occurs, women start losing muscle mass but fat storage tends to increase; thus, body composition tends to put women at higher risk for development of metabolic disease (especially heart disease and diabetes).

CDC: https://www.cdc.gov/nchs/nhanes/

Coronary Artery Disease and Menopause

- Leading cause of death in postmenopausal women.
- The beneficial effect of estrogen on CAD and mortality is due to many factors but one prominent mechanism noted was the effect of estrogen on lipid metabolism. Estrogen decreases LDL and increases HDL → some studies noted that the best predictors of CAD in men and women are different and triglycerides, HDL and Lipoprotein(a) may be more significant in women.

Kannel WB, The Framingham study. Ann Intern Med. 1979 Oct. 85(4):447-52. [Medline]
Eriksson M,; Artriroscler Thromb Vasc Biol. 1999 Jan. 19(1):67-72: [Medline]

Study of Women's Health Across the Nation (SWAN)

Hormone or hormone surrogate	OR (95% CI)	p
Testosterone	0.96 (0.86-1.06)	0.40
Bioavailable testosterone	1.10 (1.01-1.20)	0.02
S ex- hormone-binding globulin	0.87 (0.81-0.93)	<0.001
Estradiol	0.97 (0.88-1.06)	0.49

- SWAN is a multiethnic, community based, longitudinal cohort study of natural history of menopause transition of 3302 women at 7 sites in the US.
- Noted finding was development of metabolic syndrome, with its multiple co-morbid risks, was probably as a result of progressive androgenicity of the hormonal milieu. Which is different than current thought of a result in decline of estrogen.
- Testosterone predominance was significantly and independently linked to 3 out 5 components of metabolic syndrome: elevated WC, triglyceride, and decrease HDL.
- Adjusted odds of changes in hormones or hormone measure for prediction of incident of metabolic syndrome

Janssen I,; The Study of Women's Health Across the Nation. Arch Intern Med 2008; 168:1568-1575.

Study of Women's Health Across the Nation (SWAN)

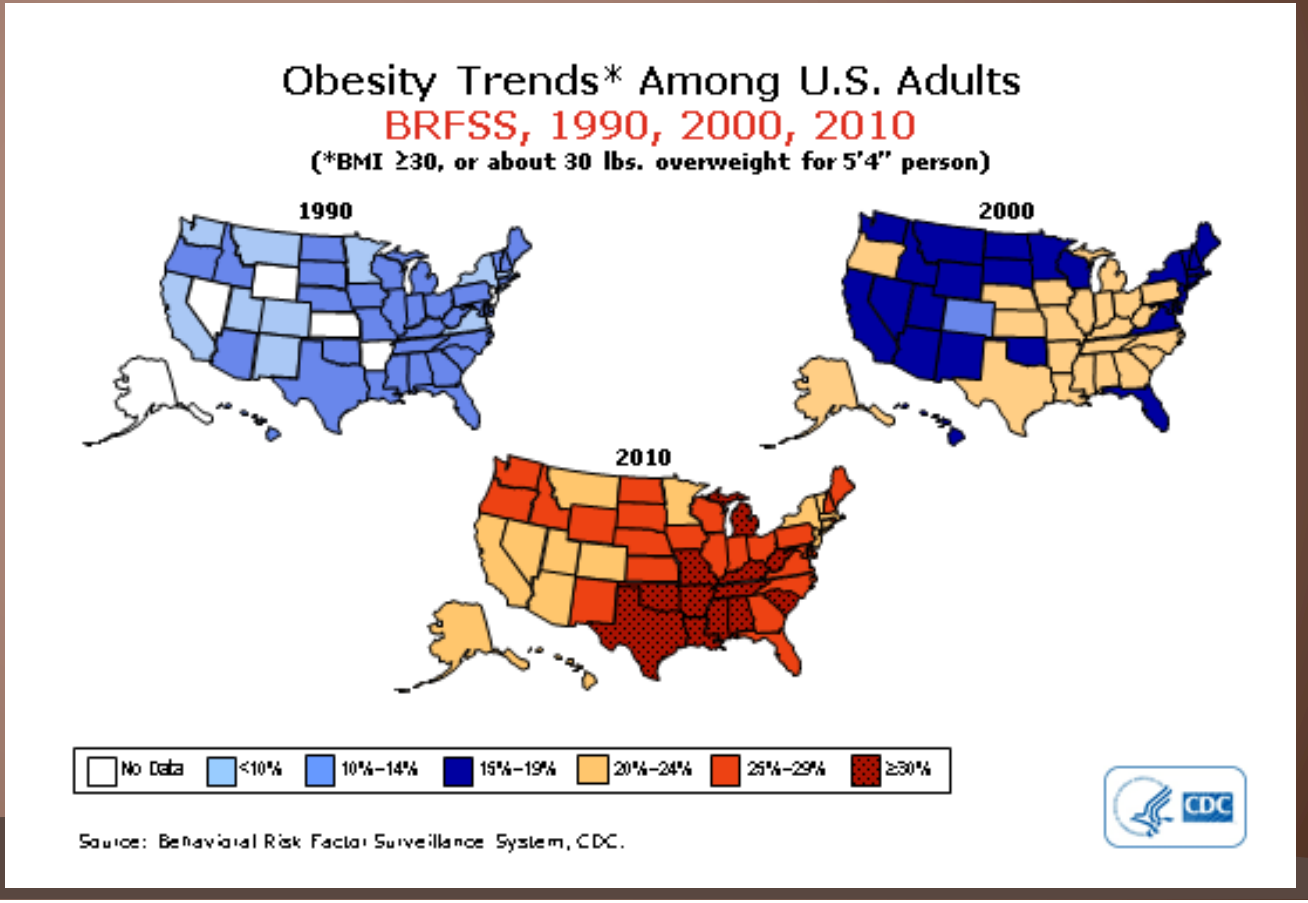
- New onset Metabolic syndrome was noted by the time of Final Menstrual Period (FMP) in 13.7% of the cohort. But it not associated with levels of either total testosterone or total estradiol.
- New onset Metabolic syndrome was found significantly associated with changes in bioavailable testosterone. "For every 1SD increase in bioavailable testosterone levels, the odds of developing metabolic syndrome increased by 10%."

Janssen I,; The Study of Women's Health Across the Nation. Arch Intern Med 2008; 168:1568-1575.

Obesity Epidemic Prevalence Map

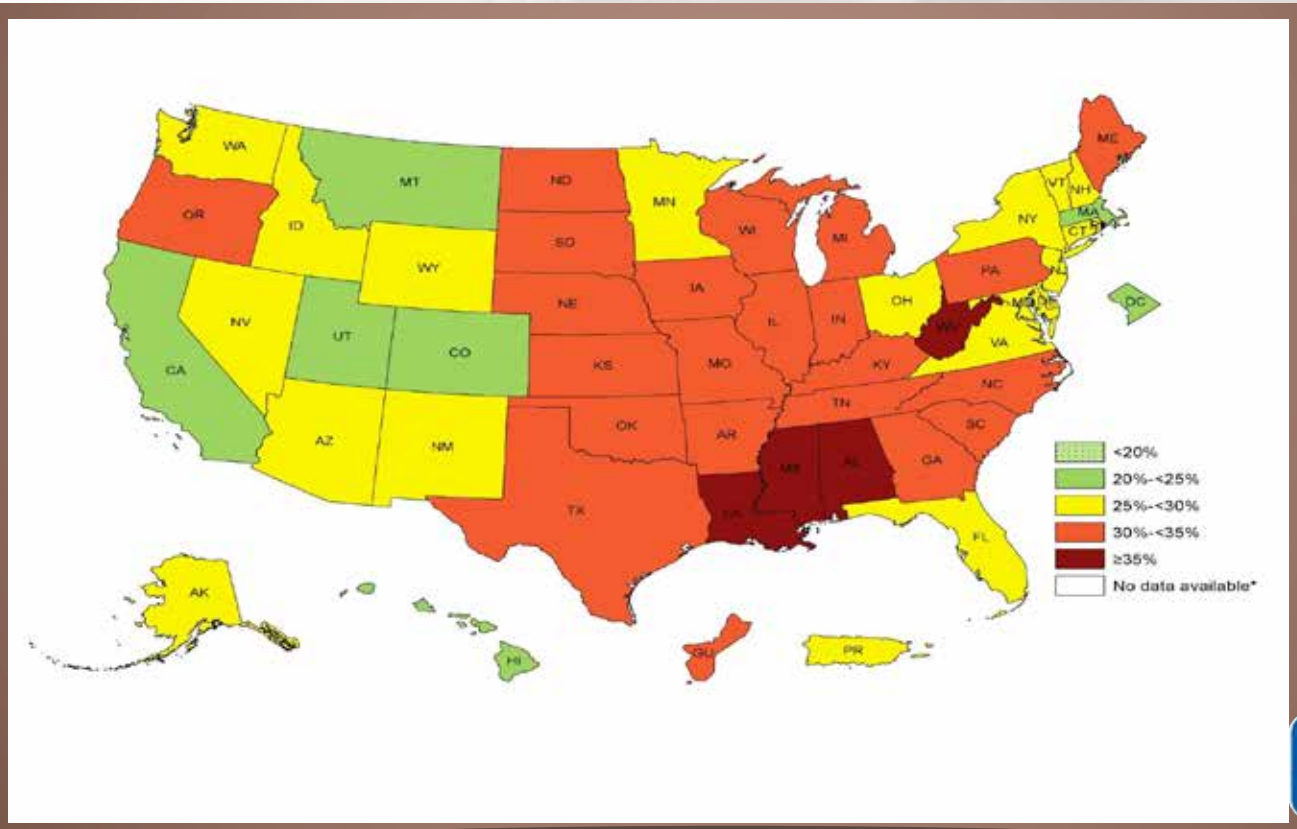
Higher prevalence found in the South (30.2%) and Midwest (30.1%)

Lower prevalence noted in the Northeast (25.6%) and West (24.9%)



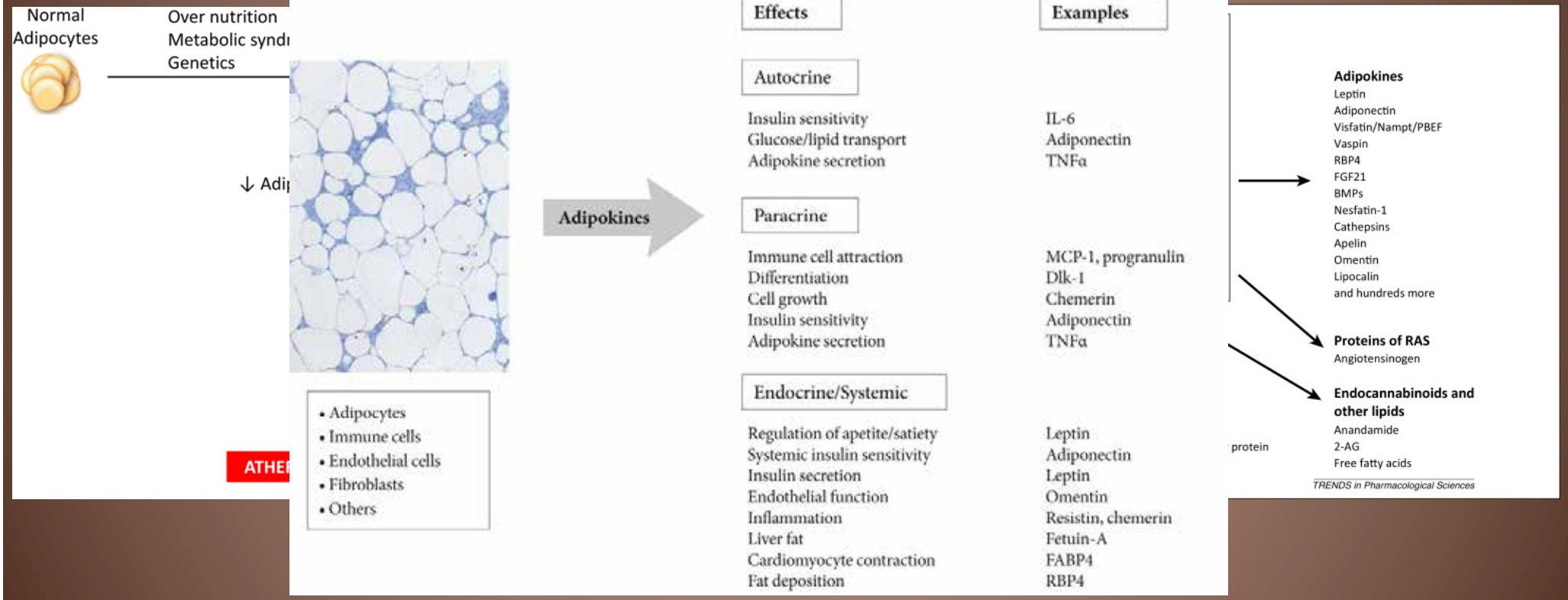
Center for Disease Control
https://www.cdc.gov/obesity/data/prevalence-maps.html

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2015



¶ **Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.**

Adipose Cells and Physiology

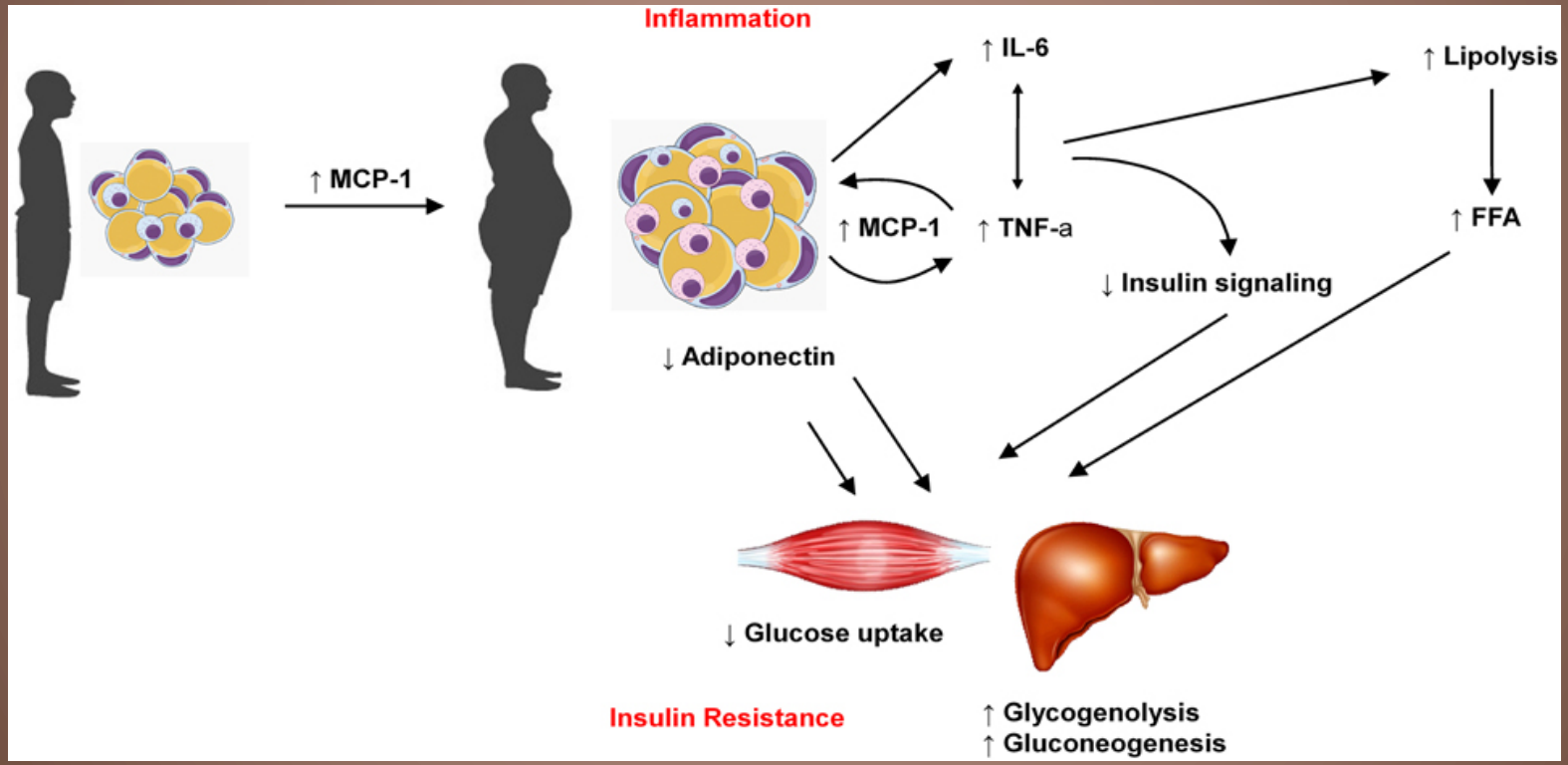


Bluher, M,; Diabetes Metab J. 2012 Oct,36(5):317-327

Mathias, F.; Trends in Pharmacological Sciences, Vol 36, Issue 7, July 2015, pages 461-470

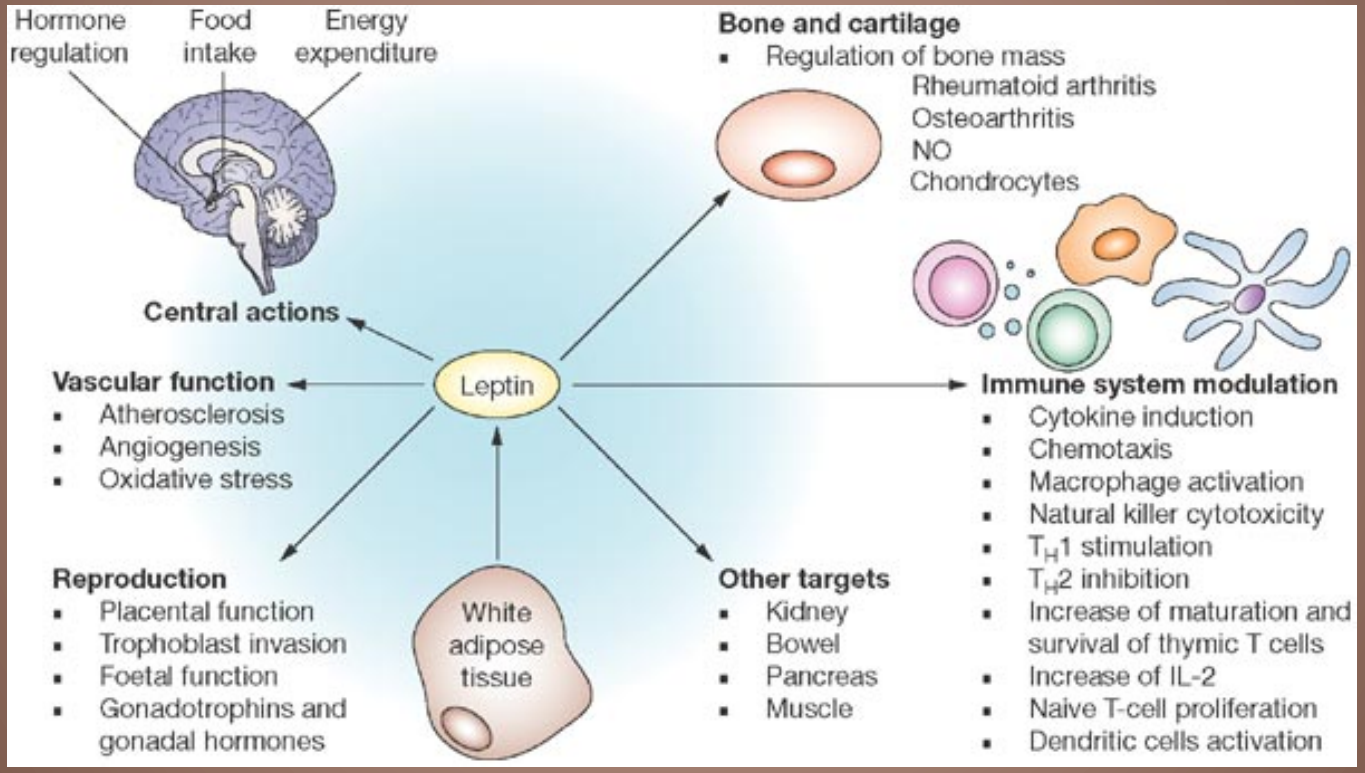
Leandro C,; Front Physiology., Adipokins, diabetes and atherosclerosis: an inflammatory association. 03 Nov 2015

Obesity leading to Insulin Resistance



Leandro C,; Front Physiology., Adipokins, diabetes and atherosclerosis: an inflammatory association. 03 Nov 2015

Pleiotropic nature of Leptin

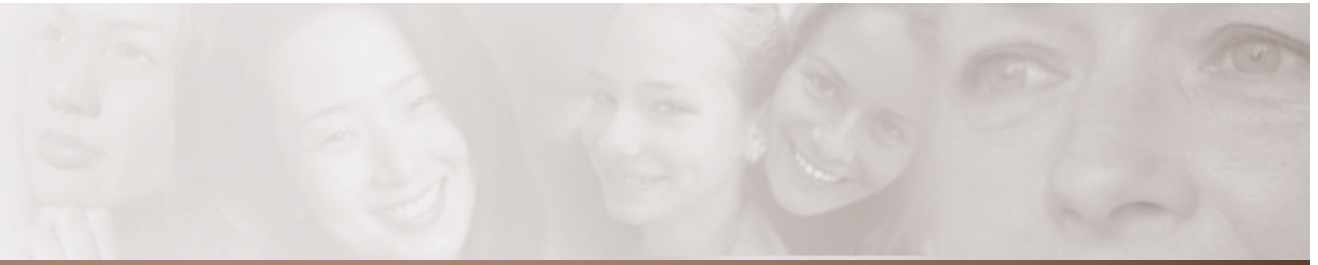


Lago, F,; Adipokines as emerging mediators of immune response and inflammation., Nature Clinical Practice Rheumatology (2007) 3, 716-724

Is Obesity a Disease?

PROS	CONS
"Obesity is a complex, **multifactorial disease** that develops from the interaction between genotype and the environment. Our understanding of how and why obesity occurs is incomplete; however, it involves the **integration of social, behavioral, cultural, and physiological, metabolic, and genetic factors**" 1998 - National Heart, Lung, and Blood Institute (NHLBI) "Overweight and obesity are **chronic diseases with behavioral origins** that can be traced back to childhood" 2013 - American Academy of Family Physicians	"…If obesity is truly a disease, then over 78 million adults and 12 million children in America just got classified as sick...Everyone has friends and acquintances who now qualify as diseased. Yet many sensible people, from physicians to philosophers, know that declaring obesity a disease is a mistake. Simply put, obesity is not a disease. To be sure, **it is a risk factor for some diseases**. But it would be false to say that everyone who is obese is sick as to say that every normal weight person is well" 2013 - Richard B. Gunderman, MD, PhD

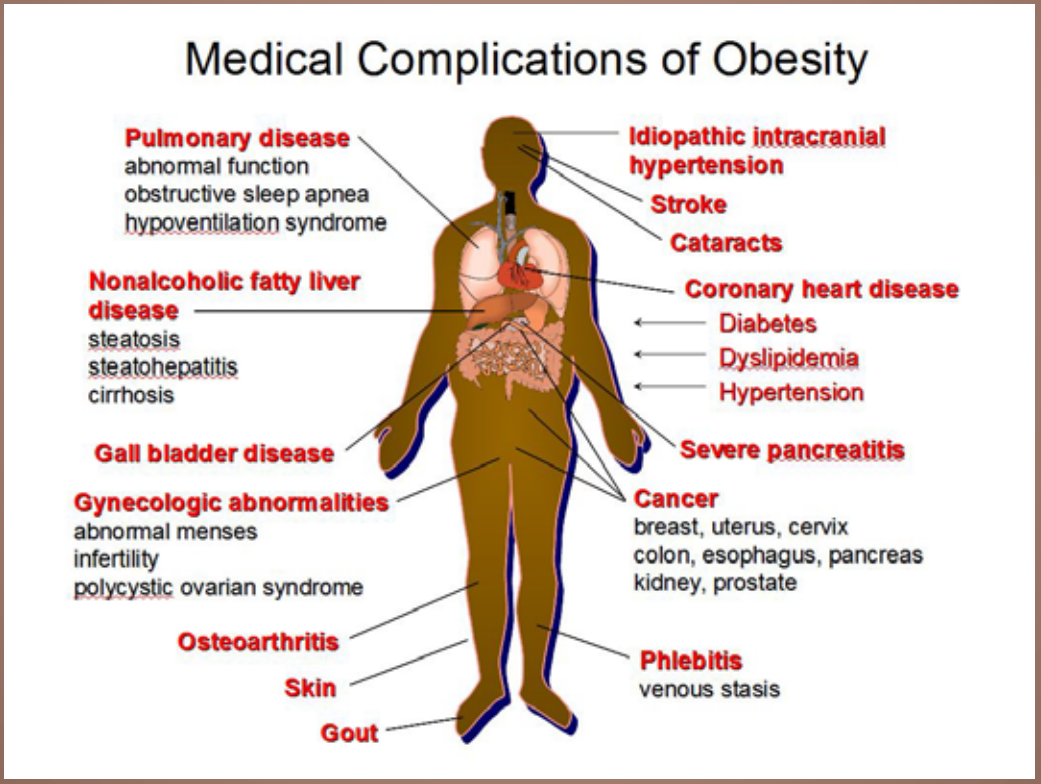
The Disease of Obesity



American Medical Association position statement in 2014:
"Recognizing obesity as a disease will help change the way the medical community tackles this complex issue that affects approximately one in three Americans"

AMA position statement. At: http://www.ama-assn.org. Accessed Oct 2014.

Obesity Related Disorders



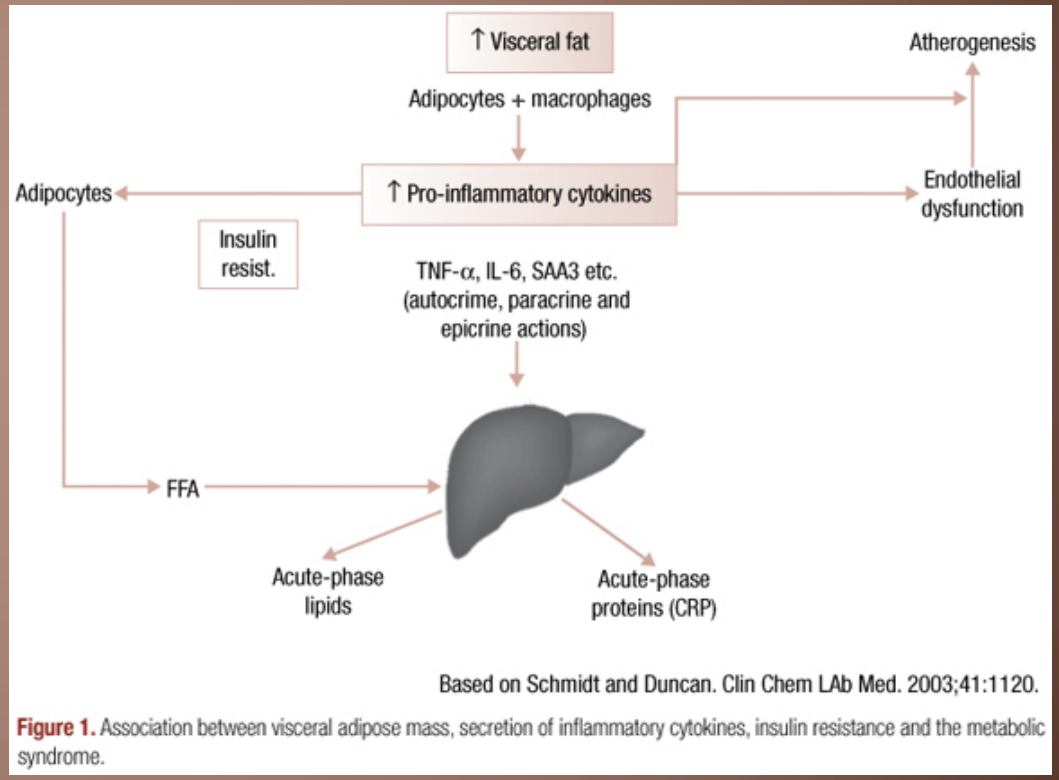
Visceral Fat

- During MT, increase in fat depositions especially in the intrabdominal area (aka Visceral fat) is noted with little change to muscle mass.
- It is thought that visceral fat cells have direct access to portal blood entering the liver and carry a significant source of many of proinflammatory proteins and are responsible for increase cardiovascular heart disease. This increase was suppressed in pre-menopausal state due to anti-inflammatory protection of estrogen.
- Visceral obesity correlates closely to an increase in insulin resistance →elevated insulin → abnormal glucose metabolism → reduction in fat breakdown and stimulation of more fat storage/deposition.

Kassem M, ISRN Inflamm; 2013, 2013: 139239

Metabolic Syndrome and Visceral Adipose Tissue Association

- Visceral adipose and inflammation: Adipose tissue is an ACTIVE ENDOCRINE ORGAN secreting adipokines, producing increased low level systemic inflammation that promote metabolic-associated pathologies such as atherosclerosis.

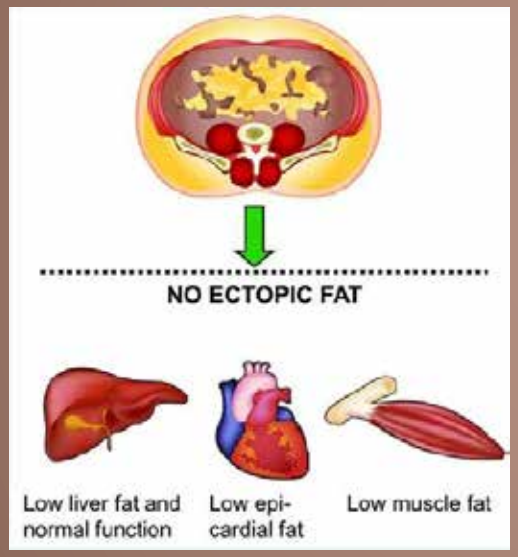


Based on Schmidt and Duncan. Clin Chem LAb Med. 2003;41:1120.

Figure 1. Association between visceral adipose mass, secretion of inflammatory cytokines, insulin resistance and the metabolic syndrome.

Influence of Fat distribution on Cardiometabolic Risk

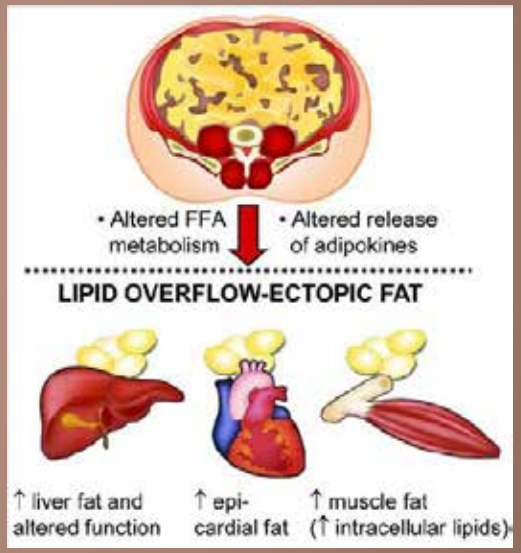
Subcutaneous obesity
"Healthy" adipose tissue



Normal metabolic profile

Absence of metabolic
Syndrome clinical criteria

Visceral obesity
Dysfunctional adipose tissue

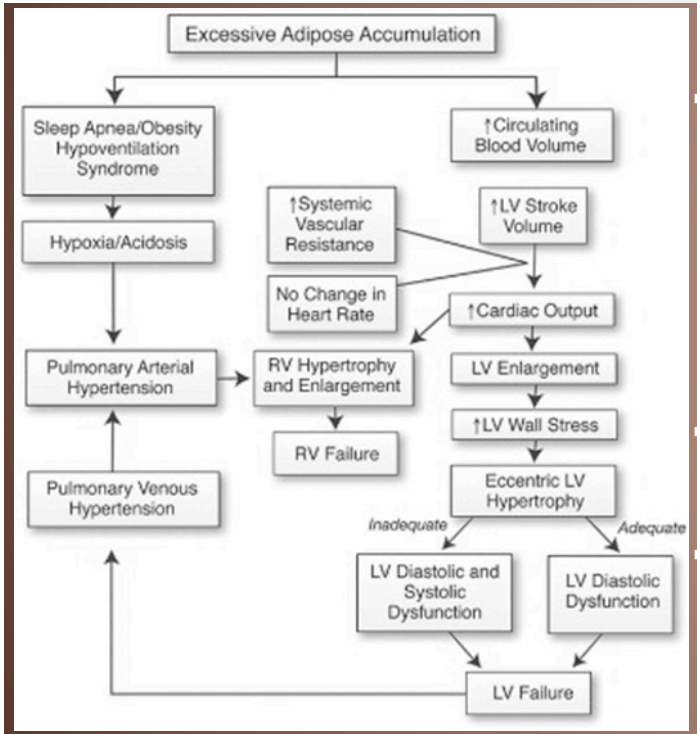


Altered metabolic profile

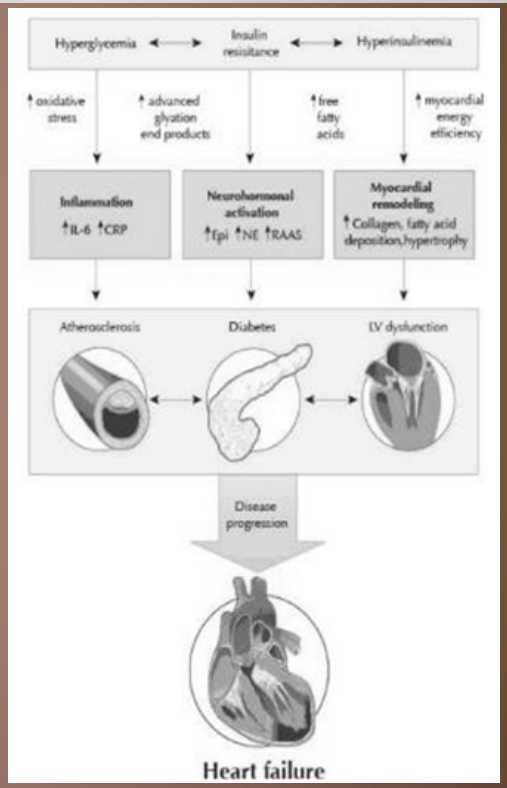
Presence of metabolic
Syndrome clinical criteria
(Hypertiglyceridemia and increase waist)

Jean-Pierre Despres Circulation. 2012; 126:1301-1313

Obesity and Insulin Resistance relevance to Heart Disease and Heart Failure



- Obesity has been associated with alternations in the Myocardium structure and Arterial wall remodeling, which leads to LV dysfunction (from Increased cardiac output) and Increased risk of Heart Failure
- Increased intra-myocardial Fatty acid deposition
- For each incremental increase of BMI by 1 unit, there is an increase risk of HF developing by 5% in men and 7% in women



Horwich, et al. Glucose, obesity, metabolic syndrome, and diabetes relevance to incidence of heart failure. J Am Coll Cardiol 2010 Jan 26;55(4) 283-293.

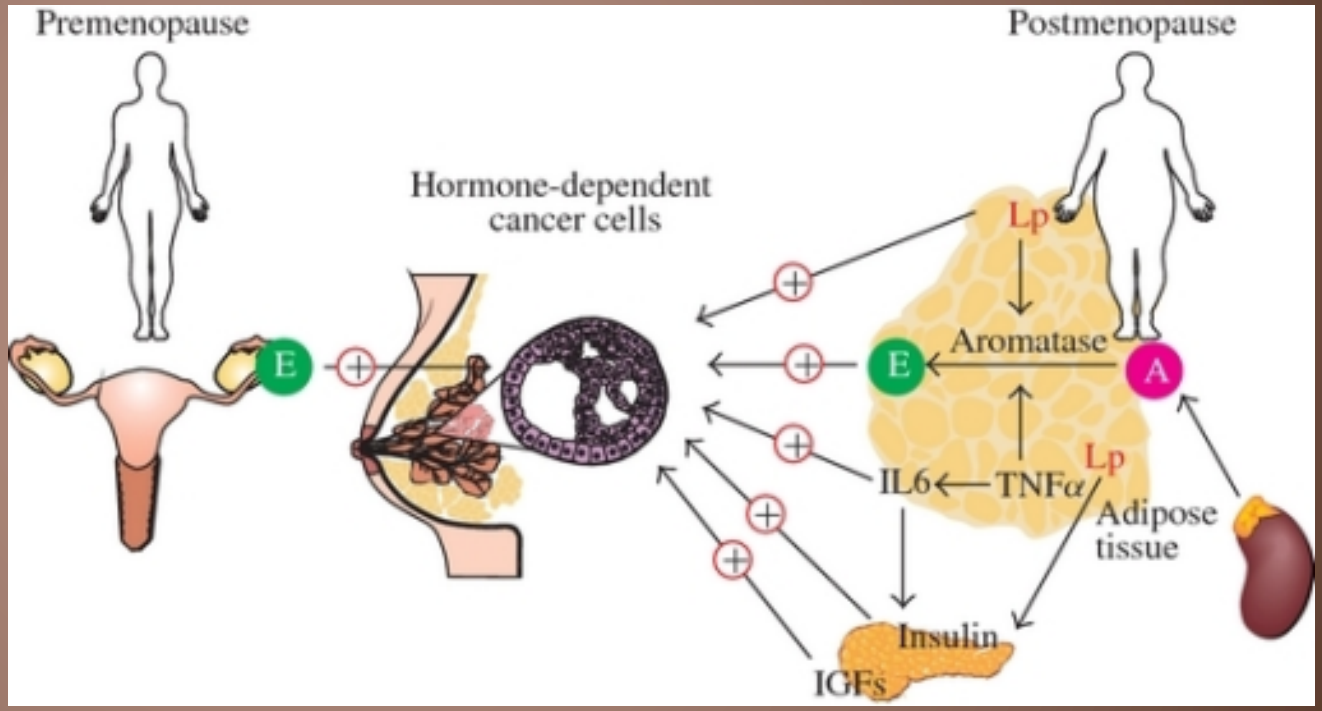
Lavie, C et al. Obesity and Cardiovascular Disease. J Am Coll Cardiol 2009 May 21;53(21):1925-1932.

Bray at al. Handbook of Obesity Clinical Applications, Fourth Ed, Vol 2.

Kenchaiah, S, et al. Obesity and the risk of heart failure. N Engl J Med, 2002 Aug 1;347(5):305-13.

Obesity, Inflammation and postmenopausal breast caner

Obesity-associated factors, including leptin, insulin and inflammatory mediators, seem to influence breast cancer growth and prognosis independently of estrogens and at least in part by interacting with estrogen signaling at a cellular level

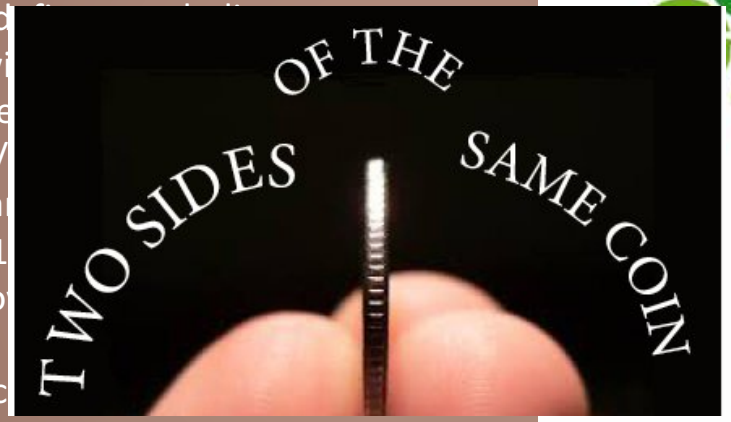


Maccio A, et al. Obesity, inflammation and postmenopausal breast cancer: Theraputic Implaction; Scientific World Journal, 2011

Metabolic Syndrome

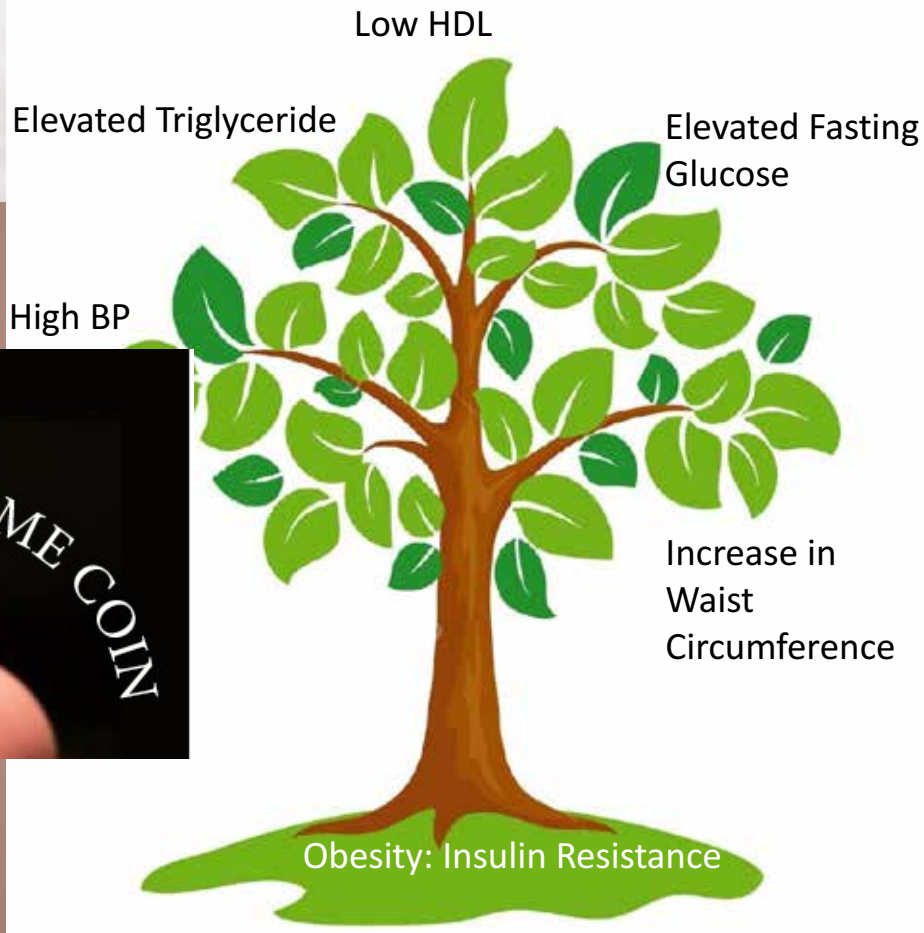
National Heart, Lung, Blood Institute (NHLBI) and American Heart Association (AHA) d
syndrome when three of the followi

1. waist circumference gre
2. HDL-C less than 50 mg/
3. Triglyceride greater tha
4. Blood pressure above 1
5. Fasting blood glucose o



While the greatest risk of metabolic
cardiovascular disease this risk was also noted to be age related.

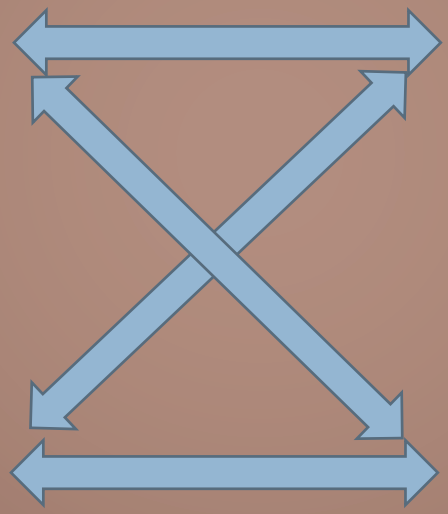
- 22% of general population meet criteria
- 60% of postmenopausal women are affected



Mathew J, J Am Heart Assoc. 2016;5:e003609 NHLBI American Heart Association

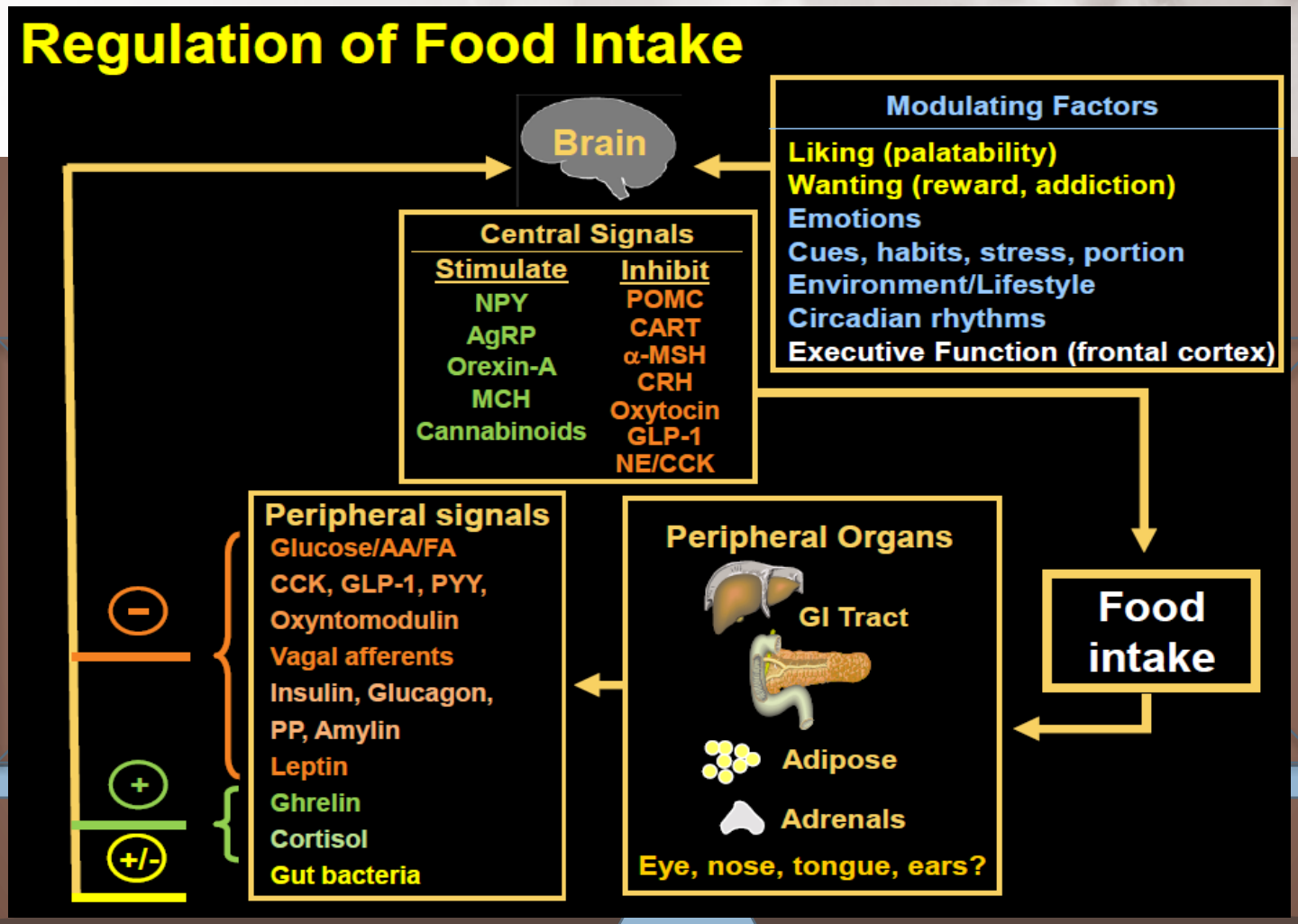
Determinants of Body Weight

- **Genes**
  - Protective and at risk alleles for weight gain
  - Race (ancestral admixture)
  - Gene-gene interactions
- **Biological factors**
  - In utero environment
  - Birth weight
  - Gender
  - Age
  - Concurrent diseases

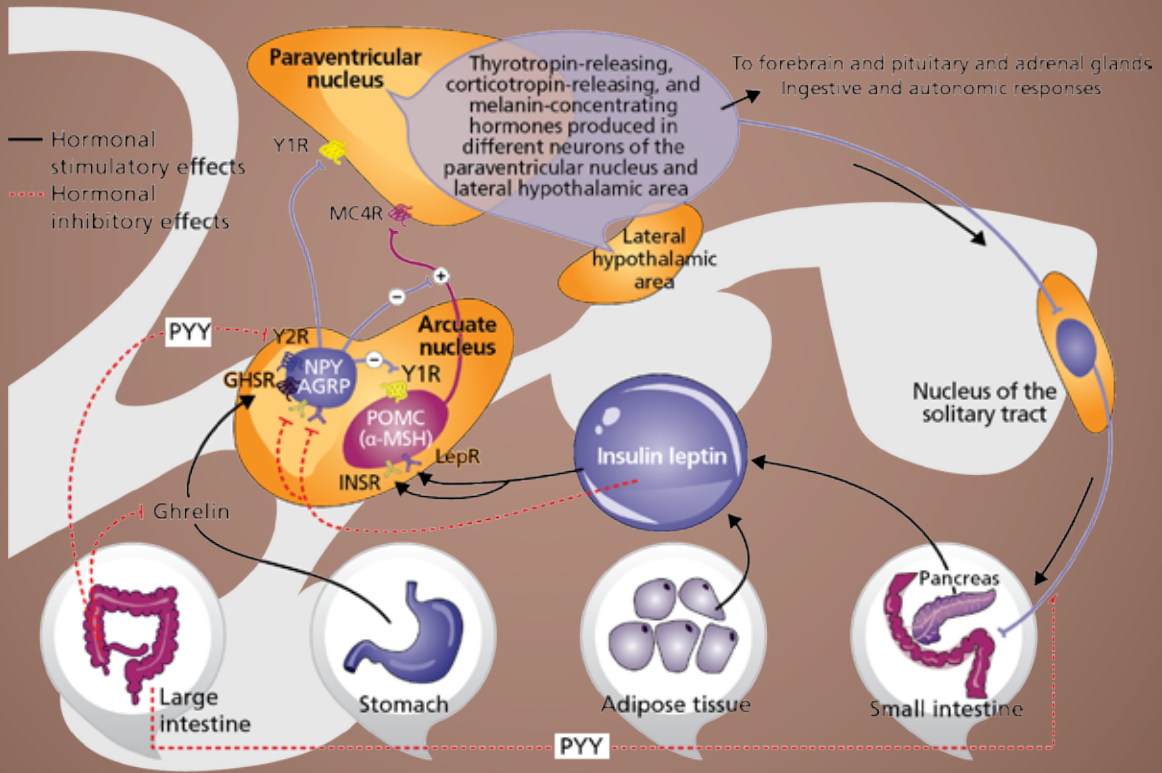


- **Environment**
  - Food availability
  - Food quality
  - Built environment
  - Socioeconomic status
  - education
- **Behavior**
  - Dietary preferences
  - Physical activity
  - Psychological factors
  - Cultural factors
  - Diurnal life patterns

Cause of

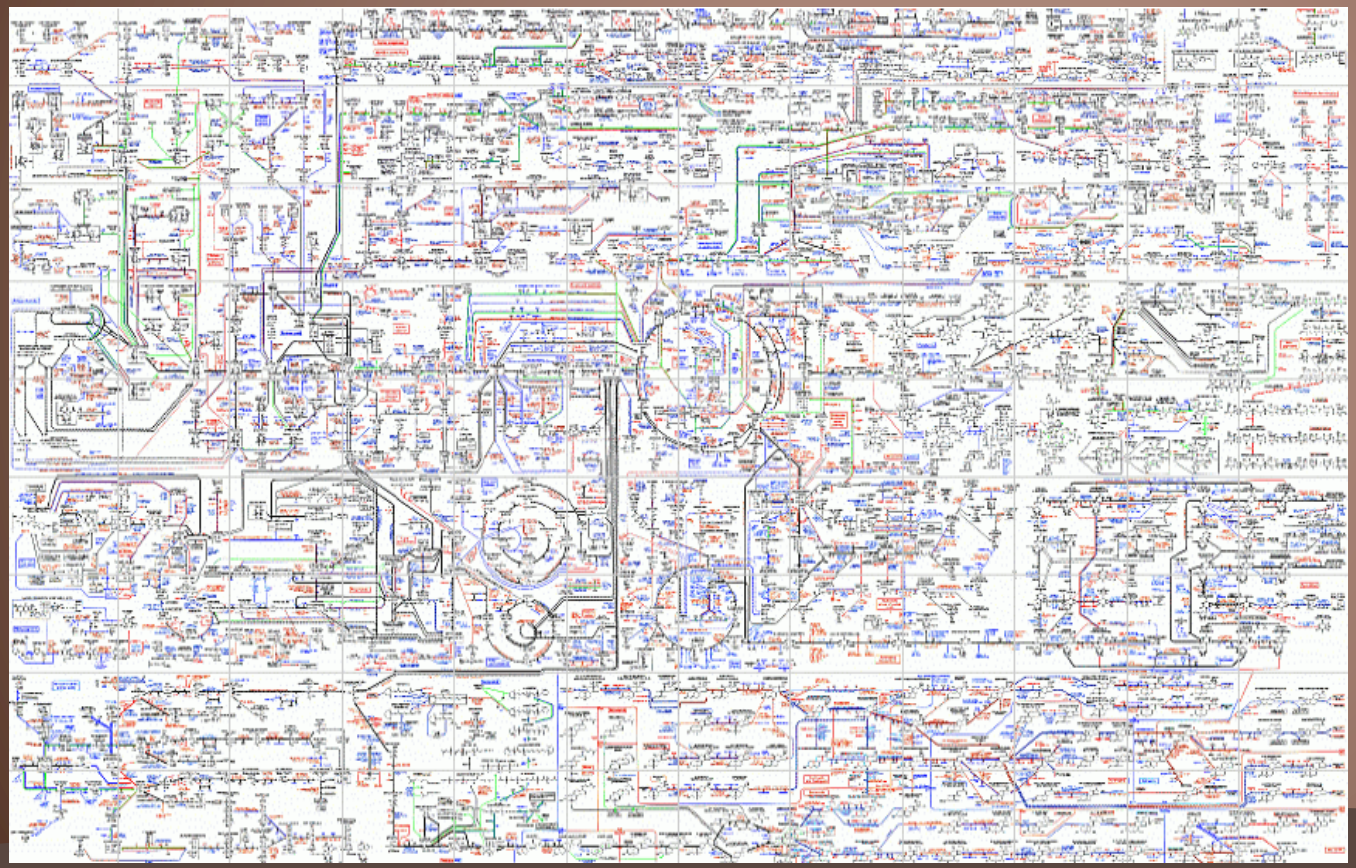

Regulation of Food Intake
Brain
Modulating Factors
Liking (palatability)
Wanting (reward, addiction)
Emotions
Cues, habits, stress, portion
Environment/Lifestyle
Circadian rhythms
Executive Function (frontal cortex)
Central Signals
Stimulate
NPY
AgRP
Orexin-A
MCH
Cannabinoids
Inhibit
POMC
CART
α-MSH
CRH
Oxytocin
GLP-1
NE/CCK
Peripheral signals
Glucose/AA/FA
CCK, GLP-1, PYY,
Oxyntomodulin
Vagal afferents
Insulin, Glucagon,
PP, Amylin
Leptin
Ghrelin
Cortisol
Gut bacteria
Peripheral Organs
GI Tract
Adipose
Adrenals
Eye, nose, tongue, ears?
Food intake

Complexities of Appetite Regulation



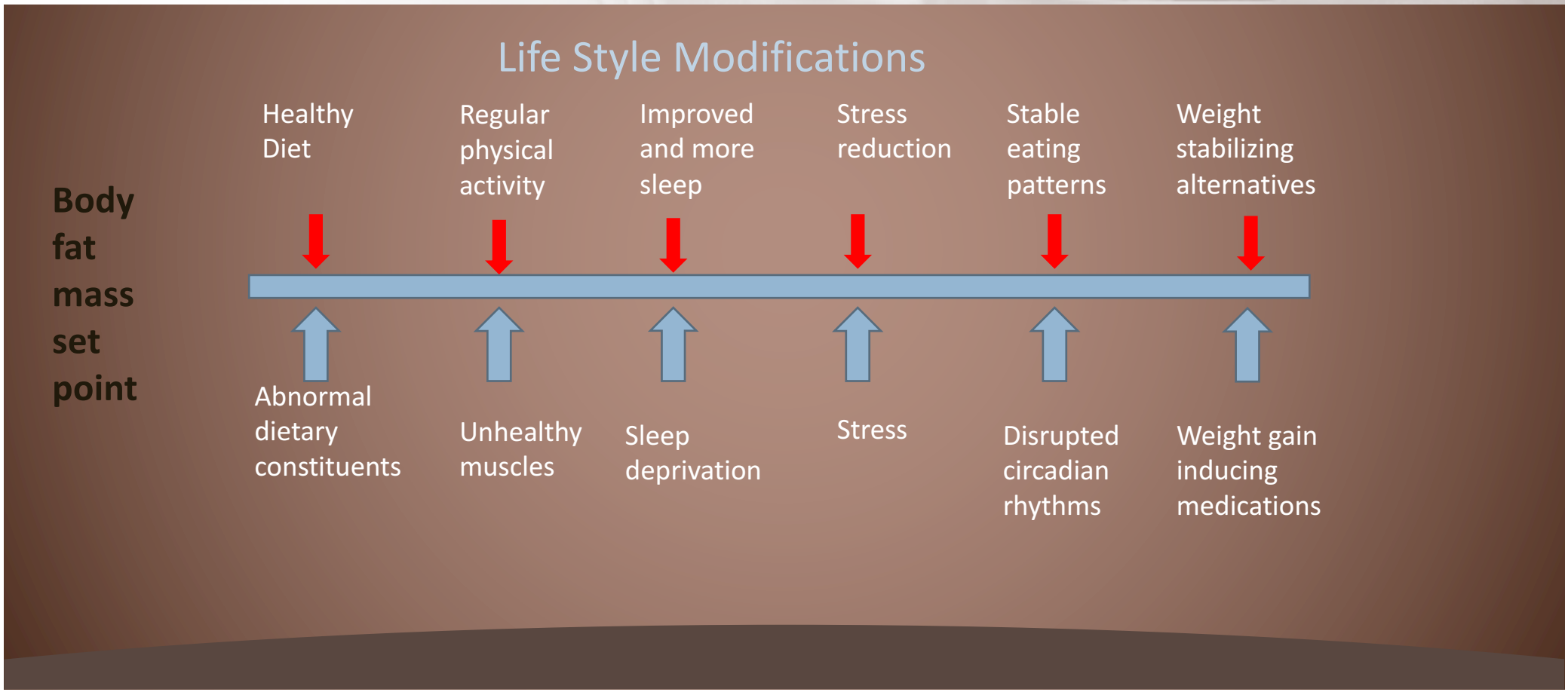
AGRP: agouti-related peptide; α-MSH: α-melanocyte-stimulating hormone; GHSR: growth hormone secretagogue receptor; INSR: insulin receptor; LepR: leptin receptor; MC4R: melanocortin-4 receptor; NPY: neuropeptide Y; POMC: proopiomelanocortin; PYY: peptide YY; Y1R; neuropeptide Y1 receptor; Y2R: neuropeptide Y2 receptor. Apovian CM, Aronne LJ, Bessesen D et al. *J Clin Endocrinol Metab*. 2015;100:342-362.

Complex Biology of Obesity



Obesity related pathway signaling

Obesity is a result of a battle of forces



Foundation of Obesity Treatment

1. Achieve an effective treatment to reduce the elevated fat mass set point
2. Recognizing and addressing the wide heterogeneity in the causes and manifestations of obesity
3. This result in a wide patient to patient variability in the response to all anti-obesity therapies
4. Patients who respond to one therapy might not show the same response to another.
5. Best is to match each patient with the most effective treatment to them

Evaluation of Patient affected by Obesity Disease

History:

- Medical
- Psychological
- Surgical, Gynecological
- Family
- Social
- Nutrition
- Physical Activity
- Review of Systems
- Medications/Supplements

Physical Exam:

- Age, race, gender, ethnicity
- Physical Exam
- Body Composition
- Laboratory
- Radiology
- Cardiology, Pulmonary, Sleep, other

Diagnostic Staging

Gender Related History:

Females:

- Menstrual, menopause
- Fertility issues
- Pregnancy issues
- Contraception
- Cancer screenings
- Hormonal medications
- Hirsuitism, acne, etc.

Males:

- Andropause
- Gynecomastia
- Fat distribution
- Erectile dysfunction

Both:

- Sexual quality of life
- Birth history and early childhood feeding Hx
- Hygiene Issues

Rasmussen K. *Curr Opin Obstet Gynecol*. 2009.

Common Medications Promoting Weight Gain

Example of common medications promoting weight gain:

1. CNS Drugs:
    a. Atypical Antiphyschotics: Olanzipine
    b. Anti-epileptics: Valproate
    c. Mood stabilizer: Lithium
    d. Anti-depressants: SSRI (paroxetine), Tricyclic agents (Nortripyline)
    e. Miscellaneous: Venlafaxine and mirtazapine
2. Endocrine agents:
    a. Glucocorticoids: prednisone
    b. OCP: medroxyprogesterone
    c. Diabetic agents: Insulin, Sulfonylureas (glyburide), Thiazolidenediones (pioglitazone)
3. Miscellaneous:
    a. Beta blockers: metoprolol
    b. Antihistamines: diphenhydramine
    c. Sleep aids: zolpidem

Effect of sleep on obesity regulation

- Timings
- Duration
- Nocturnal awakenings
- Quality
- OSA Screen
- Sleep Hygiene Tips

Sle

Sleep Hygiene Instructions

1. Avoid caffeine, nicotine, alcohol
2. Make bedroom sleep-inducing
3. Establish soothing pre-sleep routine
4. Go to bed when truly tired
5. Don't be a night-time clock-watcher
6. Use light to your advantage
7. Be consistent with sleep schedule
8. Nap early or not at all
9. Lighten up on evening meals
10. Balance fluid intake
11. Exercise early
12. Follow thru

http://healthysleep.med.harvard.edu/healthy/getting/overcoming/tips

Obesity

Patel & Hu, Obesity. 16(3): 643-53 .2008
Knutson et al. Sleep Med Rev. 11(3): 163-78. 2007

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):

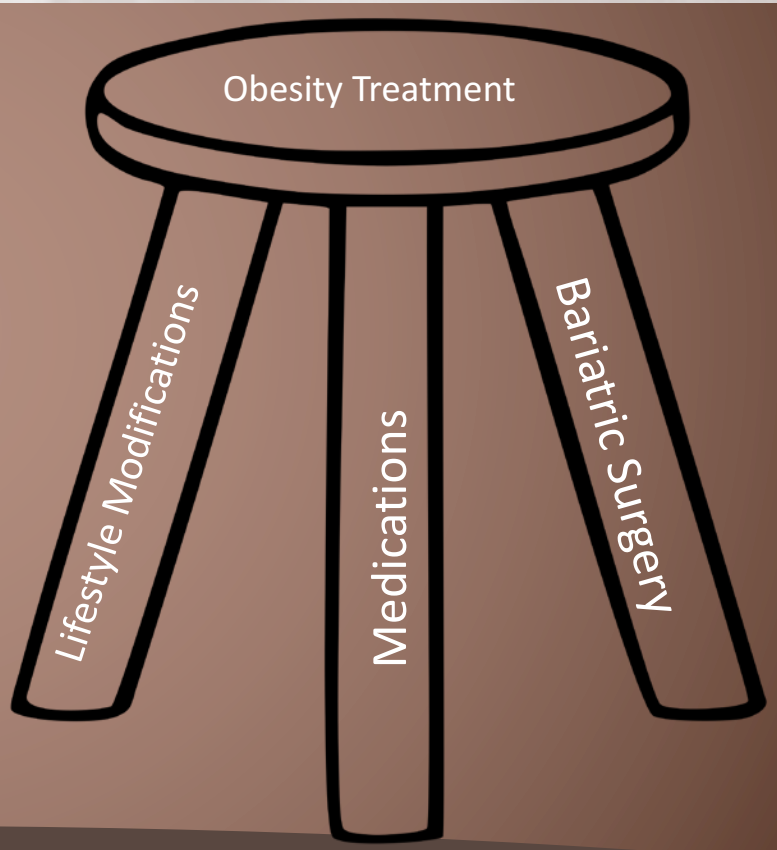
Body Mass Index (BMI)	18.5-24.9 kg/m^2	25.0-29.9 kg/m^2	$\geq$30 kg/m^2
Percent Body Fat	Male: <25% Female: <32%		Male: >25% Female: >32%
Waist Circumference	Male: <40 in. Female: <35 in.		Male: >40 in. Female: >35 in.
Edmonton Obesity Staging System	Stage 0, 1, 2, 3, 4		

No Obesity	**Overweight**	**Obesity** Class I: BMI 30.0-34.9 Class II: BMI 35-39.9 Class III: BMI $\geq$ 40.0
Prevention	Primary care provider or dietitian	
	If treatment is ineffective, refer to an obesity medicine specialist.	Consider referring to an obesity medicine specialist.

Obesity Medicine Association: Algorithm 2016

Overview Treatment of Obesity

A Guide to Selecting Treatment					
	BMI Category				
Treatment	25–26.9	27–29.9	30–34.9	35–39.9	≥40
Diet, physical activity, and behavior	Appropriate NHLBI Guidelines	+	+	+	+
Pharmacotherapy	No	With comorbidities	+	+	+
Surgery*	No	No	No LAGB only	With comorbidities	+



https://www.nhlbi.nih.gov/files/docs/guidelines/prctgd_c.pdf

Recommendation for Therapeutic Weight Loss

OBESITY COMPLICATION	% weight loss required for therapeutic benefit	Notes	References
Diabetes Prevention	3% to 10%	Maximum benefit 10%	DPP (Lancet, 2009) SEQUEL (Garvey et al, 2013)
Hypertension	5% to >15%	BP still decreasing >15%	Look AHEAD (Wing, 2011)
Dyslipidemia	3% to >15%	TG still decreasing at >15%	Look AHEAD (Wing, 2011)
HbA1c	3% to >15%	HbA1c still decreasing at >15%	Look AHEAD (Wing, 2011)
NAFLD	10%	Improves steatosis, inflammation, mild fibrosis	Assy et al, 2007; Dixon et al, 2004; Anish et al, 2009
Sleep Apnea (AHI)	10%	Little benefit at ≤ 5%	Sleep AHEAD (Foster, 2009) Winslow et al, 2012
Osteoarthritis	5-10%	Improves symptoms and joint stress mechanics	Christensen et al, 2007 Felson et al, 1992; Aaboe et al, 2011
Stress Incontinence	5-10%		Burgio et al, 2007 Leslee et al, 2009
GERD	5-10% women 10% men		Singh et al, 2013 Tutuljan R, 2011
PCOS	5-15% (>10% optimal)	Lowers androgens, improves ovulation, increases insulin sensitivity	Panidis D et al, 2008 Norman et al, 2002 Moran et al, 2013

But first: patient readiness to change

Is the patient ready and motivated to lose weight? Evaluation of readiness should include the following:

1) reasons and motivation for weight loss
2) previous attempts at weight loss
3) support expected from family and friends
4) understanding of risks and benefits
5) attitudes toward physical activity
6) time availability
7) potential barriers to the patient's adoption of change

5 A's of Obesity Management

Ask	- Ask for permission to discuss body weight - Explore readiness for change
Assess	- Assess BMI, WC, and Obesity stage - Explore drivers and complications of excess weight
Advice	- Advice the patient about the health risks of obesity, the benefits of modest weight loss, 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.

Searight R: Realistic approaches to counseling in the office setting. Am Fam Physician 2009 79:277-284.
Foote J, DeLuca A, Magura S, Warner A, Grand A, Rosenblum A, Stahl S: A group motivational treatment for chemical dependency. J Subst Abuse Treat 1999 17:181-192.
Vallis M, Piccinini-Vallis H, Sharma AM, Freedhoff Y: Clinical review: modified 5 As: minimal intervention for obesity counseling in primary care. Can Fam Physician 2013 59:27-31

Goals of Therapy

Goals of therapy are to reduce body weight and maintain a lower body weight for the long term; the prevention of further weight gain is the minimum goal.

1) An initial weight loss of 5-10 percent of body weight achieved over 6 months is a recommended target.

2) The rate of weight loss should be 1 to 2 pounds per week.

3) Greater rates of weight loss do not achieve better long-term results.

4) After the first 6 months of weight loss therapy, the priority should be weight maintenance achieved through combined changes in diet, physical activity, and behavior.

5) Further weight loss can be considered after a period of weight maintenance.

Key Components of Lifestyle Therapy

- Dietary Therapy
- Physical Therapy
- Cognitive behavioral therapy

New Treatment Paradigm is by treating WEIGHT FIRST then Comorbidities

Pharmacological Therapy

- Review current medications and identify ones that can cause an increase in weight
- Discuss with primary care and specialists to consider and change medications to alternate medications that are weight neutral or weight reducing medications.
- Initiate weight loss medication after establishing lifestyle modification goals and plans.
- Reevaluate medication every 3 month to assure benefits. Stop medication if appropriate weight loss was not achieved or side effects arise.

Pharmacotherapy

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

FDA approved meds for Obesity in the US as of 2016

Medication	Average Weight Loss*	Mechanism of Action	Potential Side Effects
Phentermine (Adipex™, Ionamin™)	~ 5%	Adrenergic	Tachycardia, hypertension
Phentermine / Topiramate (Qsymia™)	10%	Adrenergic, CNS	Tachycardia, hypertension, cognitive dysfunction, neuropathy, teratogenicity
Bupropion / Naltrexone (Contrave™)	4.5%	CNS; opioid antagonism	Seizures, confusion, anxiety, opiate withdrawal
Lorcaserin (Belviq™)	3.5%	Serotonergic ($5HT_{2C}$)	Headache
Liraglutide (Saxenda™)	7%	GLP-1 agonist	Nausea
Orlistat (Xenical™)	3%	Lipase inhibitor	Steatorrhea, incontinence

New Treatment Paradigm: WEIGHT FIRST

	Overweight/Obesity
Monitor	Weight and BMI
Diet	Any diet patient will adhere to
Exercise	150 minutes of moderate-intensity aerobic activity/wk and muscle-strengthening activities on > 2 days/wk
Meds	Orlistat, phentermine, phentermine/topiramate, lorcaserin

	Dys-lipidemia	HTN	IGT
Monitor	Lipid panels Lipoproteins subsets	Blood Pressure Ambulatory Blood Pressure	Blood sugar Glycosylated hemoglobin distribution
Diet	↓ Sat + trans fat ↑ Omega-3s ↑ MUFA ↓ Simple CHOs ↓ ETOH	DASH Diet ↓ Sodium ↓ ETOH	Glycemic index diet ↑ Fiber Diabetic diet
Meds	Statins Fibrates	ACE Inhibitors	Metformin Exenatide Liraglutide

DRUG-ASSOCIATED WEIGHT CHANGE REFERENCE

Therapeutic Category	Drug Class	May Cause Weight Gain	Alternatives That Cause Less Weight Gain, Weight Loss, or are Weight Neutral
Psychiatry	Antipsychotic	• Clozapine [1-5] • Risperidone [1, 4, 5] • Olanzapine [1-5] • Quetiapine [2] • Other [1-3, 5, 7]	• Ziprasidone [1, 4] • Aripiprazole [6]
	Antidepressants and Mood Stabilizers	• Citalopram [8] • Escitalopram [8] • Fluvoxamine [8] • Lithium [3, 5, 9] • MAOIs [5, 9] • Mirtazapine [8] • Paroxetine [11] • TCAs [3, 5, 9] • Venlafaxine [8]	• Bupropion [12] • Nefazodone [4, 10] • Fluoxetine (short term: <1 year) [12, 13] • Sertraline (short term: <1 year) [13]
Neurology	Anticonvulsants	• Carbamazepine [10, 14] • Gabapentin [15, 15, 16] • Valproate [10, 14]	• Lamotrigine [16] • Topiramate [17-20] • Zonisamide [21]
Endocrinology	Diabetes Treatments	• Insulin [3, 22] • Sulfonylureas [3, 23] • Thiazolidinedione [24]	• Metformin [3, 23] • Acarbose [3] • Miglitol [25] • Pramlintide [26] • Exenatide [27] • Sitagliptin [28]
Obstetrics & Gynecology	Oral Contraceptives	• Progestational steroids [3] • Hormonal contraceptives containing progestational steroids [9, 29]	• Barrier methods • IUDs
	Endometriosis Treatment	• Depot leuprolide acetate [30]	• Surgical methods
Cardiology	Antihypertensives	• α-blocker [3] • β-blocker [3]	• ACE inhibitors • Calcium channel blockers
Infectious Disease	Antiretroviral Therapy	• Protease inhibitors [31, 32]	• None
General	Steroid Hormones	• Corticosteroids [3] • Progestational steroids [3]	• NSAIDs
	Antihistamines/ Anticholinergics	• Diphenhydramine • Doxepin • Cyproheptadine [33, 34] • Other potent antihistamines [35, 36]	• Decongestants • Steroid inhalers

Bariatric Surgical Procedures

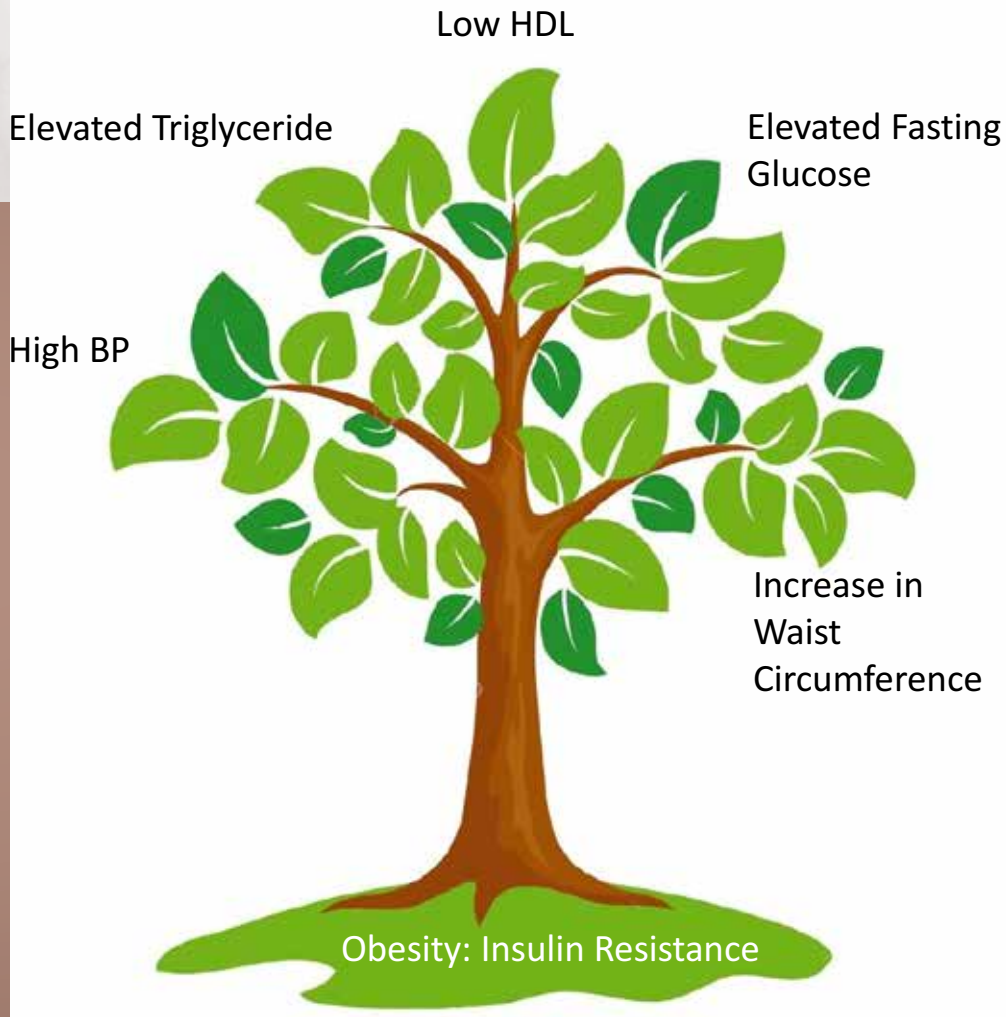
	Pros	Cons	Expected loss in percent excess body weight* at two years	Optimally suited for patients with:	Other comments
Roux-en-Y Gastric Bypass	Greater improvement in metabolic disease	Increased risk of malabsorptive complications over sleeve	60-75%	Higher BMI, GERD, Type 2 DM	Largest data set, more 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)

Metabolic Syndrome and Obesity Tree

Obesity and Metabolic disease treatment is an energy balance that is much more about the physiology (signaling and homeostasis) than the physics (calories in and out)

The driving forces to consume food (whether it is homeostatic, hedonic or both) and the autonomic thermogenesis are more a response to the body's perceived needs than primary driver of fat mass and weight.



Summary

- Obesity is a disease that could present at any point in a patient's life and it is a chronic disease.
- Peri and Post menopausal women tend to have higher incidence of obesity and metabolic syndrome related health problems.
- Hormonal treatment for women is a good initial step in treatment of the symptoms of menopause but not enough to address obesity. Practitioners should address risk factors that lead to obesity and educate patients about prevention and treatment of obesity and metabolic syndrome prior to menopause.
- Refer to obesity medicine specialist or bariatric surgeon for additional help.

Thank you