Obesity in the United States: Pearls for the Primary Care Internist to Treat and Destigmatize the Disease

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Objectives

- Develop an approach to the patient who has difficulty losing weight and learn the labs and elements of the history and physical which are helpful to management.
- Discern the considerations for prescribing medications for weight reduction and the recommended follow up for maximizing success with these patients.
- Determine when surgical interventions are indicated and how they should be prepared for this consultation.

Body Mass Index Calculation

Metric measurements:

$$\frac{\text{Weight (kg)}}{\text{Height (m)}^2}$$

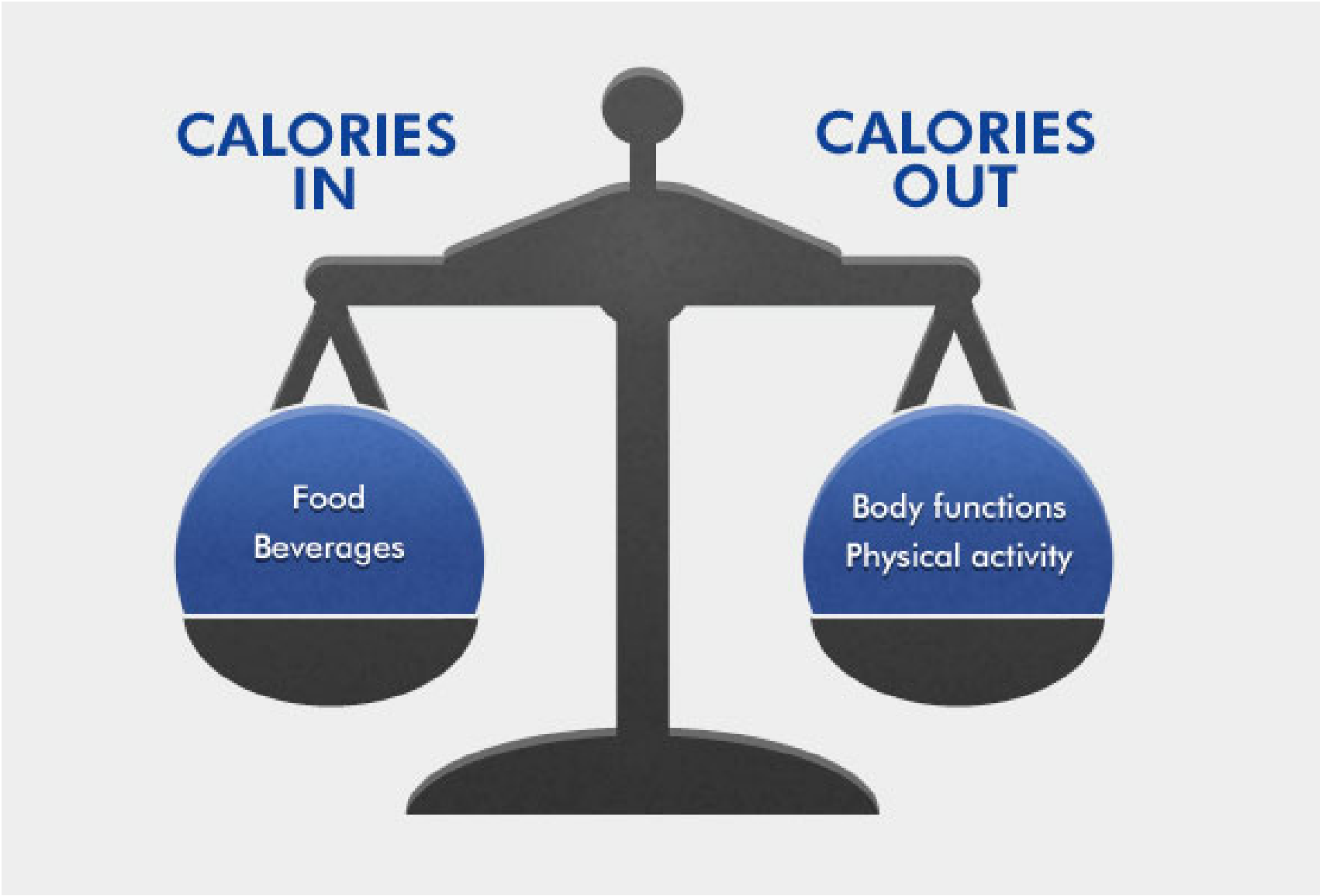
English measurements:

$$\frac{\text{Weight (lb) X 703}}{\text{Height (in)}^2}$$

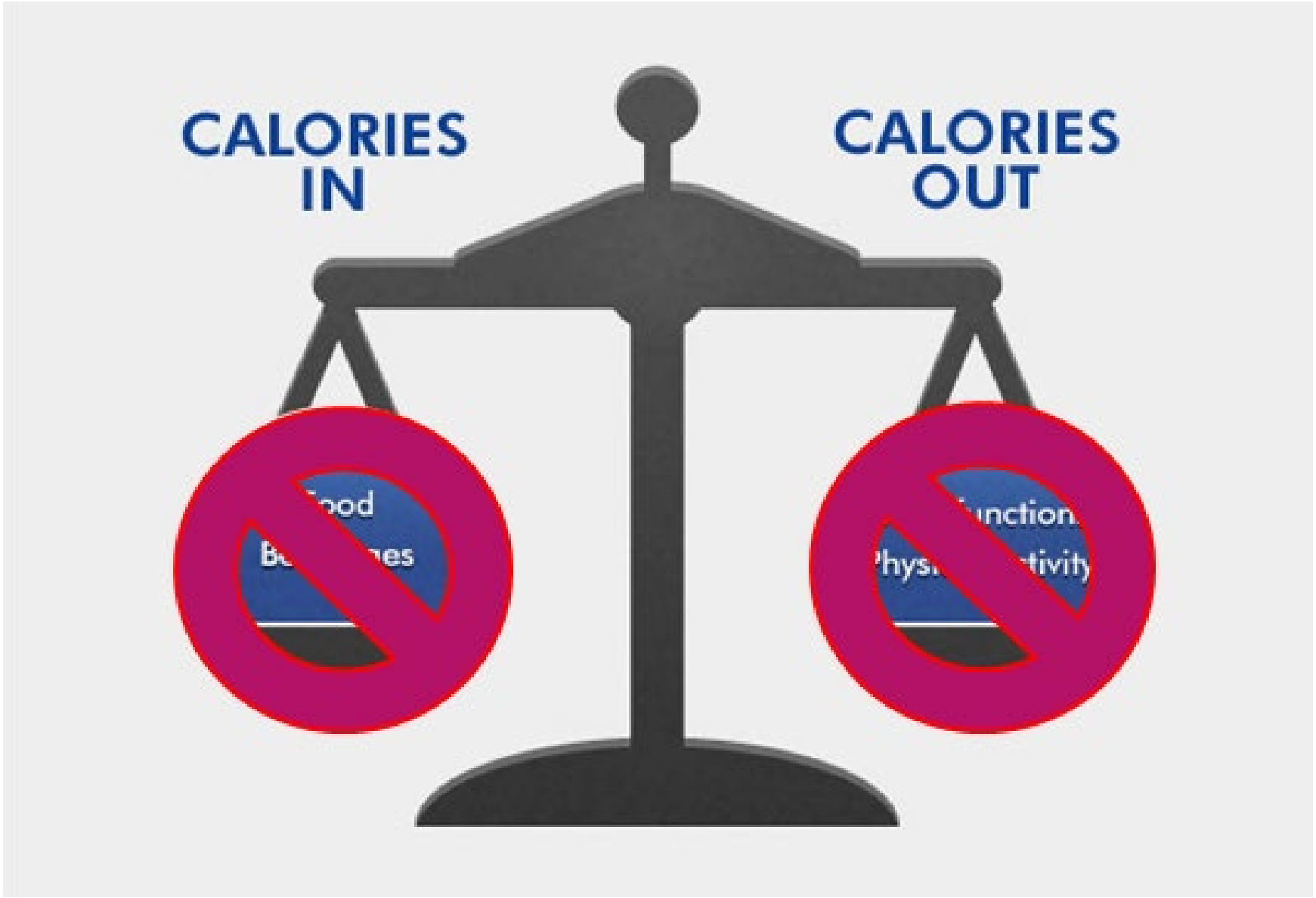
How is Obesity defined in Adults?

Weight Status Category	Body Mass Index (BMI)
Underweight	< 18.5
Normal Weight	18.5-24.9
Overweight	25- 29.9
Class I Obesity	30-34.9
Class II Obesity	35-39.9
Class III Obesity	≥40

Energy Balance (simple)



Energy Balance (simple)



All Calories are NOT created EQUAL

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Obesity: A Multi-factorial Disorder

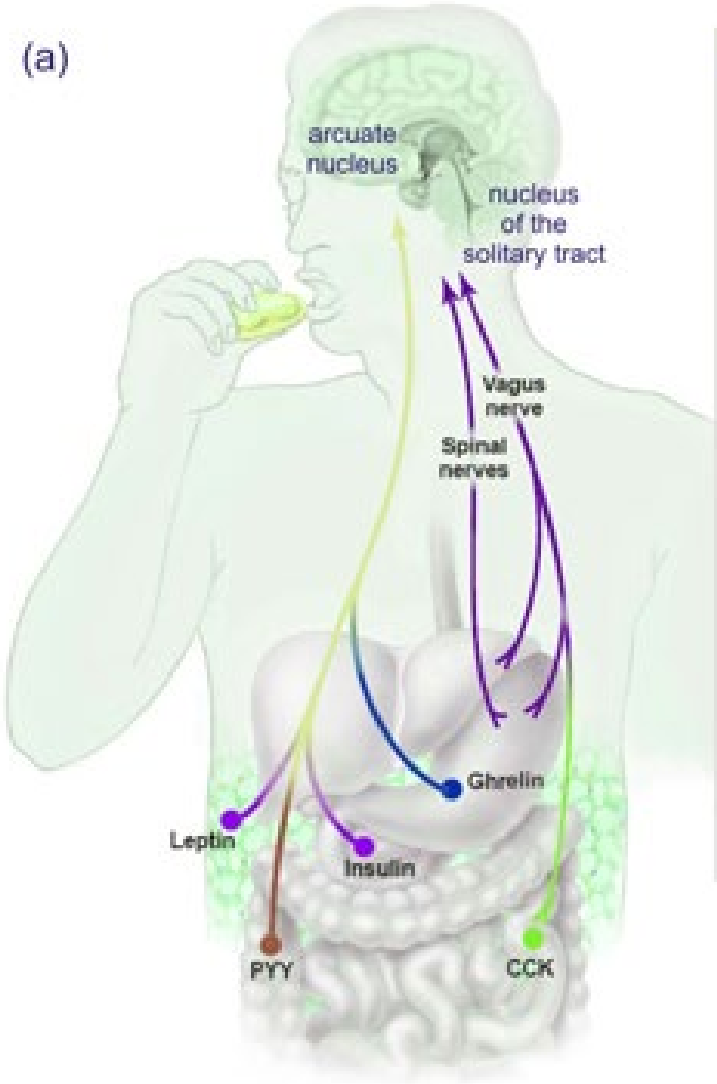
Genetics

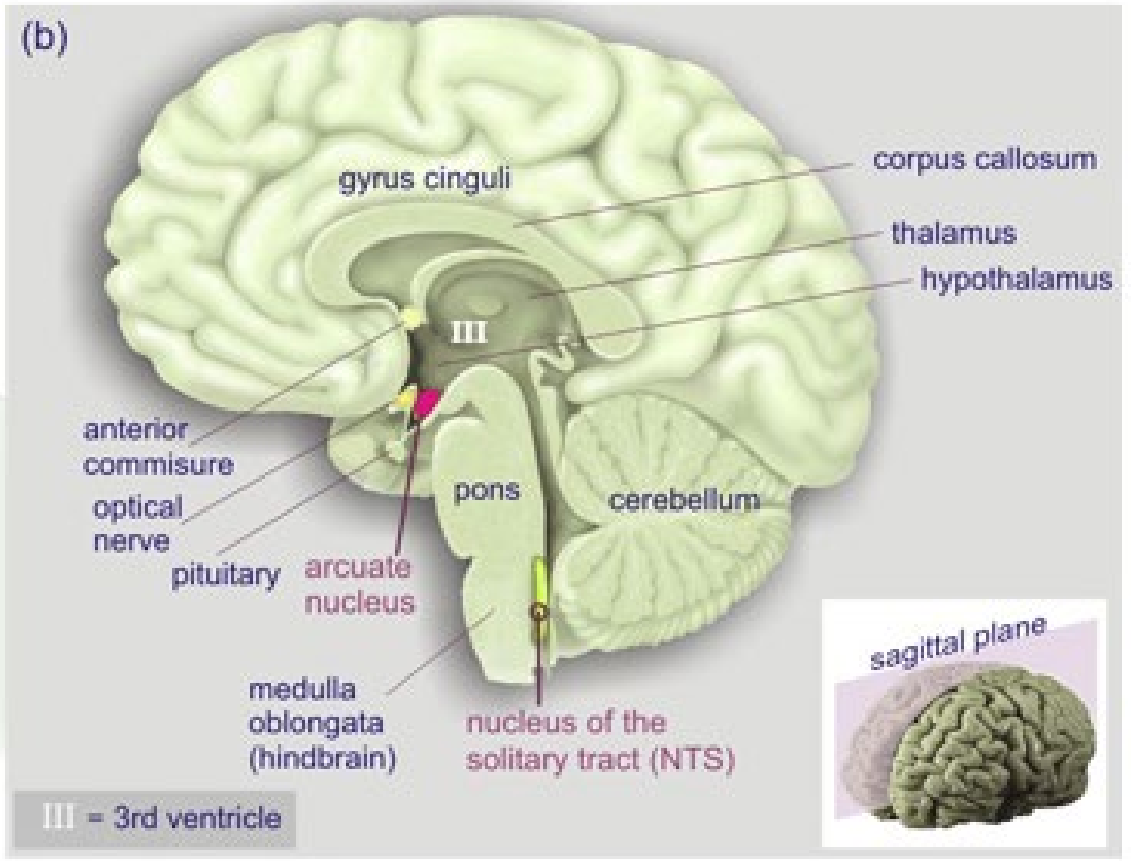
Environment

Development

Behavior

Regulation of Food Intake





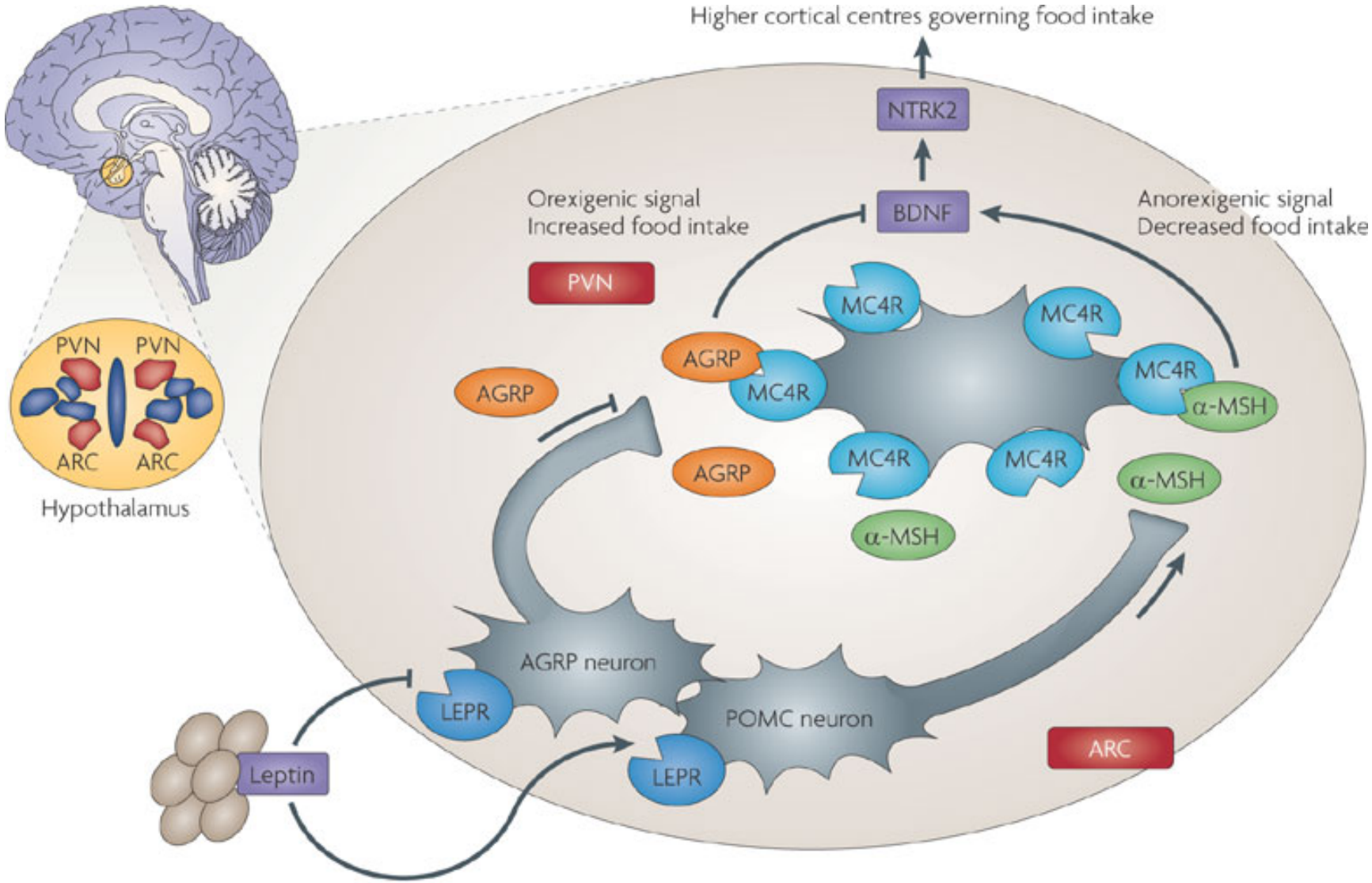
http://www.cellbiol.net/ste/alpobesity2.php

Regulation of Food Intake

Substance	Production Site	Effect (Relevant for Feeding)
Ghrelin (grow)	•Stomach (fundus region, entero-endocrine cells) •Neurons in the hypothalamus	Appetite (orexigenic)
Anandamide (endocannabinoide, ananda; bliss, delight + amide)	Small intestine	Appetite (orexigenic)
Insulin (insula; island or islet)	Pancreas (β-cells in islets of Langerhans)	•Satiety (anorexigenic) •glycogen and lipid storage
Leptin (leptos, thin)	•Adipocytes (long term) •Stomach (short term)	Satiety (anorexigenic)
CCK (cholecystokinin, "move the bile-sac")	Small intestine	•Early satiety (anorexigenic) •release of digestive enzymes from exocrine pancreas, bile from the gallbladder and H+ from parietal cells in stomach
PYY (peptide tyrosine tyrosine)	•Ileum •colon	Satiety (anorexigenic)

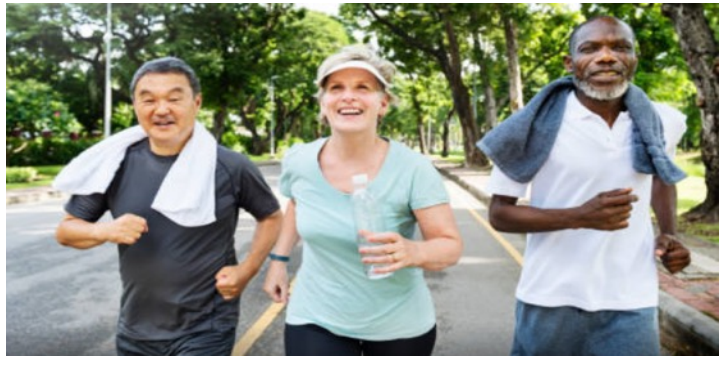
http://www.cellbiol.net/ste/alpobesity4.php

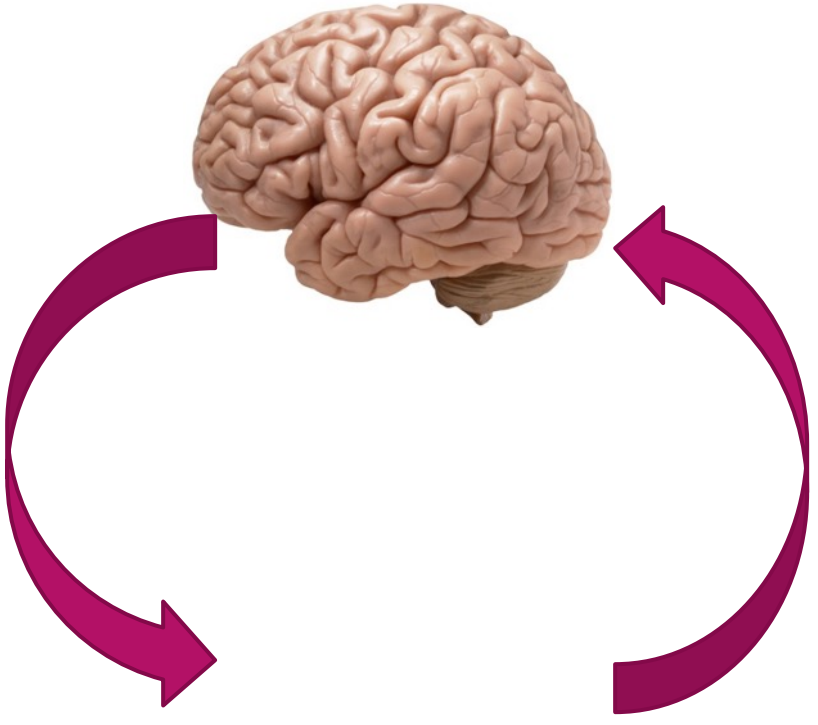
Regulation of Food Intake

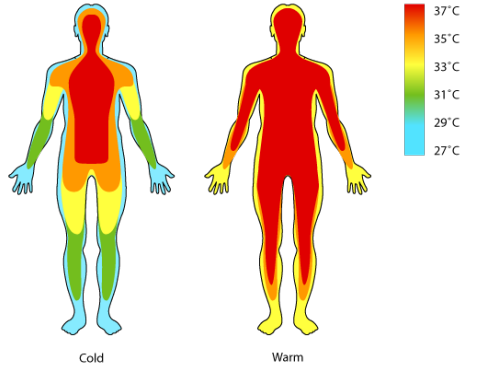


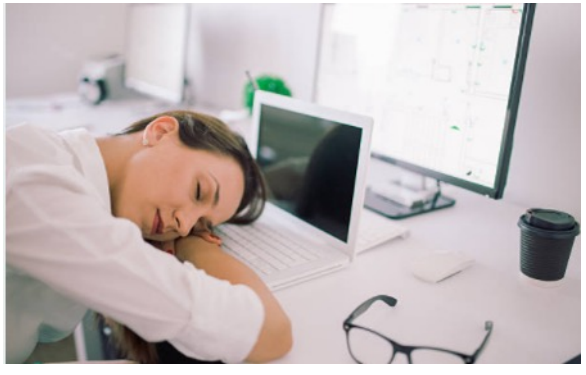
Nature Reviews Genetics **10**, 431-442 (July 2009)

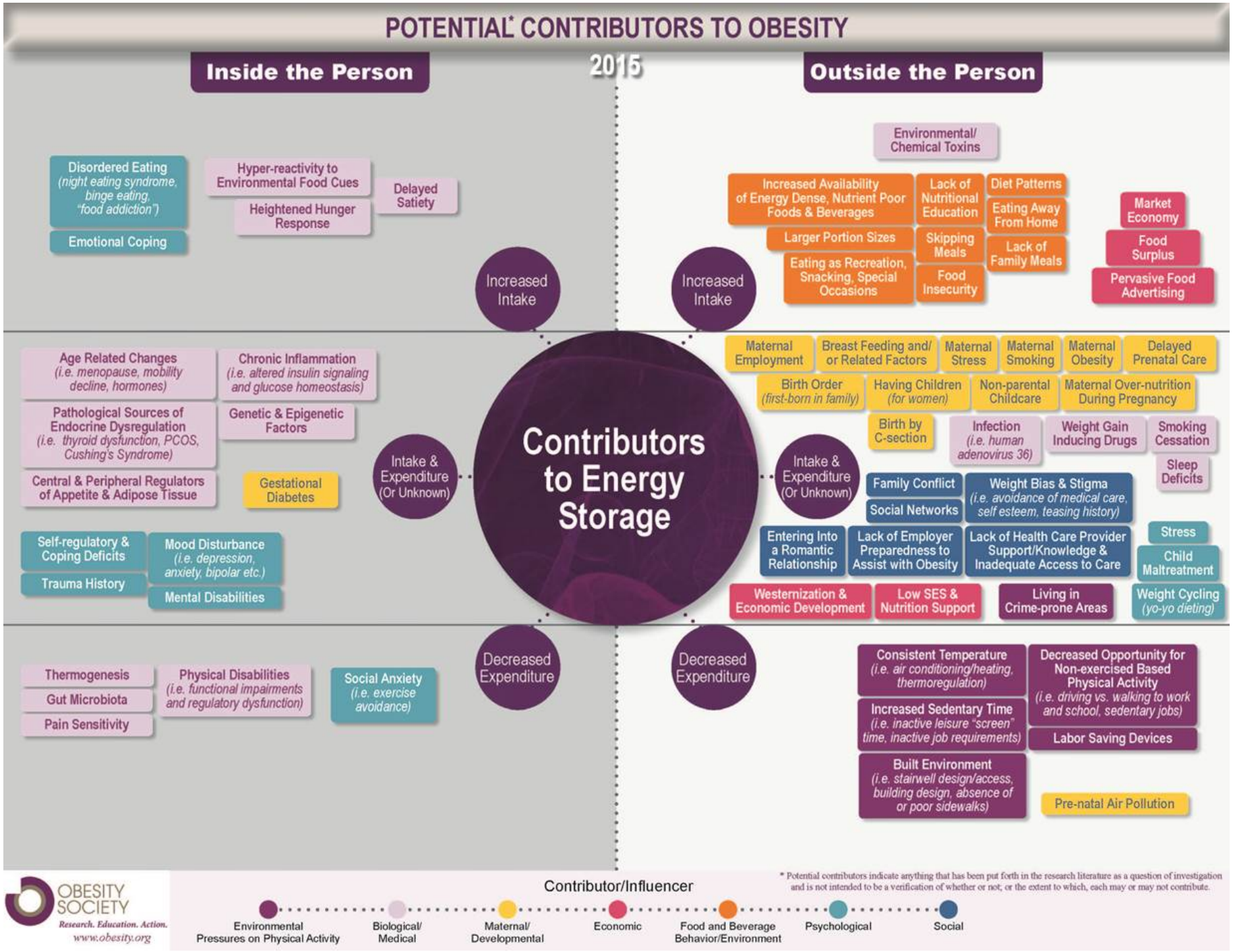
Central Nervous System regulates weight










POTENTIAL* CONTRIBUTORS TO OBESITY
2015
Inside the Person
Outside the Person
Disordered Eating (night eating syndrome, binge eating, "food addiction")
Emotional Coping
Hyper-reactivity to Environmental Food Cues
Heightened Hunger Response
Delayed Satiety
Increased Intake
Environmental/ Chemical Toxins
Increased Availability of Energy Dense, Nutrient Poor Foods & Beverages
Larger Portion Sizes
Eating as Recreation, Snacking, Special Occasions
Lack of Nutritional Education
Skipping Meals
Food Insecurity
Diet Patterns
Eating Away From Home
Lack of Family Meals
Market Economy
Food Surplus
Pervasive Food Advertising
Increased Intake
Age Related Changes (i.e. menopause, mobility decline, hormones)
Pathological Sources of Endocrine Dysregulation (i.e. thyroid dysfunction, PCOS, Cushing's Syndrome)
Central & Peripheral Regulators of Appetite & Adipose Tissue
Chronic Inflammation (i.e. altered insulin signaling and glucose homeostasis)
Genetic & Epigenetic Factors
Gestational Diabetes
Intake & Expenditure (Or Unknown)
Contributors to Energy Storage
Intake & Expenditure (Or Unknown)
Maternal Employment
Breast Feeding and/ or Related Factors
Maternal Stress
Maternal Smoking
Maternal Obesity
Delayed Prenatal Care
Birth Order (first-born in family)
Having Children (for women)
Non-parental Childcare
Maternal Over-nutrition During Pregnancy
Birth by C-section
Infection (i.e. human adenovirus 36)
Weight Gain Inducing Drugs
Smoking Cessation
Sleep Deficits
Family Conflict
Social Networks
Weight Bias & Stigma (i.e. avoidance of medical care, self esteem, teasing history)
Entering Into a Romantic Relationship
Lack of Employer Preparedness to Assist with Obesity
Lack of Health Care Provider Support/Knowledge & Inadequate Access to Care
Stress
Child Maltreatment
Weight Cycling (yo-yo dieting)
Westernization & Economic Development
Low SES & Nutrition Support
Living in Crime-prone Areas
Self-regulatory & Coping Deficits
Trauma History
Mood Disturbance (i.e. depression, anxiety, bipolar etc.)
Mental Disabilities
Decreased Expenditure
Decreased Expenditure
Thermogenesis
Gut Microbiota
Pain Sensitivity
Physical Disabilities (i.e. functional impairments and regulatory dysfunction)
Social Anxiety (i.e. exercise avoidance)
Consistent Temperature (i.e. air conditioning/heating, thermoregulation)
Increased Sedentary Time (i.e. inactive leisure "screen" time, inactive job requirements)
Built Environment (i.e. stairwell design/access, building design, absence of or poor sidewalks)
Decreased Opportunity for Non-exercised Based Physical Activity (i.e. driving vs. walking to work and school, sedentary jobs)
Labor Saving Devices
Pre-natal Air Pollution
OBESITY SOCIETY
Research. Education. Action.
www.obesity.org
Contributor/Influencer
Environmental Pressures on Physical Activity
Biological/ Medical
Maternal/ Developmental
Economic
Food and Beverage Behavior/Environment
Psychological
Social
* Potential contributors indicate anything that has been put forth in the research literature as a question of investigation and is not intended to be a verification of whether or not; or the extent to which, each may or may not contribute.

Contributors/ Influencers to Obesity

Biological/ Medical

Food & Beverage Behavior/ Environment

Maternal/ Developmental

Social

Psychological

Economic

Environmental Pressures on Physical Activity

Contributors to Obesity- **Inside** the Person

↑Intake

- Hyper-reactivity to Environmental Food Cues
- Delayed Satiety
- Disordered Eating

↓Expenditure

- Gut Microbiota
- Thermogenesis
- Physical Disabilities

↑ Intake/ ↓Expenditure

- Genetic and Epigenetic Factors
- Age Related Changes
- Mood Disturbances

Contributors to Obesity- **Outside** the Person

↑Intake

- Environmental/ Chemical Toxins
- Pervasive Food advertising
- Large Portion Sizes

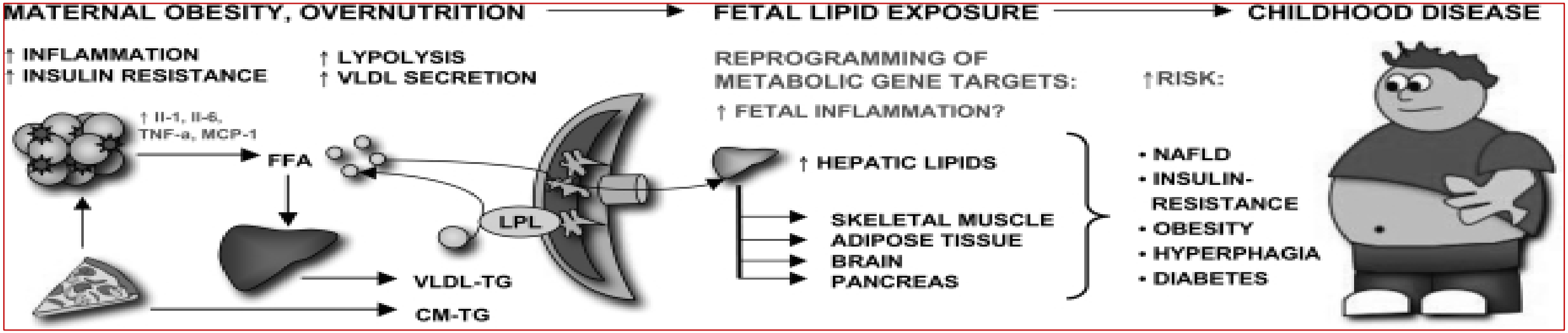
↓Expenditure

- Built Environment
- Sedentary Time
- Labor Saving Devices

↑ Intake/ ↓Expenditure

- Stress
- Weight Cycling
- Maternal/Paternal Obesity

Development- Fetal Programming



Am J Physiol Regul Integr Comp Physiol. 2010 September; 299(3): R711–R722.

Anthropometric and Plasma Profile of Children Born BMS vs. AMS

	BMS (n=54)	AMS (n=57)	P-value
Male/Female	26/28	24/33	NS
Birth weight (kg)	3.3± 0.1	2.9 ± 0.1	0.003
Macrosomia	8 (14.8%)	1 (1.8%)	0.03
Age	16.6 ± 0.6 (6.8-25.5)	10.7 ± 0.5 (2.4-20.8)	<0.0001
BMI %	79.4 ± 3.4	68.4± 4.0	0.04
Weight (kg)	74.5 ± 4.5	46.5 ± 3.5	<0.0001
Body Fat %	29.7 ± 2.3	24.1 ± 2.1	0.08
Insulin (μU/ml)	21.1 ± 1.8	15.1 ± 1.5	0.01
Glucose (mmol/L)	5.08 ± 0.06	4.86 ± 0.05	0.008

J Clin Endocrinol Metab. 2009 Nov;94(11):4275-83

Children Born AMS vs. BMS

- 3-fold ↓ prevalence of severe obesity (11 *vs.* 35%, *P* = 0.004)
- ↑ insulin sensitivity (homeostasis model assessment of insulin resistance index 3.4 ± 0.3 *vs.* 4.8 ± 0.5, *P* = 0.02)
- Improved lipid profile
  - cholesterol/HDL cholesterol 2.96 ± 0.11 *vs* 3.40 ± 0.18, *P* = 0.03
  - HDL cholesterol 1.50 ± 0.05 *vs.* 1.35 ± 0.05 mmol/liter, *P* = 0.04)
- ↓ CRP (0.88 ± 0.17 *vs.* 2.00 ± 0.34 µg/ml, *P* = 0.004)
- ↑ Leptin (11.5 ± 1.5 *vs.* 19.7 ± 2.5 ng/ml, *P* = 0.005)
- ↓ ghrelin (1.28 ± 0.06 *vs.* 1.03 ± 0.06 ng/ml, *P* = 0.005)

J Clin Endocrinol Metab. 2009 Nov;94(11):4275-83

Initial Steps to Assess Patients with Obesity (AHA/ACC/TOS guidelines)

- Patient Encounter
- Measure Height, Weight, and Calculate BMI
- Determine Weight Category
- Assess and Treat CVD risk factors and obesity related co-morbidities
- Assess Weight and Lifestyle Histories

Assess and treat CVD risk factors and obesity related co-morbidities

- History and physical examination
- Clinical and laboratory assessments
  - Blood pressure
  - Fasting blood glucose
  - Fasting lipid panel (expert opinion)
  - Waist circumference measurement (BMI 25- ≤ 35)
    - (>88 cm or >35 in for women and >102 cm or >40 in for men
  - Intensive Management of CVD risk factors (these and host of others):
    - Hypertension
    - Dyslipidemia
    - Prediabetes/ Diabetes
    - Obstructive Sleep Apnea (OSA)

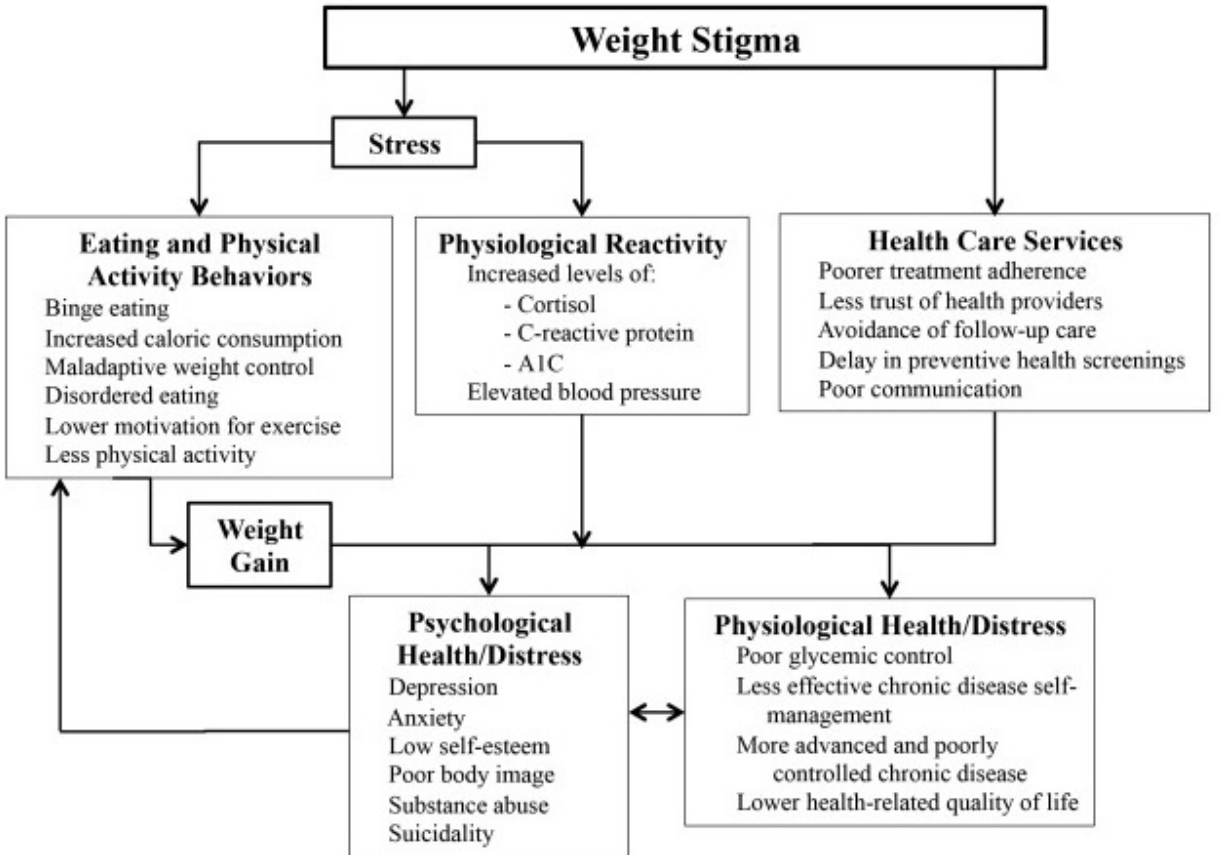
Assess Weight and Lifestyle Histories

- Ask questions about history of weight gain and loss over time
- Details of previous weight loss attempts
- Dietary habits
- Physical activity
- Family history of obesity
- Other medical conditions or medications that may affect weight

Next Steps to Assess Patients with Obesity

- Assess need to lose weight
- Advise to avoid weight gain and address other risk factors
- Assess readiness to make change and identify barriers to success
- Determine weight loss and health goals and intervention strategies
- Comprehensive lifestyle therapies alone or in conjunction with adjunctive therapies

Overcoming Weight Stigma in the Treatment of Obesity



Clin Diabetes. 2016 Jan;34(1):44-50.

Guidelines for Selecting Obesity Treatment

BMI Category

Treatment	25-26.9	27-29.9	30-34.9	35-39.9	≥40
Diet, PA, & Behavioral Therapy	With co-morbidities	With co-morbidities	+	+	+
Pharmacotherapy		With co-morbidities	+	+	+
Weight Loss Surgery			With co-morbidities		

•Prevention of weight gain with lifestyle therapy is indicated in any patient with a BMI ≥ 25 kg/m2, even without co-morbidities, while weight loss is not necessarily recommended for those with a BMI of 25–29.9 kg/m2 or a high waist circumference, unless they have two or more co-morbidities.

•Consider pharmacotherapy only if a patient has not lost 1 pound per week after 6 months of combined lifestyle therapy.

The **+** represents the use of indicated treatment regardless of co-morbidities.

Common Weight Promoting Medications

- **Anti-psychotics**
  - Risperidone
  - Lithium
  - Quetiapine
  - Aripiprazole
  - Olanzapine
  - Valproic Acid
- **Anti-depressants**
  - Citalopram
  - Duloxetine
  - Venlafaxine
- **Sleep Agents**
  - Zolpidem
  - Eszopiclone
  - Trazadone
  - Zaleplon
- **Neuropathic Agents**
  - Gabapentin
  - Pregablin
- **β-Blockers**
- **Steroids**
- **Insulin**
- **Hypoglycemic Agents**

Treatment Strategy for Weight Promoting Medications

- Investigate whether medications are a likely source of weight gain in patients.
- If a weight promoting drug may be discontinued, discontinue the agent.
- If discontinuation of a weight promoting medication is not feasible, consider the use of anti-obesity pharmacotherapy for weight loss in conjunction with appropriate lifestyle changes.

Anti-obesity pharmacotherapy agents

- Most agents may be characterized into **3 primary groups**
  1) Centrally acting medications that impair dietary intake
  2) Medications that act peripherally to impair dietary absorption
  3) Medications that increase energy expenditure

FDA Approved Anti-obesity pharmacotherapy agents

Drug class/name
CNS Stimulants/ Anorexiants: Phentermine *Phentermine/topiramate *Lorcaserin Diethylpropion Phendimetrazine Benzphetamine
Anti-Depressants/ Dopamine Reuptake Inhibitors/ Opioid Antagaonists: *Bupropion/ Naltrexone
Gastrointestinal Agents/Other: *Orlistat *GLP-1 agonists (liraglutide)

Other Anti-obesity pharmacotherapy agents

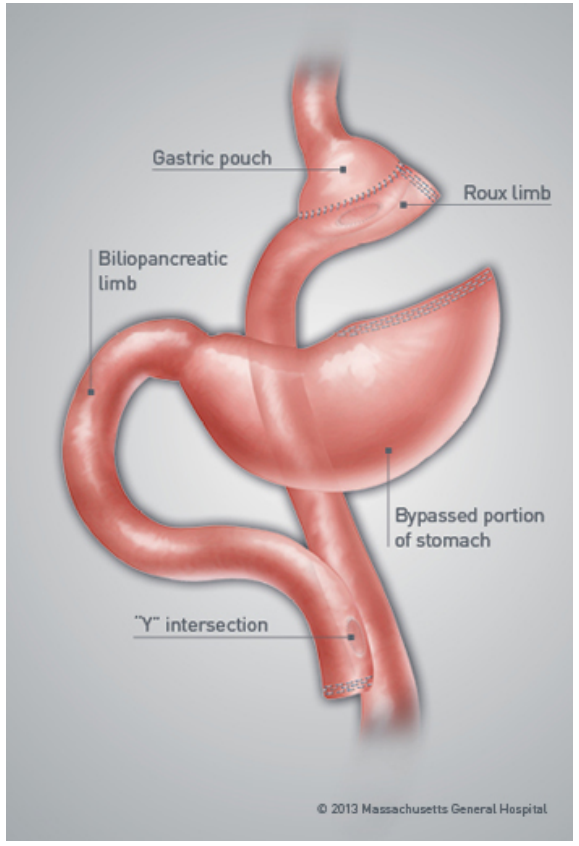
Drug class/name
Topiramate
Zonisamide
Bupropion
Metformin
Amylin agonist (pramlinitide)
SGLT2 Inhibitors (canagliflozin, dapaglifozin)

Criteria for Weight Loss Surgery

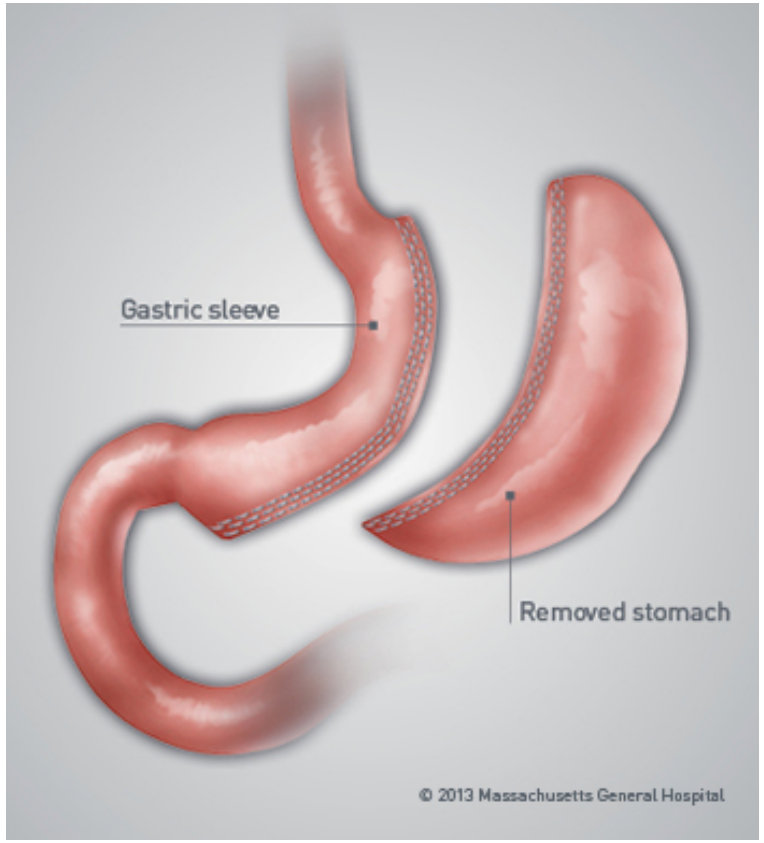
- Body Mass Index (BMI) ≥40 OR
- BMI of 35-39.9 + 1 serious co-morbidity
  - Type 2 Diabetes Mellitus
  - Coronary Artery Disease
  - Obstructive Sleep Apnea
- Prior Unsuccessful Weight Loss Attempts
- Acceptable operative risks
- Ability to participate in treatment and long term follow-up
- An understanding of the operation and the lifestyle changes needed to sustain long term weight loss

Most Common Weight Loss Surgeries in the US

Roux-en-Y Gastric Bypass



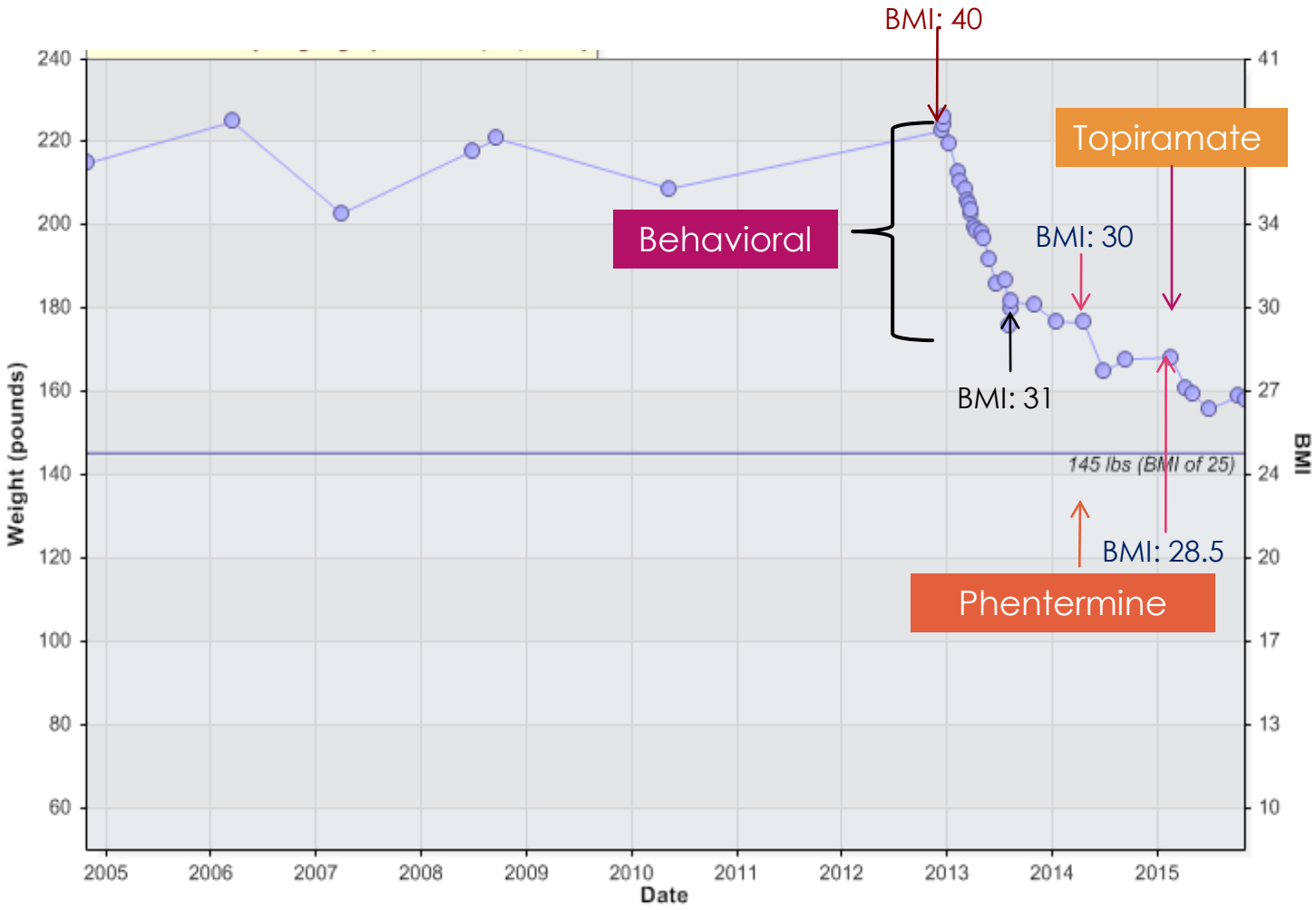
Vertical Sleeve Gastrectomy



Case #1

- 54-year-old woman
- Past medical history:
  - Untreated hypertension
  - Migraine headaches
  - GERD
  - Irritable Bowel Syndrome
  - Metabolic syndrome
- Retained 20 lbs with each of her 2 pregnancies
- Tried many commercial programs which lead to 20 lbs of unsustainable weight loss with each attempt
- Most significant weight loss with the use of phen-fen in the 1990's (~50 lbs over 6 months)
- Interested in weight loss medications + behavioral Tx

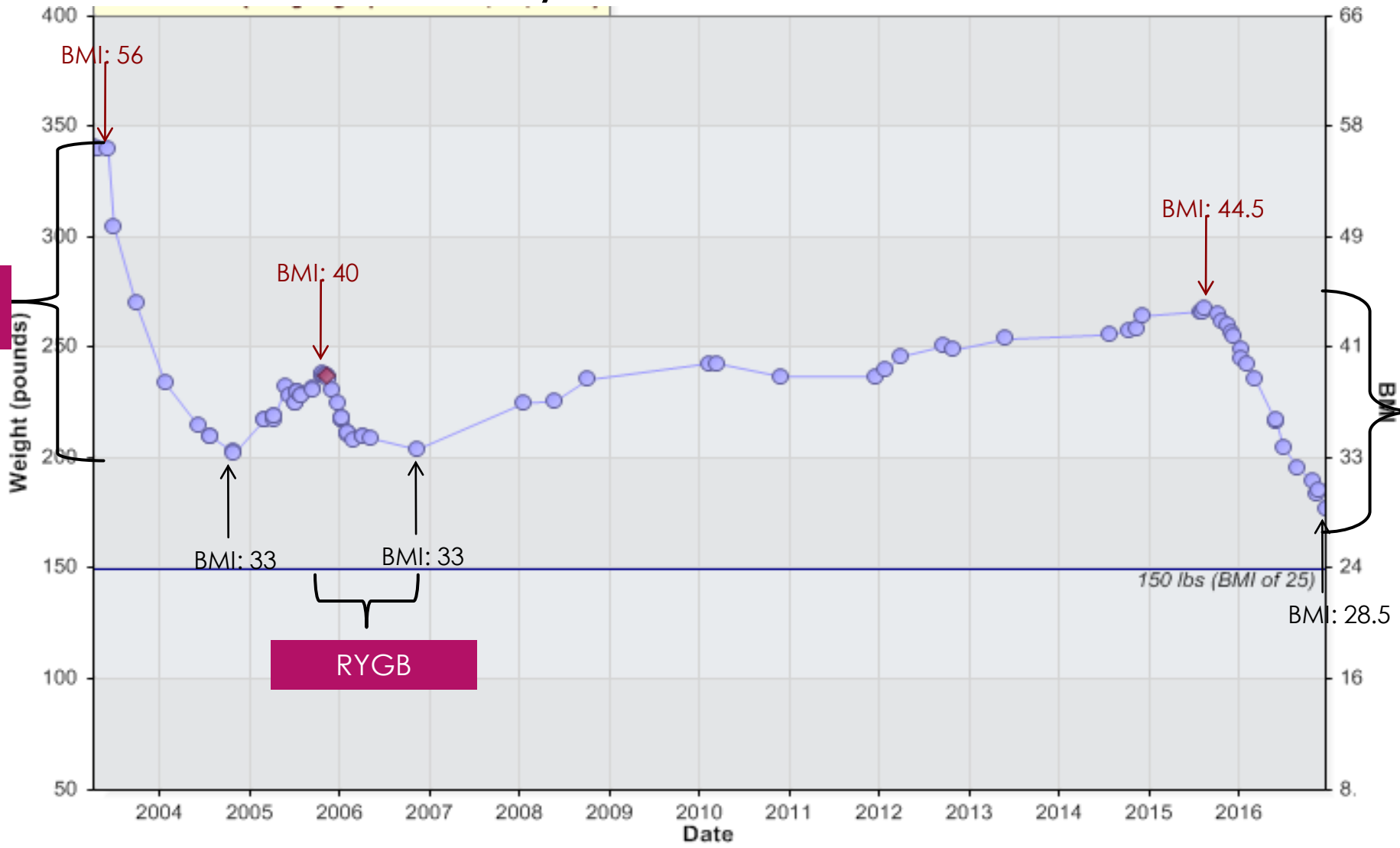
54-year-old woman



Case #2

- 57-year-old woman
- Past medical history:
  - Dyslipidemia
  - Breast Cancer
  - Hypertension
  - Depression
  - Pernicious Anemia
- Diet:
  - Breakfast: Brown Rice, Cashews, Goat Cheese
  - Snack: Denies
  - Lunch: Fish; may be on a sandwich with vegetables
  - Snack: Cheese and Crackers, Cashew nuts, Protein Bars
  - Dinner: Salad (Spinach) with cucumbers, tomatoes, goat cheese, peppers, vinaigrette
  - Snack: Cheese and Crackers, Cashew nuts, Protein Bars
- Activity: Exercise class (cardio interval circuit- 3 times per week, 1 hour); 2 videos 1/2 hour (low impact cardio); Yoga at night
- Sleep: 8 hours per night of restful sleep

57-year-old woman



Phentermine/ Topiramate

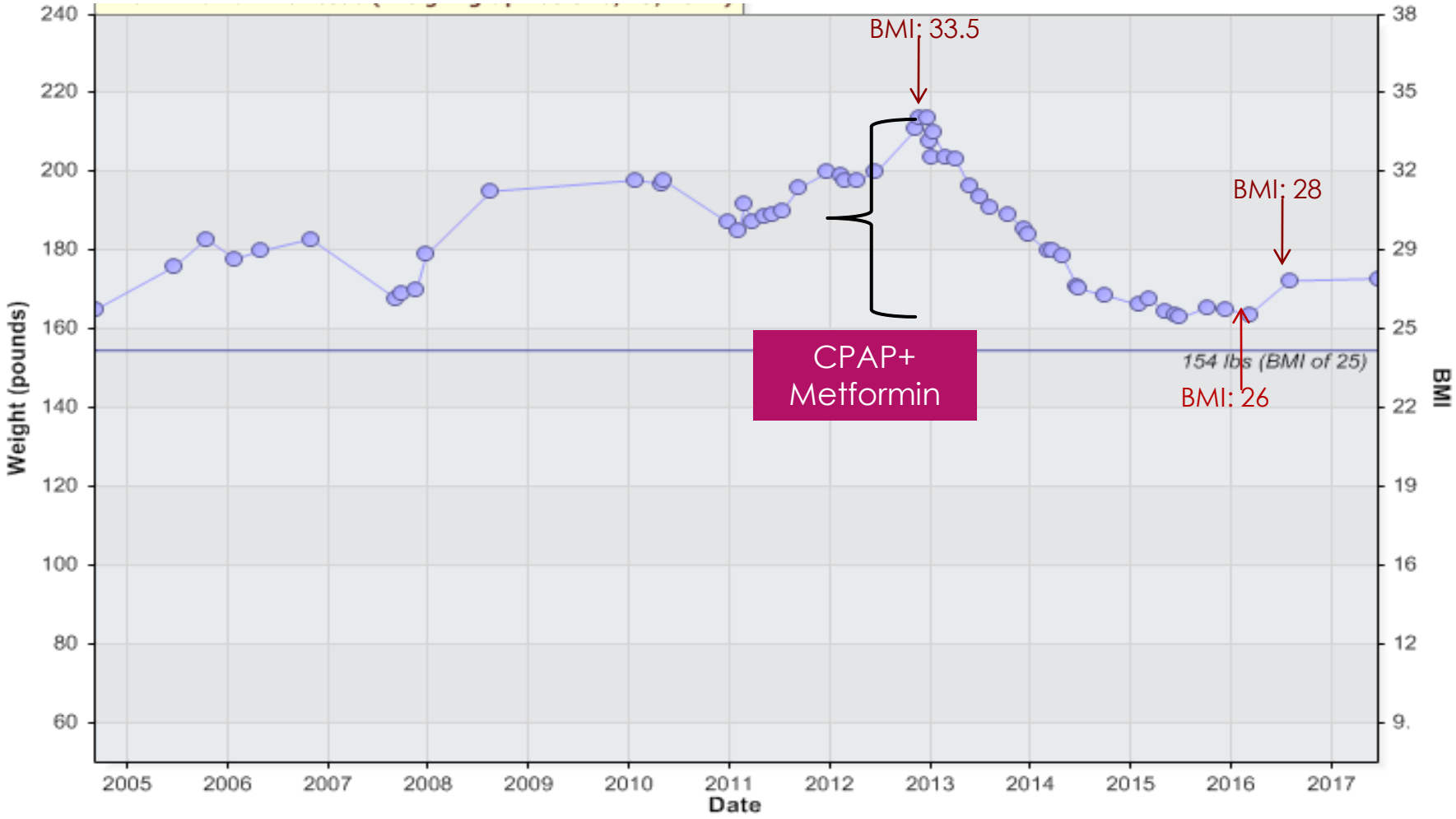
RYGB

Phentermine +Topiramate

Case #3

- 46-year-old woman
- Past medical history:
  - Hypertension
  - Anxiety/ Depression
  - Asthma
  - Fibromyalgia
  - Bipolar disorder
  - Gastroesophageal reflux disease
  - Metabolic syndrome X
- History of being on several weight promoting: Ziprasidone, Quetiapine, Duloxetine, Citalopram, Fluoxetine, Zolpidem, Trazodone, Atenolol, Pregablin, and Nortriptyline
- Postpartum weight retention of 20 pounds
- Poor sleep- daytime hypersomnolence, snoring, morning headache

46-year-old woman



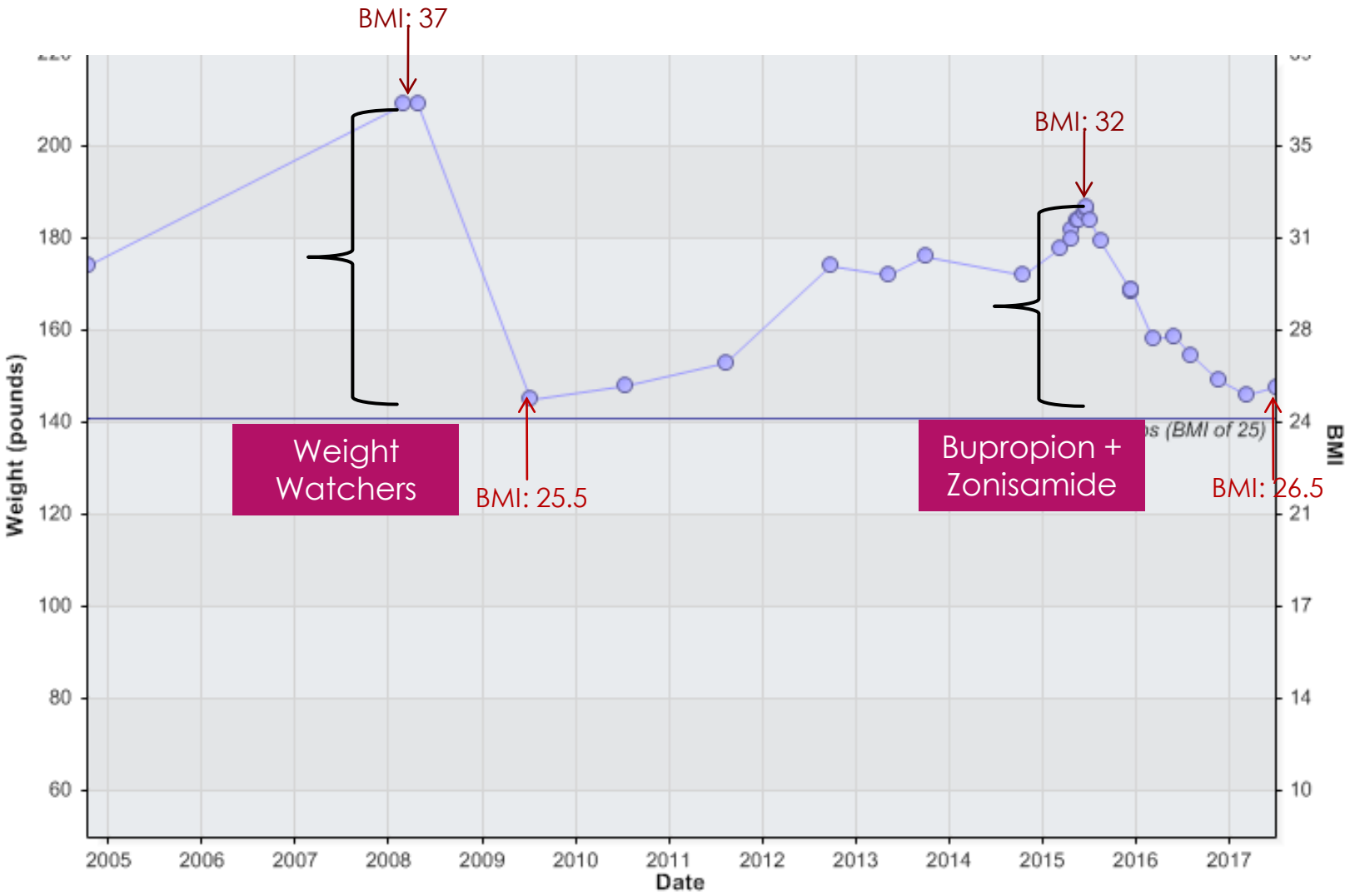
Ann Pharmacother. 2010 Apr;44(4):668-79

Am J Psychiatry. 2013 Sep;170(9):947-52.

Case #4

- 34-year-old woman
- Past medical history:
  - Migraine headaches
  - Asthma
  - Hypothyroidism
  - Depression
  - Generalized Anxiety Disorder (GAD)
  - Anorexia Nervosa
  - Gastroesophageal reflux disease
  - Chondromalacia of the knee
  - Vitamin D deficiency
  - Suicidal ideation
- History of being on fluoxetine for depression

34-year-old woman



J Clin Psychiatry. 2007 Aug;68(8):1226-9.

Case #5

- 60 year old man

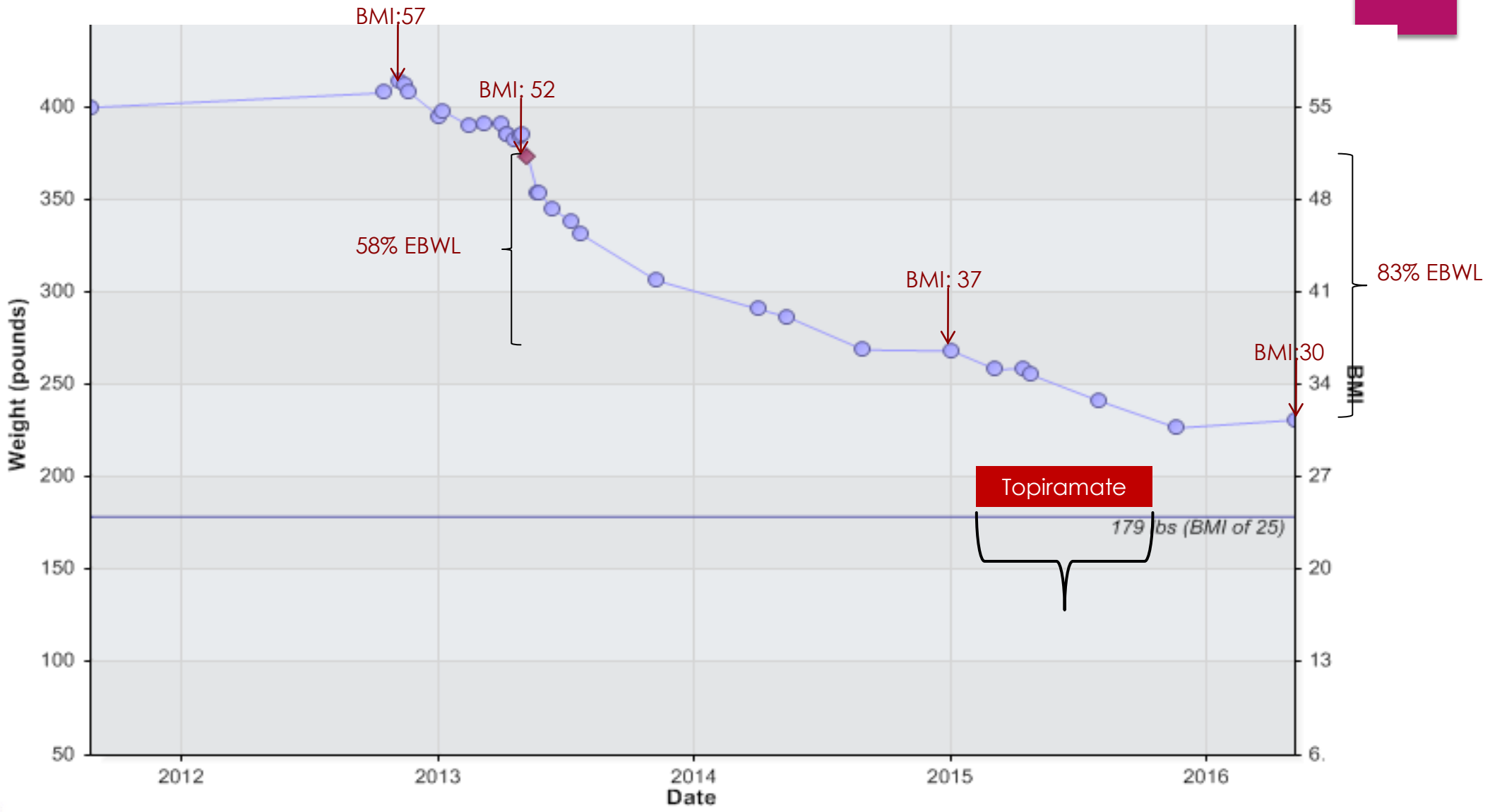
Past medical history:

- Hypertension
- Type 2 Diabetes Mellitus
- Dyslipidemia
- Hypogonadism
- Depression

Diet : Breakfast: Fiber one bar (or 2), OR Bagel with cream cheese
Snack: Denies
Lunch: Chicken Salad Sandwich (1/2), or Chicken Caesar Salad, or 1 Hot Dog, or 1 slice of Pizza
Snack: Denies
Dinner: Chicken, Vegetables, Salad, Or Roast Beef/ Steak, Bread
Eliminated: Rice and Pasta

Exercise: Walking (1.5 hours daily) (40-45 min- afternoon, push-ups and bicep curls)

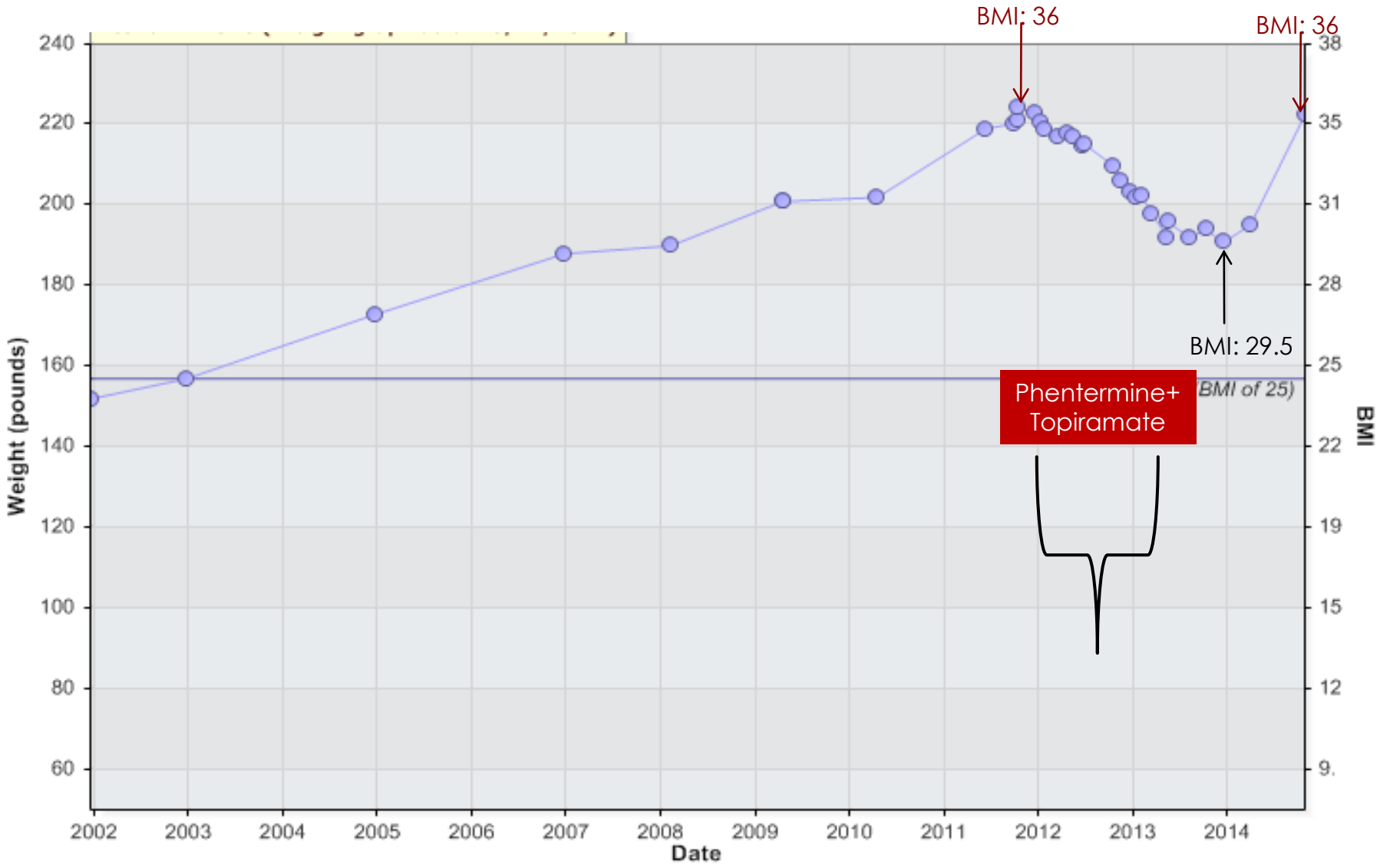
60-Year-Old Man s/p VSG



Case #6

- 36-year-old woman
- Past medical history:
  - Hypothyroidism
  - Dysthymia
  - Allergic Rhinitis
  - Chronic Back Pain
  - Migraine Headaches
- Diet:
  - Breakfast: Oatmeal and Egg Whites
  - Lunch: Salad with Chicken
  - Snack: Fruit (Less Recently)
  - Dinner: Fruit, Chicken, Rice, Broccoli, Increase in Plant Based Protein
- Activity: Cardio at gym- 5 days per week (elliptical)-1 hour; Walks at lunch time (45 minutes); strength training with 3 times per week- 1 hour
- Sleep: 6-7 hours per night of restful sleep

36-year-old woman



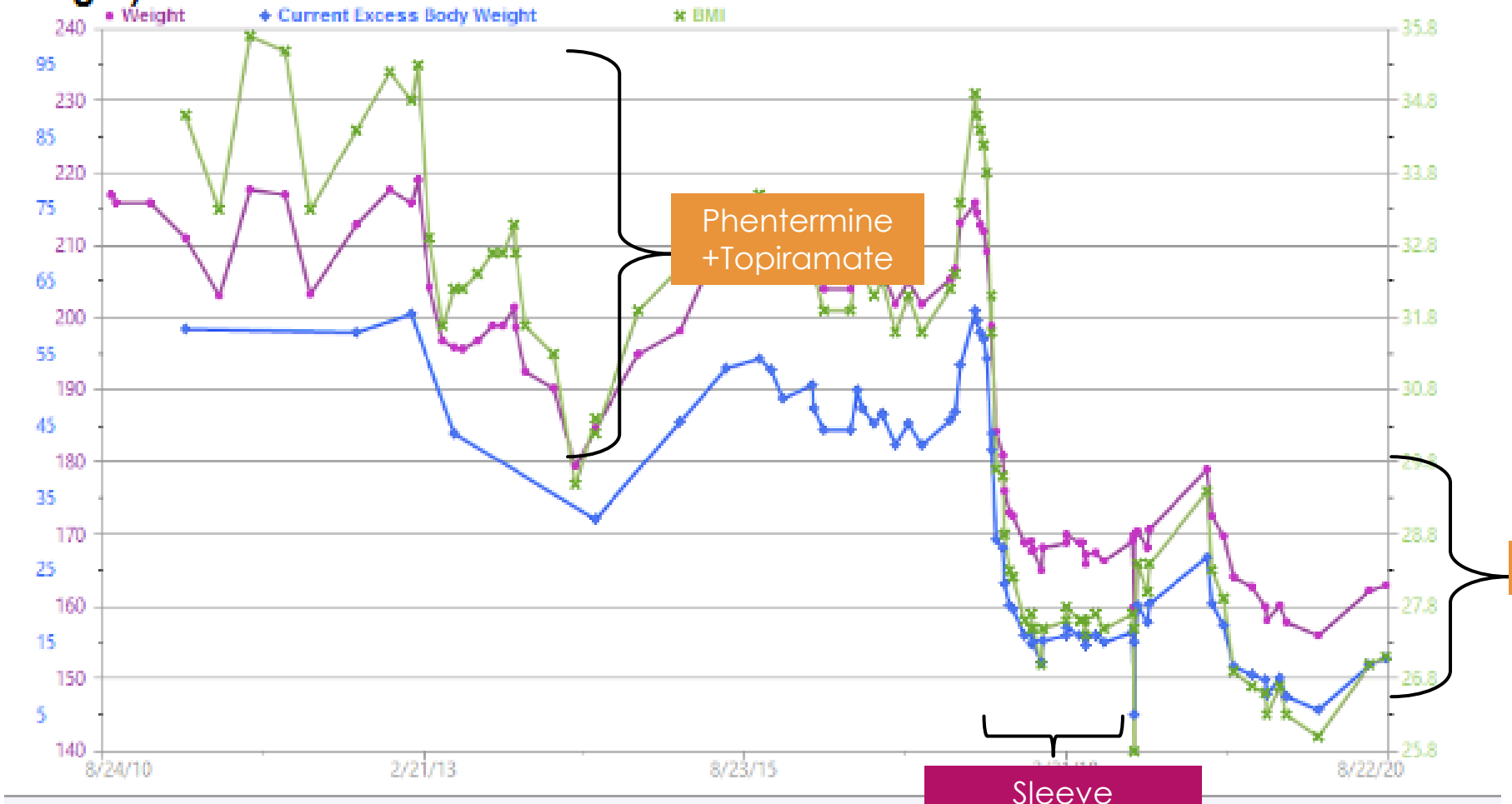
Case #7

- 64-year-old man
- Past medical history:
  - Type 2 Diabetes Mellitus
  - Male hypogonadism
  - Vitamin D deficiency
  - Obstructive sleep apnea on CPAP
  - Dyslipidemia
  - Hypertensive disorder
  - Steatosis of liver
- Hunger: Normal to high on topiramate; liraglutide
- Satiety: Fills Quickly
- Physical Activity: Peloton- 3-4 times per week (45 minutes)
- Sleep: 7 hours on CPAP
- Stress: Normal

64-year-old man

At this time, he has lost 92.2% of his excess body weight and 22.4% of his total body weight

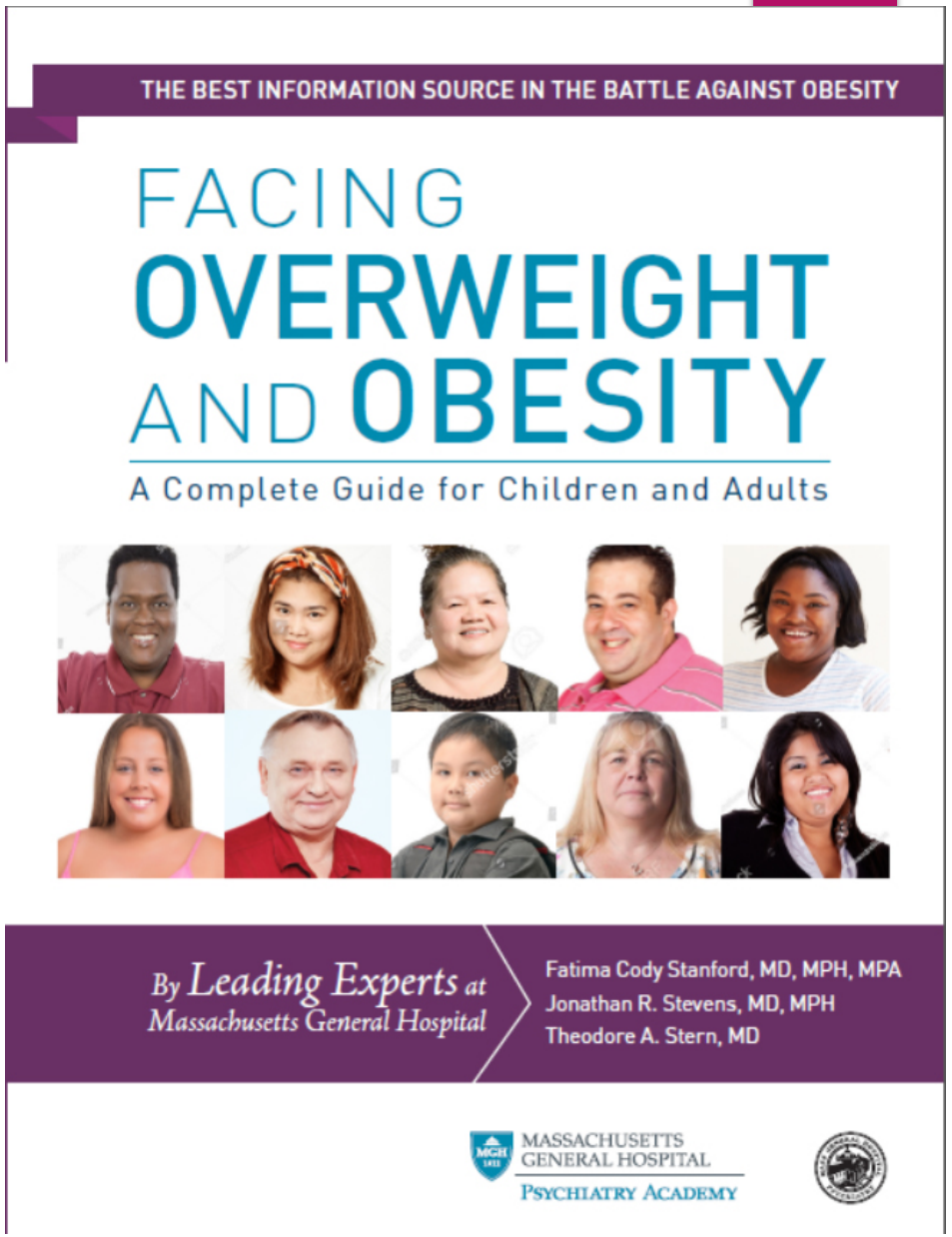
(NADIR post op: Lost 81.5% of his excess body weight and 20.4% of his total body weight)



Take Home Points

- Track weight loss progress in terms of excess body weight and total body weight at each visit.
- Listen to patient cues about hunger, satiety, and side effects to drive weight management.
- Continue to encourage healthy lifestyle behaviors as weight loss medications should serve an adjunct to these.
- If a patient has a superior response to medication (5-10% of total body weight loss), continue medications indefinitely.
- Advise women of childbearing age about discontinuing medication prior to conception.

Reference for Physicians and Patients



Thank You For Your Time

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