

Medical Weight Loss Overview

2021

Learning Objectives

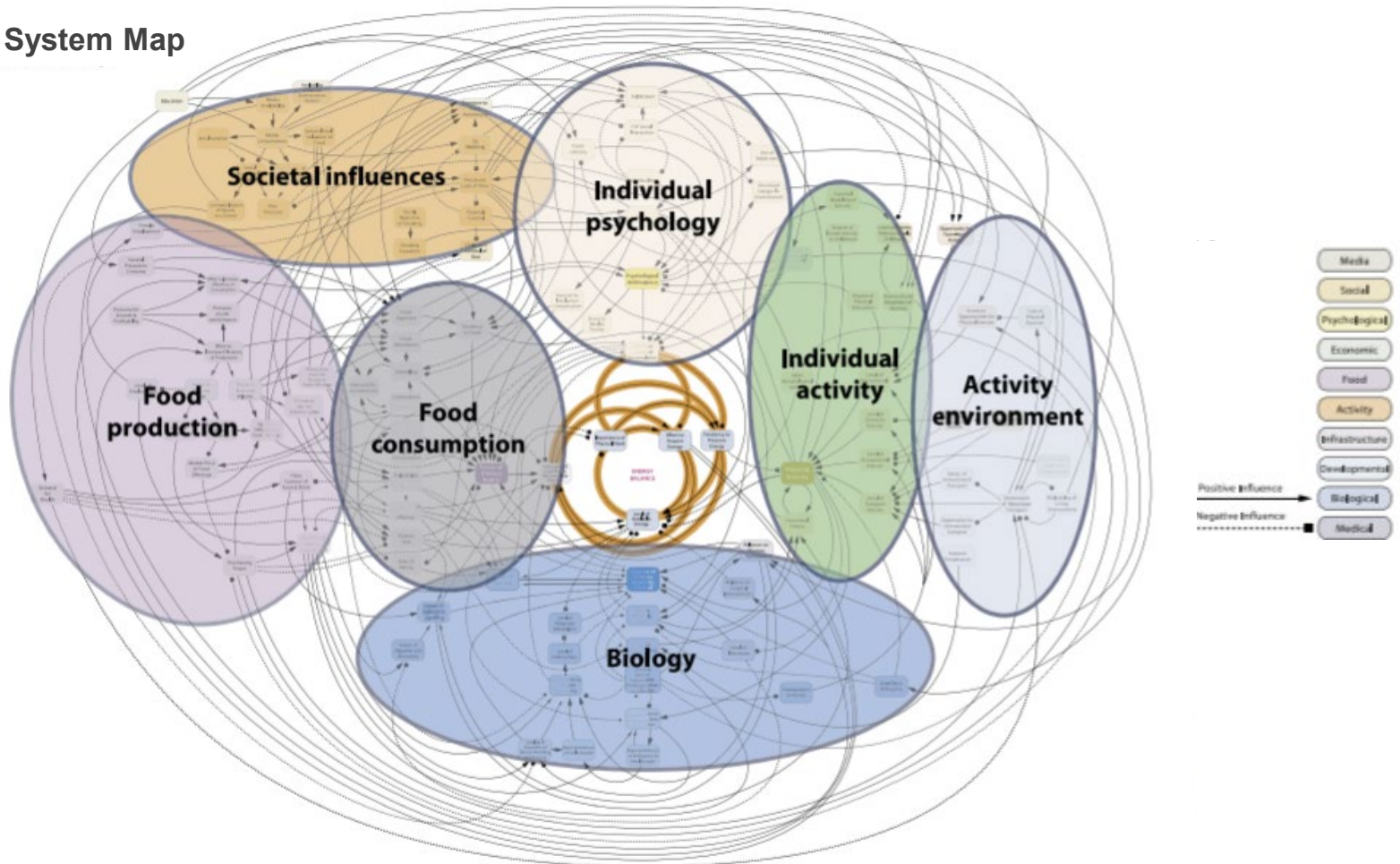
- Discuss obesity as a chronic and complex disease and describe its short- and long-term physiological effects on physical and mental health
- Describe the factors that make long term weight loss difficult to sustain
- Review the classification of obesity
- Recognize how the medical weight loss program (MWL) is structured to promote sustainability

Why Obesity?

- Obesity is a progressive, chronic, relapsing, neuroendocrine and epigenetic multifactorial disease
 - Associated with excess adipose tissue deposition that promotes neuroendocrine and inflammatory dysfunction
 - Associated with over 200 other diseases
 - Most commonly discussed in terms of body mass index (BMI)

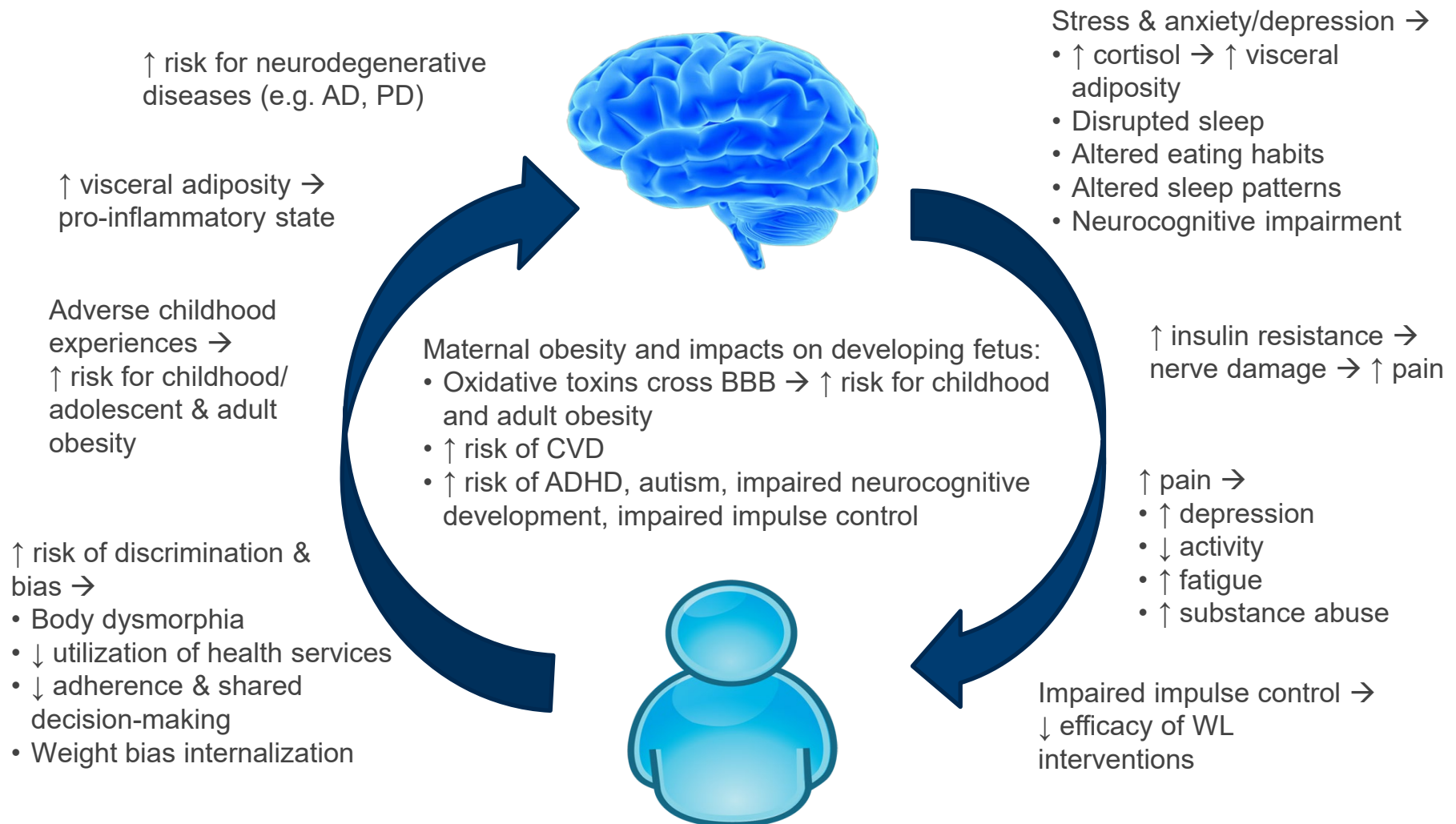
Obesity is Not Unidimensional and Cannot be Treated as Such

Obesity System Map

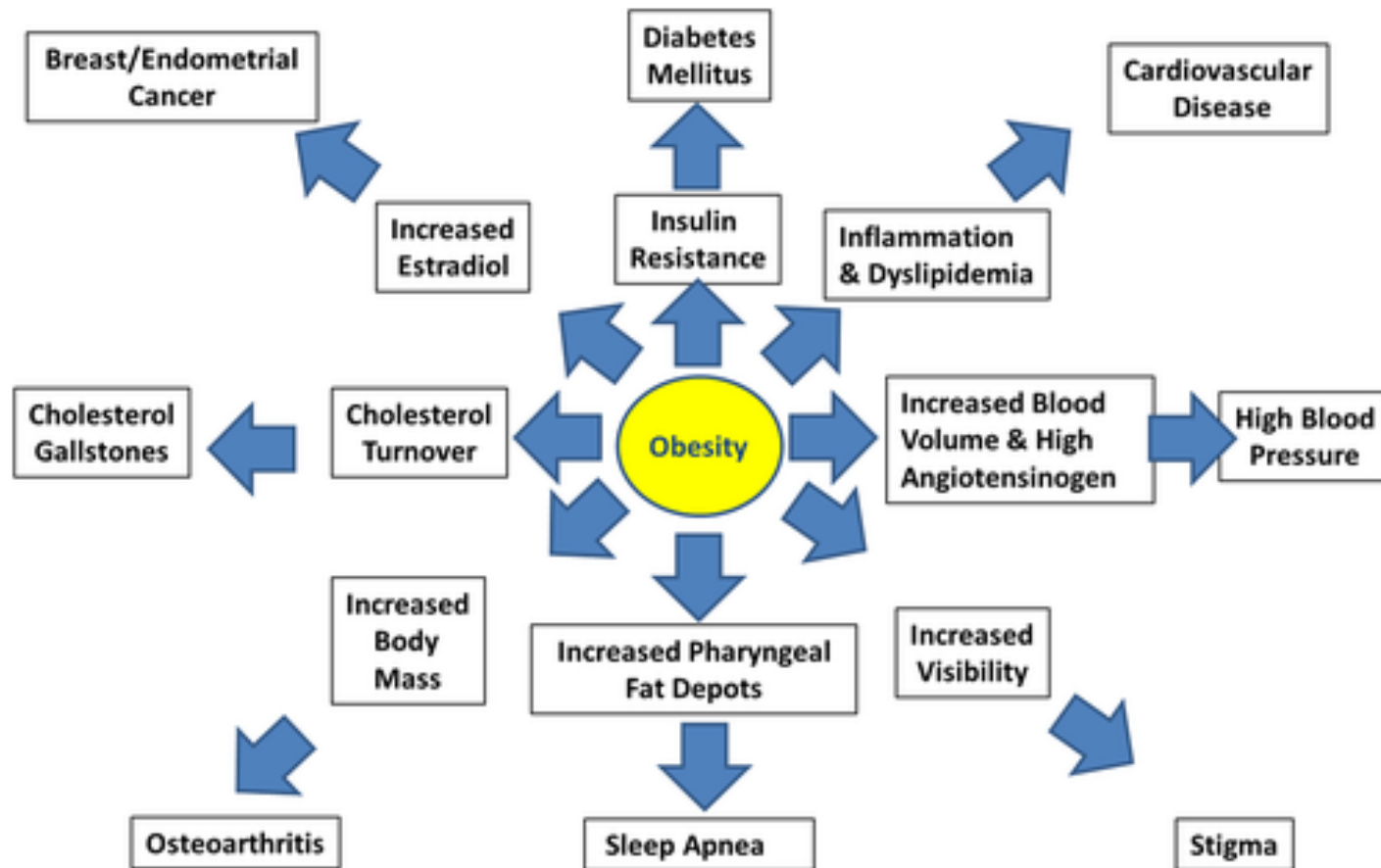


Source: Government Office for Science (2007), FORESIGHT Tackling Obesity: Future Choices–Project Report 2nd edition: [www.gov.uk/government/publications/ reducing-obesity-future-choices](http://www.gov.uk/government/publications/reducing-obesity-future-choices).

Complex Neural/Psychiatric Interactions



Obesity Affects Every Aspect of Our Health



Bray GA, et al. *Obes Rev*. 2017;18(7):715-723. doi: 10.1111/obr.12551.

Obesity is Expensive

America's Obesity Crisis: The Health and Economic Costs of Excess Weight
– Milken Institute, 2018

Most expensive conditions:

- HTN
- T2DM
- OA
- Chronic back pain
- Alzheimer's disease

TABLE 9

Total Costs of Obesity and Being Overweight, 2016

Condition	Costs (in \$ Millions), 2016		
	Direct Costs	Indirect Costs	Total
Alzheimer's and Vascular Dementia	\$73,572	\$32,606	\$106,178
Asthma and COPD	\$10,564	\$16,234	\$26,798
Breast Cancer	\$5,900	\$3,669	\$9,569
Chronic Back Pain	\$38,476	\$217,291	\$255,768
Colorectal Cancer	\$6,151	\$5,425	\$11,576
Congestive Heart Failure	\$5,201	\$2,039	\$7,239
Coronary Heart Disease	\$22,700	\$39,315	\$62,015
Diabetes (Type 2)	\$120,707	\$214,500	\$335,208
Dyslipidemia	\$28,619	†	\$28,619
End Stage Renal Disease	\$3,716	††	\$3,716
Endometrial Cancer	\$189	\$158	\$347
Esophageal Adenocarcinoma	\$970	\$92	\$1,061
Gallbladder Cancer	\$22	\$17	\$39
Gallbladder Disease	\$26,863	\$27,401	\$54,264
Gastric Cardia Adenocarcinoma	\$1,433	\$136	\$1,568
Hypertension	\$29,323	\$432,230	\$461,553
Liver Cancer	\$87	\$67	\$154
Osteoarthritis	\$86,480	\$215,303	\$301,783
Ovarian Cancer	\$1,152	\$152	\$1,304
Pancreatic Cancer	\$146	\$738	\$884
Prostate Cancer	\$1,983	\$13,411	\$15,393
Renal Cancer	\$2,254	\$559	\$2,813
Stroke	\$14,148	\$14,527	\$28,674
	\$480,655	\$1,235,869	\$1,716,523

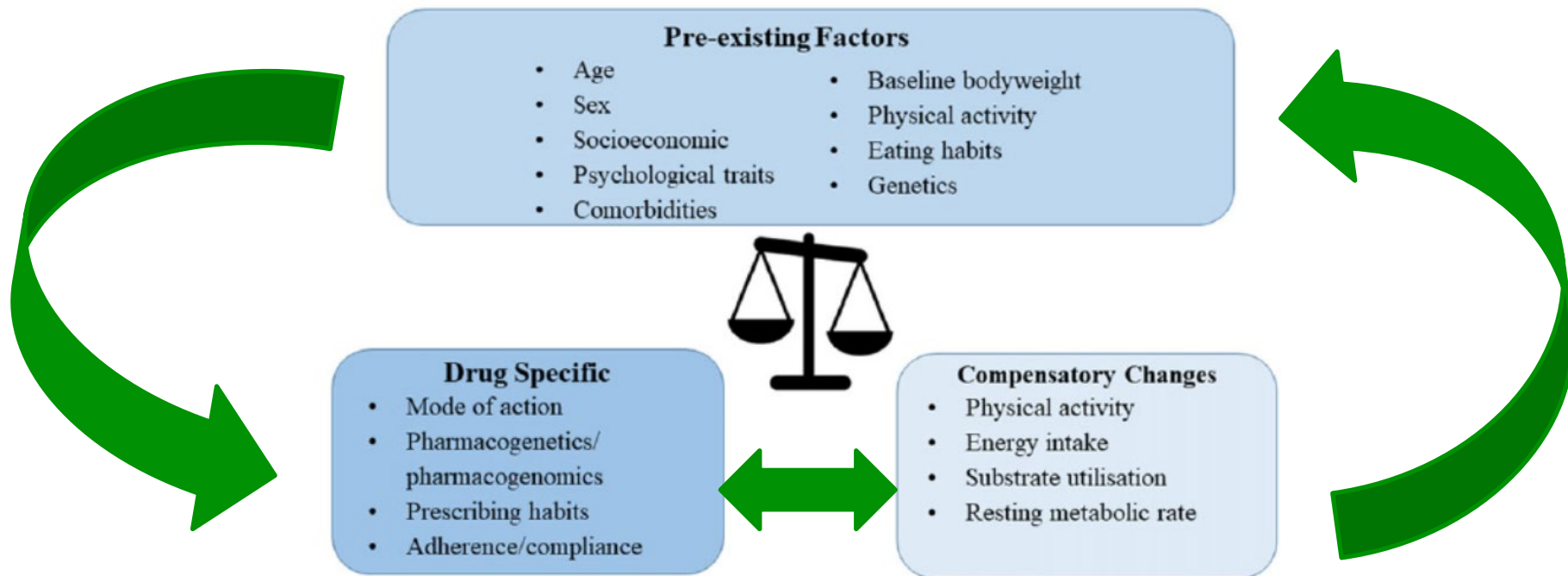
† Included in heart disease, diabetes, and stroke.¹

†† Included in diabetes and hypertension.

Source: Milken Institute.

One Solution Does Not Work for All ...

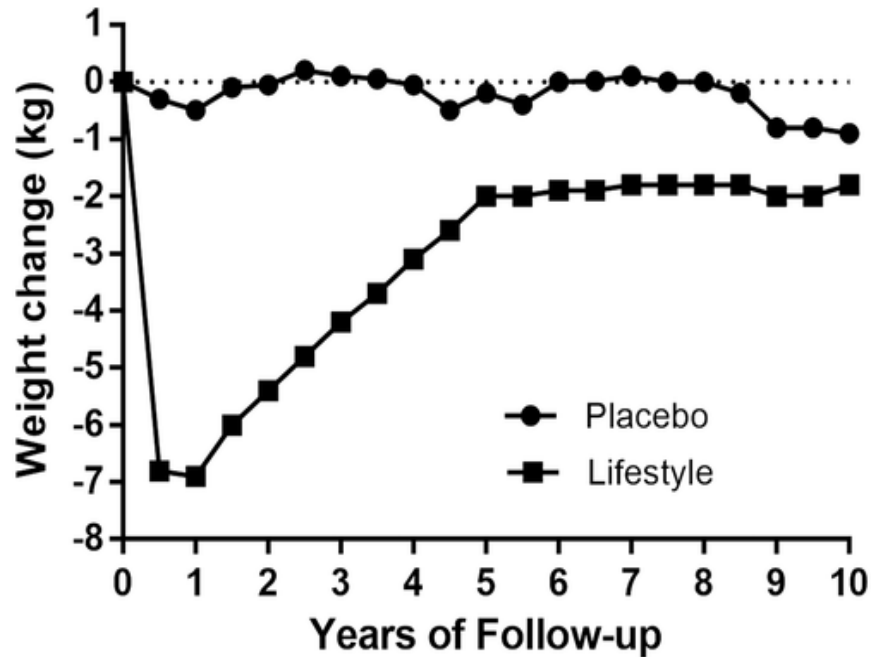
Variability is to be expected, no matter what lifestyle, medical or surgical approach is used to promote weight loss



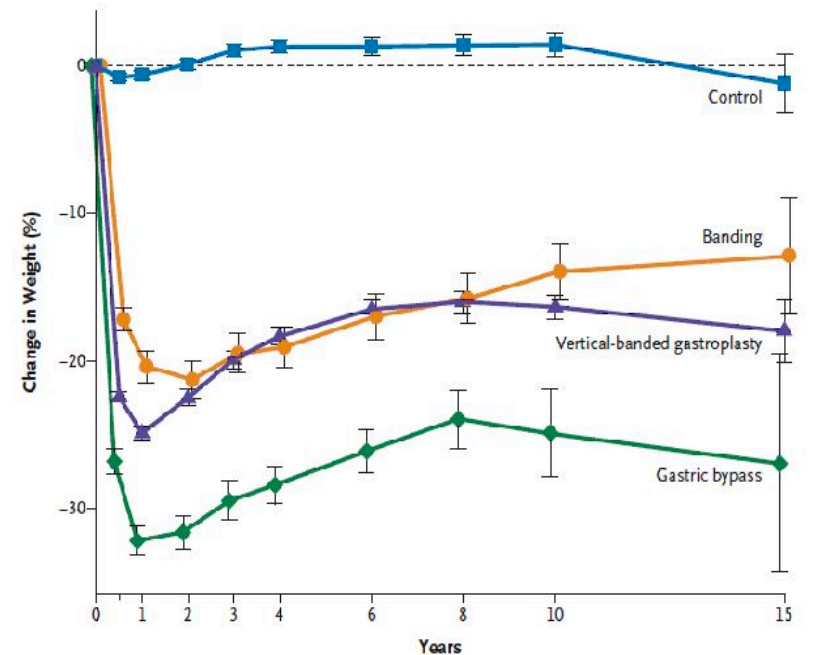
We Have Evolved to Keep Weight On During Times of Scarcity ...

- Weight gain is the result of an imbalance of *energy in* and *energy out*
 - This is a very simplistic way of thinking of a VERY complex problem
- Millions of years of adaptation → Have made us very metabolically efficient
 - Don't like to lose weight once we have it
 - Genetics greatly affect this

Obesity is a Relapsing Chronic Disease



Adapted from Venditti et al Int J Obes 2008;32:1537-44



Source: <https://www.georgiasurgicare.com/advanced-weight-loss-center/weight-regain-care-after-weight-loss-surgery-postbariatric-care/>

Why is It So Hard to Maintain Weight Loss?

- Difficult to maintain long term adherence to the “restrictive regimens” that allowed success in the first place
- Weight loss → both physiological and psychological changes which promote weight regain



Figure: MacLean PS, et al. *Obesity* (Silver Spring). 2015;23(1):7-15. doi:10.1002/oby.20967.

Drivers of Weight Regain/Disease Relapse

- Metabolic adaptations of weight loss:
 - ↓ total energy expenditure
 - ↑ hunger feelings (↑ ghrelin)
 - ↓ post prandial satiety hormones
- Neuronal changes:
 - WL → neuronal changes to food-related cues related to dysregulation of energy changes



©design36/Shutterstock.com



It's Not Their Fault ...

Change	Weight loss leads to ...
Physiologic Priority Imbalance	<ul style="list-style-type: none"> ➤ Neuro-biologic processes strongly resist undernutrition ➤ Neuro-biologic processes weakly resist over-nutrition <p>“Prefer the path of least resistance”</p>
Neurobiology	<p>Weight loss alters neuroendocrine factors → results in:</p> <ul style="list-style-type: none"> ➤ ↓ in post-prandial levels of hormones that + satiety: <ul style="list-style-type: none"> ➤ GLP-1 ➤ CCK ➤ Peptide YY ➤ ↑ Ghrelin → ↑ Appetite <p>Insulin and leptin resistance → limit appetite reduction</p> <p><i>Exercise increases brain's sensitivity to insulin and leptin</i></p>
Energy Expenditure	<p>↓ in resting energy expenditure with weight loss due to loss of body tissue → greater muscle efficiency → less energy expenditure with physical activity</p> <p>↑ <i>resistance training to further improve muscle efficiency</i></p>

It's Not Their Fault ... (cont.)

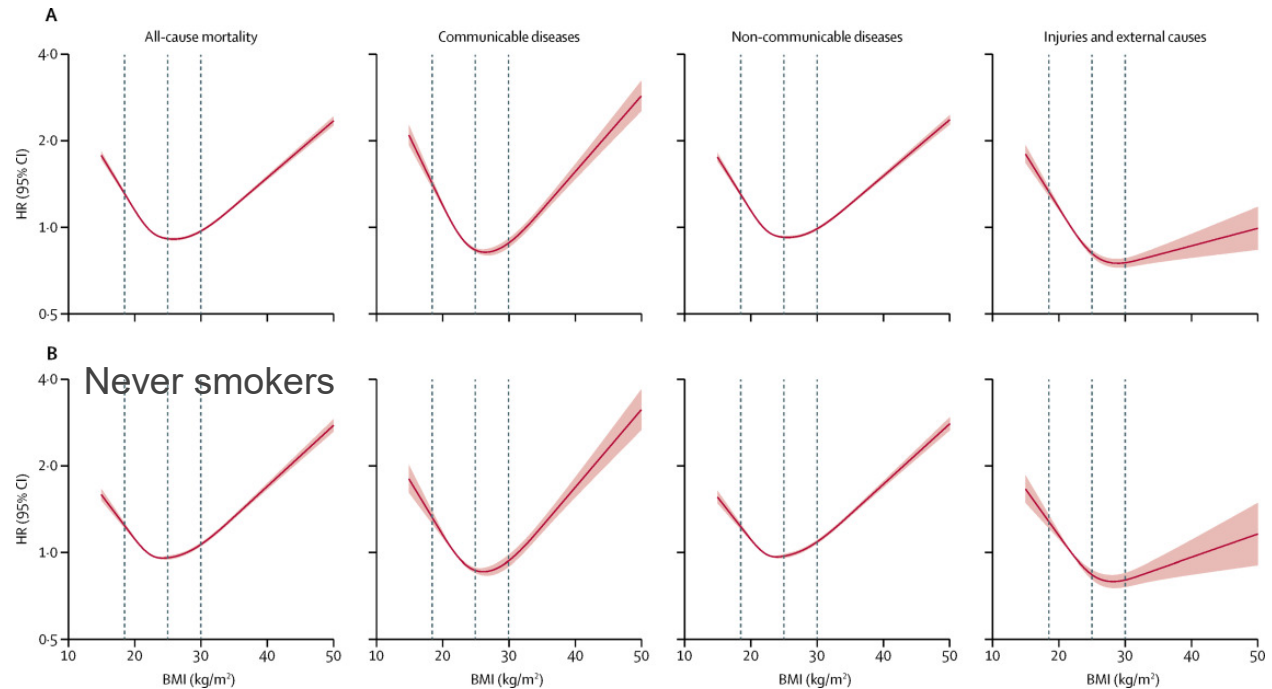
Change	Weight loss leads to ...	Strategies to try to overcome barriers:
Behavior	<p>Commitment amnesia:</p> <ul style="list-style-type: none"> ➤ Forgets the degree of commitment and dedication to lifestyle change needed to achieve initial success <ul style="list-style-type: none"> ➤ Including tracking and logging of food and physical activity <p>Change in life circumstances and priorities:</p> <ul style="list-style-type: none"> ➤ Stress ➤ Change in life circumstances <p>“Set point fallacy” The mistaken belief that once you have achieved your desired weight that weight loss will persist, and that you no longer need to do anything to maintain the lifestyle changes that helped you to achieve the weight loss.</p>	<p>If mental health concerns are beginning to affect their weight loss priorities, inform them of the importance of dealing with mental health and help connect them to a MH resource (i.e., encourage them to get help)</p> <p>The brain will always remember a person's highest weight and will try to push the weight back to that high weight → medications can help counter the physiologic measures trying to push weight back up</p>

Set Point Theory, a.k.a. “Obesogenic Memory”

- Controversial theory
- Premise: An acquired “obesogenic memory” drives weight regain in order to maintain a previous *status quo*?
 - This is why we always ask, “***what was your highest weight ever?***”
- Bariatric surgery can help to “reset” this set-point
 - It can affect the release of:
 - ↑ Anorexigenic hormones (↑ GLP-1, CCK and PYY)
 - ↓ Orexigenic hormones (ghrelin)
 - *Likely responsible for the profound weight loss seen s/p bariatric surgery*

BMI & Classes of Obesity

Class	BMI (kg/m ²)
Underweight	< 18.5
Normal weight	18.5–24.9
Overweight	25–29.9
Class I (Mild)	30–34.9
Class II (Moderate)	35–39.9
Class III (Severe)	≥ 40



Bhaskaran K, et al. *Lancet Diabetes Endocrinol.* 2018;6(12):944–53. doi: [http://dx.doi.org/10.1016/S2213-8587\(18\)30288-2](http://dx.doi.org/10.1016/S2213-8587(18)30288-2).

* *In those of Asian descent, obesity begins at a BMI of 27 kg/m²*

Is BMI a Perfect Measure of Obesity?

- History: Developed over 200 years ago
- Not a perfect measure:
 - Does not differentiate between fat tissue and lean muscle
 - Does not take distribution of adipose tissue into consideration
 - Does not take into consideration differences in fat distribution amongst:
 - Men and women
 - Different racial and ethnic groups
- Is there a better measure?

What about Waist Circumference (WC)?

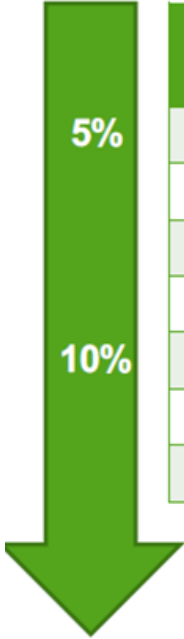
Advantages	Disadvantages
Correlates well with cardiovascular health	Not always reproducible
Increase in WC directly correlates with increase in adipose dysfunction	Not better than BMI in assessing cardiovascular risk in people with BMI >35
Inexpensive	Also affected by race/gender norms
	May not correlate with visceral fat in those s/p liposuction

Association	Men	Women
AHA/ NHBLI	> 102 cm (> 40 in)	> 88 cm (> 35 in)
International Diabetes Federation	> 90 cm (> 35.5 in)	> 80 cm (> 31.5 in)
Different cut-points for different ethnic groups		
Over BMI > 35 kg/m ² , WC does not more accurately correlate with risk		

Clinically Significant Weight Loss Allows for Improvements in Obesity Related Conditions

Weight loss impact on weight-related diseases

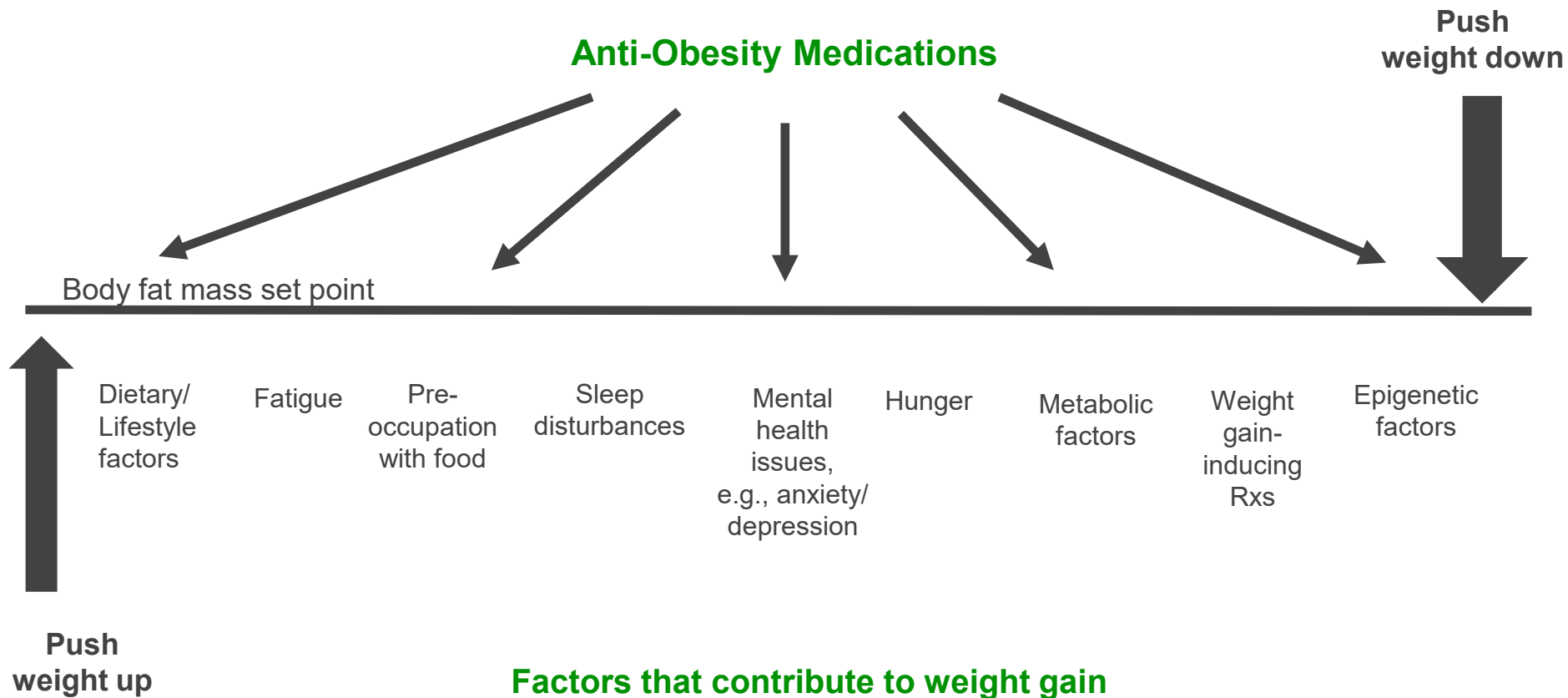
Clinically significant weight loss is defined as $\geq 5\%$ and $\geq 10\%$ weight loss



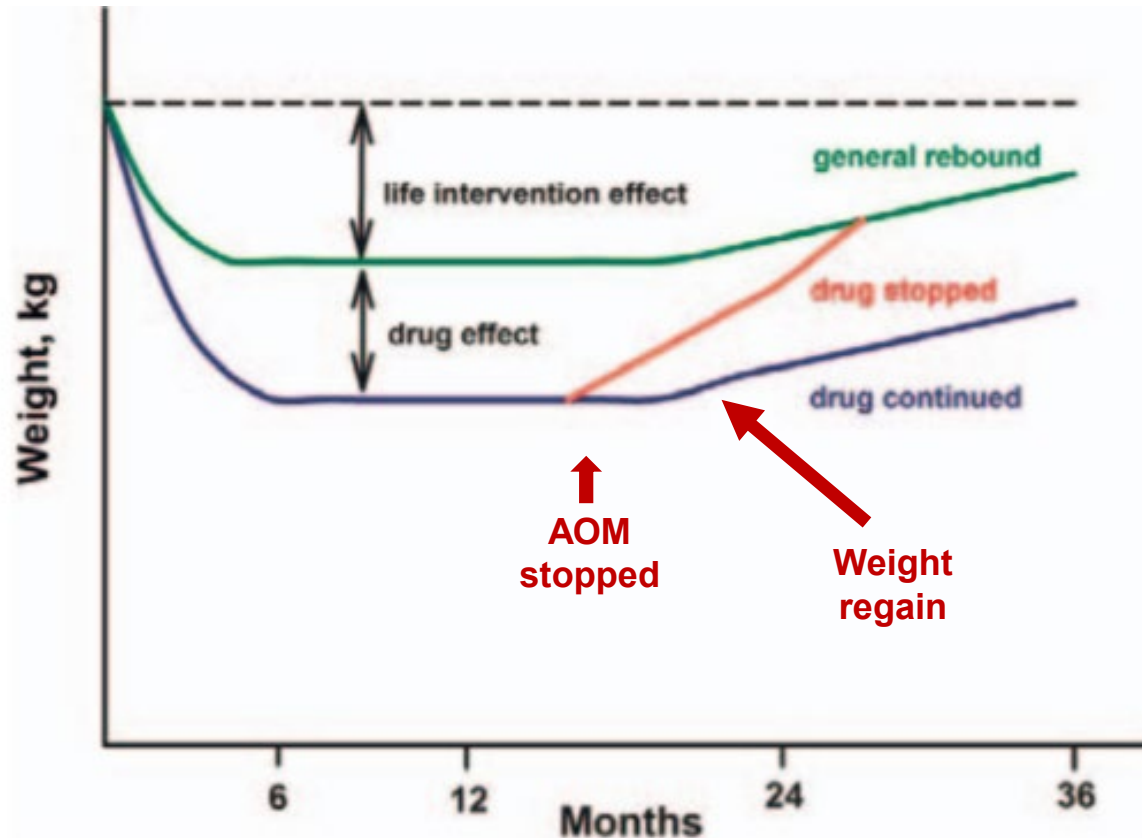
% body weight ↓	Weight-related diseases
5 to $\geq 10\%$	male hypogonadism, urinary stress incontinence
5 to $\geq 15\%$	T2D, dyslipidemia, HTN, PCOS, NAFLD
7-8%	asthma/reactive-airway disease
7-11%	obstructive sleep apnea
10%	prediabetes, metabolic syndrome, female infertility
$\geq 10\%$	osteoarthritis, GERD
10-40%	steatohepatitis

Importance of guiding patients to define health goals

How Can Anti-obesity Medications Help?

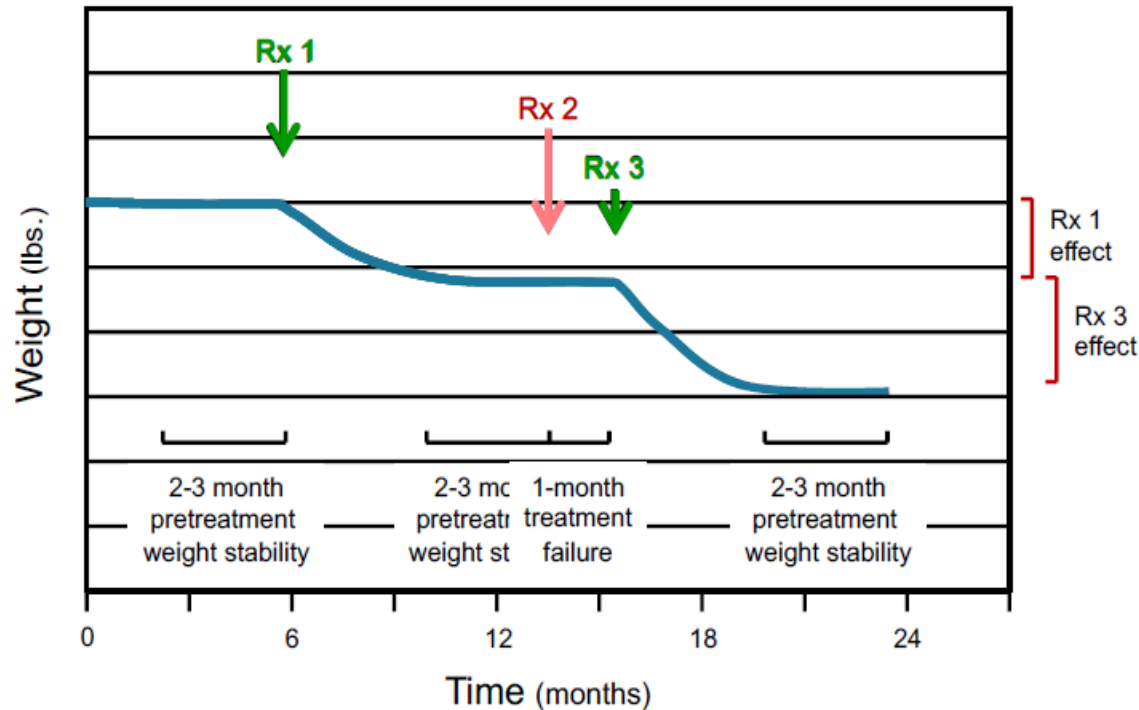


Weight Loss Over Time +/- Lifestyle Intervention and AOMs



Must set expectations for long-term use of AOMs

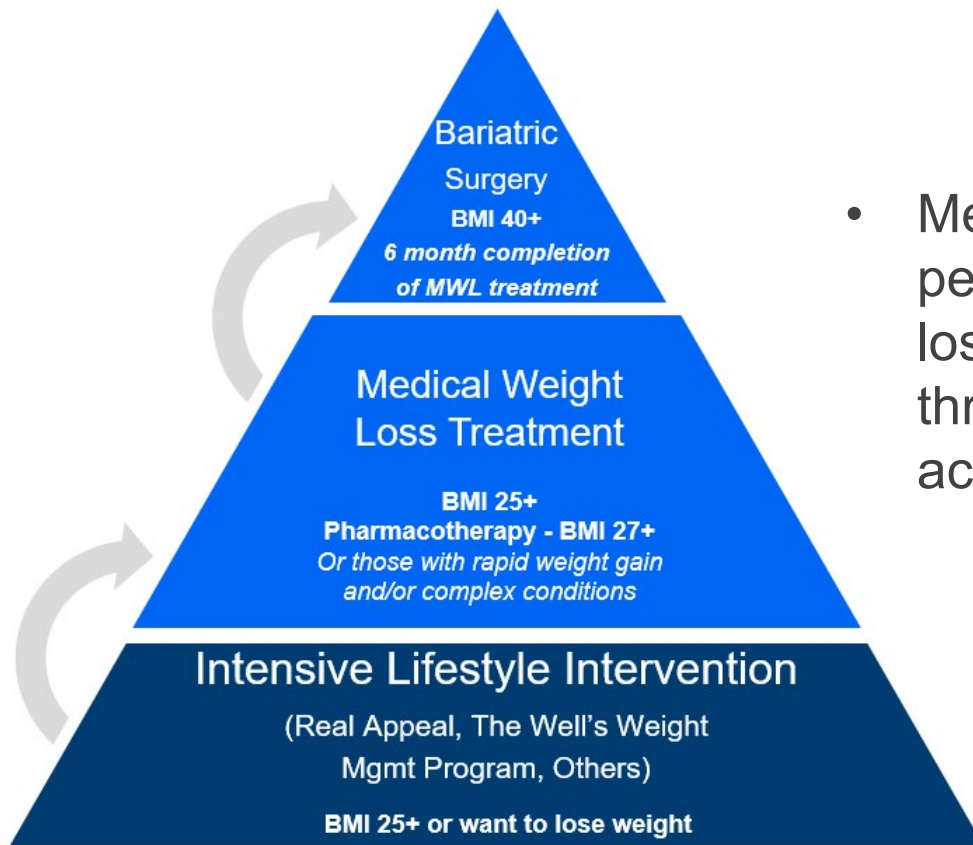
Plateaus and Escalation of AOMs



These are inevitable and will happen at some point during a person's weight loss journey.

Time horizon may vary

Medical Weight Loss Continuum



- Medical Weight Loss helps a person to navigate their weight loss journey from lifestyle changes through potentially surgery to achieve sustainable weight loss.

Optimize holistic treatment of the patient:

- *Review concomitant medications and discuss with PCP about potentially optimizing regimen*
- *Identify other areas of opportunity that may help support the person's weight loss efforts*

There are Many Medications That Have the Potential to Promote Weight Gain

Class of medication	Alternative Agents
Weight Promoting	May promote weight loss +/- weight neutral
Cardiovascular:	
Beta-blockers: ➤ Propranolol ➤ Atenolol ➤ Metoprolol	➤ Carvedilol
Older and more lipophilic CCBs may ↑ body weight 2/2 edema, e.g., nifedipine, amlodipine	
Diabetes medications:	
Insulins ➤ Sulfonylureas ➤ Thiazolidinediones ➤ Meglitinides (e.g. nateglinide, repaglinide)	May ↓ weight: ➤ Metformin ➤ GLP-1 agonists ➤ SGLT2-inhibitors ➤ Alpha glucosidase inhibitors (e.g., acarbose, miglitol) ➤ Pramlintide Weight neutral: ➤ DPP4 inhibitors (e.g., “-gliptins”)

There are Many Medications That Have the Potential to Promote Weight Gain

Class of medication	Alternative Agents
Weight Promoting	May promote weight loss +/- weight neutral
Steroids:	
Contraceptives: <ul style="list-style-type: none">➤ Progestin contraceptives (injectable or implantable)➤ OCPs➤ IUDs	<ul style="list-style-type: none">➤ Copper IUD➤ Testosterone (helpful in men, facilitates ↑ in lean body mass)
Anti-seizure medications:	
<ul style="list-style-type: none">➤ Carbamazepine➤ Gabapentin➤ Valproate➤ Pregabalin	<ul style="list-style-type: none">➤ Topiramate➤ Zonisamide

There are Many Medications That Have the Potential to Promote Weight Gain

Class of medication	Alternative Agents
Weight Promoting	May promote weight loss +/- weight neutral
Antidepressants	
Tricyclic antidepressants: <ul style="list-style-type: none">➤ Amitriptyline➤ Doxepin➤ Imipramine	Variable effect on body weight: <ul style="list-style-type: none">➤ Desipramine➤ Nortriptyline
SSRIs <ul style="list-style-type: none">➤ Paroxetine➤ Citalopram	Variable effect on body weight: <ul style="list-style-type: none">➤ Escitalopram➤ Sertraline
SNRIs <ul style="list-style-type: none">➤ Venlafaxine	<ul style="list-style-type: none">➤ Desvenlafaxine➤ Duloxetine
➤ Trazodone	Decrease weight: <ul style="list-style-type: none">➤ Bupropion➤ Fluoxetine

There are Many Medications That Have the Potential to Promote Weight Gain

Class of medication	Alternative Agents
Weight Promoting	May promote weight loss
Mood stabilizers	
<ul style="list-style-type: none">➤ Gabapentin➤ Divalproex➤ Lithium➤ Valproate➤ Carbamazepine➤ Lamotrigine➤ Oxcarbazepine	<ul style="list-style-type: none">➤ Topiramate➤ Zonisamide

What about supplements and other non-FDA reviewed adjuncts?

Supplements/Non-FDA Reviewed Strategies Espoused For Weight Loss

Substance	Mechanism of Action	Weight loss effects
Prebiotics	Indigestible oligosaccharides → stimulate intestinal growth	May promote microbiome conducive to weight loss
Probiotics	Bacteria found in fermented food that provide protection against yeast overgrowth and other pathogenic bacteria	May promote weight loss (Consistently reported in rodents)
Caffeine	<ul style="list-style-type: none"> ➤ Reduce appetite ➤ Increase fat oxidation ➤ Stimulant 	? Weight loss
Green tea	<ul style="list-style-type: none"> ➤ Contains caffeine and epicatechin <ul style="list-style-type: none"> ➤ Catechin has antioxidant effects ➤ Stimulant 	Minor weight loss
Human chorionic gonadotropin (hCG) hormone	<ul style="list-style-type: none"> ➤ ↑ metabolism ➤ Promotes fat loss 	<p>Marketed as:</p> <ul style="list-style-type: none"> ➤ “All natural” option ➤ Appetite suppressor ➤ Preserve muscle mass ➤ Often coupled with an ultra-low-calorie diet (500 cal/day) <p>Meta-analyses do not support clinically significant weight loss</p> <p>Weight loss likely due to low calorie diet vs. hCG injection</p>

Questions???

Next: Pharmacology