Obesity

St. Vincent's Hospital, Birmingham AL

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60 min

Presenter Disclosure Information

Name of Presenter: W. Timothy Garvey, MD

Research Support: (institutionally sponsored) Sanofi, Novo Nordisk, Pfizer

Board Member/Advisory Panel: Novo Nordisk, American Medical Group Association, BOYDSense, Gilead, Amgen, Boehringer-Ingelheim

Stock/Shareholder: (publicly traded) Eli Lilly, Pfizer, Novartis, Merck, Ionis, Bristol-Myers-Squibb, Affymetrix

55 yr old Caucasian female with obesity, hypertension, and dyslipidemia who seeks out your care after being told her fasting glucose was elevated.

Medical History

1. HTN – Captopril 75 mg daily; Amlodipine 10 mg daily
2. Hypercholesterolemia – Atorvastatin, 40 mg daily
3. Depression – Desipramine, 200 mg daily

Review of Systems

1. Shortness of breath on exertion, knee pain, foot pain

Social and Family History:

1. Single
2. Non smoker, 1 to 2 alcoholic beverages/week
3. Family History positive for diabetes in mother, grandmother, and 2 uncles. Father with MI age 56

Evaluation

Exam
BMI 40.2 kg/m^2 – 220 lbs and height 62 inches
Blood pressure 144/91

Laboratory
Fasting glucose 118 mg/dl, HbA1c 6.3%
Lipids (mg/dL): TC 230; LDL-c 135; HDL-c 42; TG 194

Weight History
In high school, she weighed 105 lbs. She lost her fiancé to an auto accident when she was 20. At this point she quit exercising, started overeating, and started showing signs of depression. At 30, her weight was 170 lbs. In her early 50s, she had failed to achieve weight loss in Weight Watchers due to an inability to change her lifestyle.

Which of the following is the most appropriate next step?

a. Begin metformin 2,000 mg/day
b. Initiate a Very Low Calorie Diet (VLCD) with meal replacements (shakes & bars) together with a plan for increased physical activity.
c. Place on Mediterranean diet and increase exercise
d. Structured lifestyle intervention with reduced calorie meal plan and liraglutide 3 mg/day.
e. Consider bariatric surgery

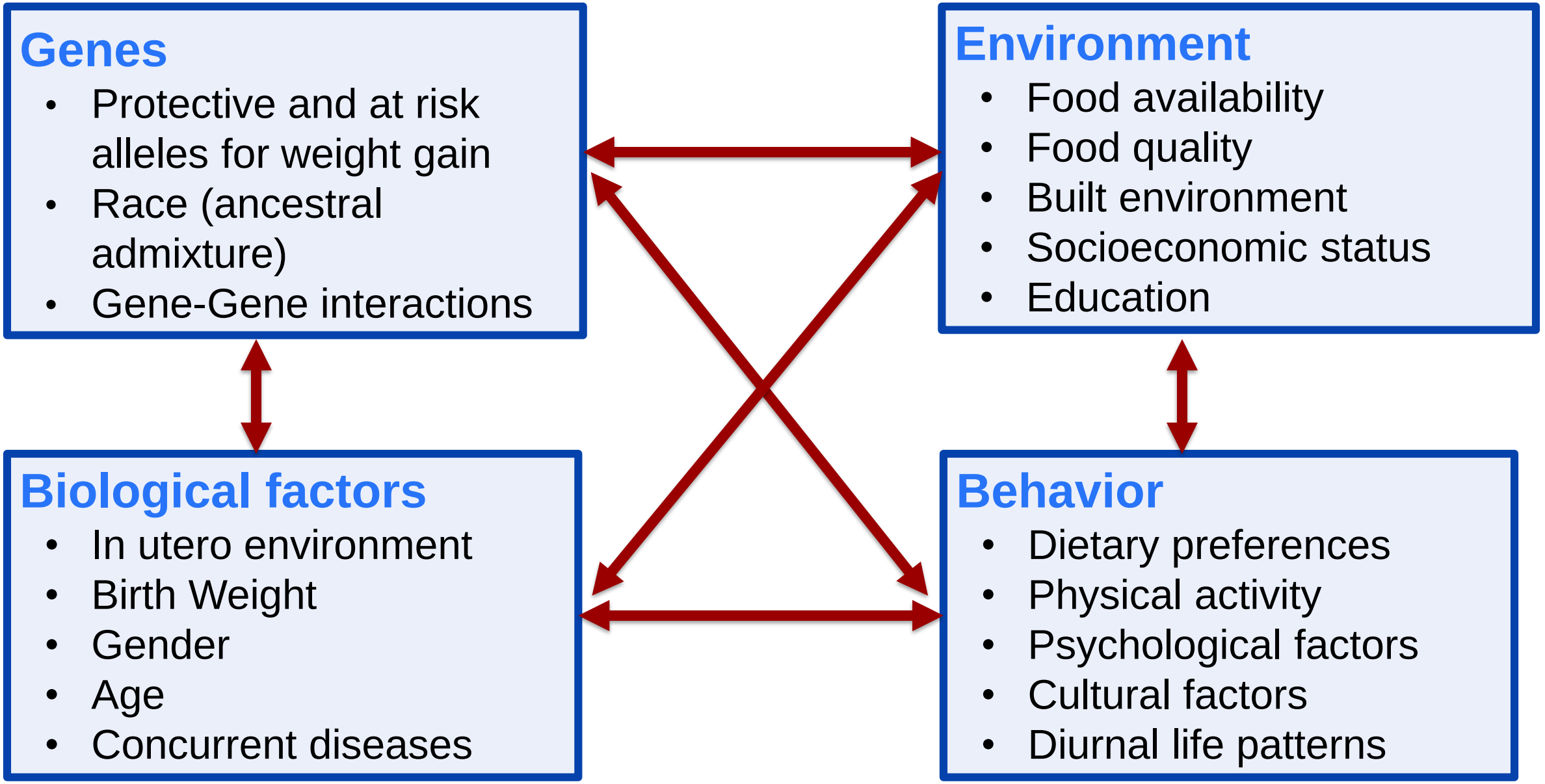
Obesity is a Disease: American Association of Clinical Endocrinologists Position Statement[1]

The American Medical Association designates obesity as a disease.

June 18, 2013, AMA House of Delegates

[1] Mechanick JI, Garber AJ, Handelsman Y, Garvey WT. *Endocr Pract*. 2012;18:642-8.

Determinants of Body Weight



Obesity is a chronic disease

that involves interactions among genetic, environmental, and behavioral factors

1. **Characteristic signs or symptoms**
   - ✓ **BMI**
2. **Impairment in the normal functioning of some aspect of the body**
   - ✓ **satiety hormone regulation of energy intake;**
   - ✓ **adipose tissue dysfunction**
3. **Results in harm or morbidity**
   - ✓ **cardiometabolic and biomechanical complications**

Criteria established by the American Medical Association (AMA), Report 4 of the Council on Scientific Affairs (A-05). Recommendations for Physician and Community Collaboration on the Management of Obesity (Resolution 421, A-04), 2005

Mechanick JI, Garber AJ, Handelsman Y, Garvey WT. *Endocr Pract*. 2012;18:642-8.

Assessing Weight: BMI and Waist Circumference

BMI = weight (kg)/height (m^2)*	
Normal weight	BMI 18.5-24.9
Overweight	BMI 25.0-29.9
Obesity class 1	BMI 30.0-34.9
Obesity class 2	BMI 35.0-39.9
Obesity class 3 (extreme)	BMI ≥40.0

Waist Circumference (Increase Risk)

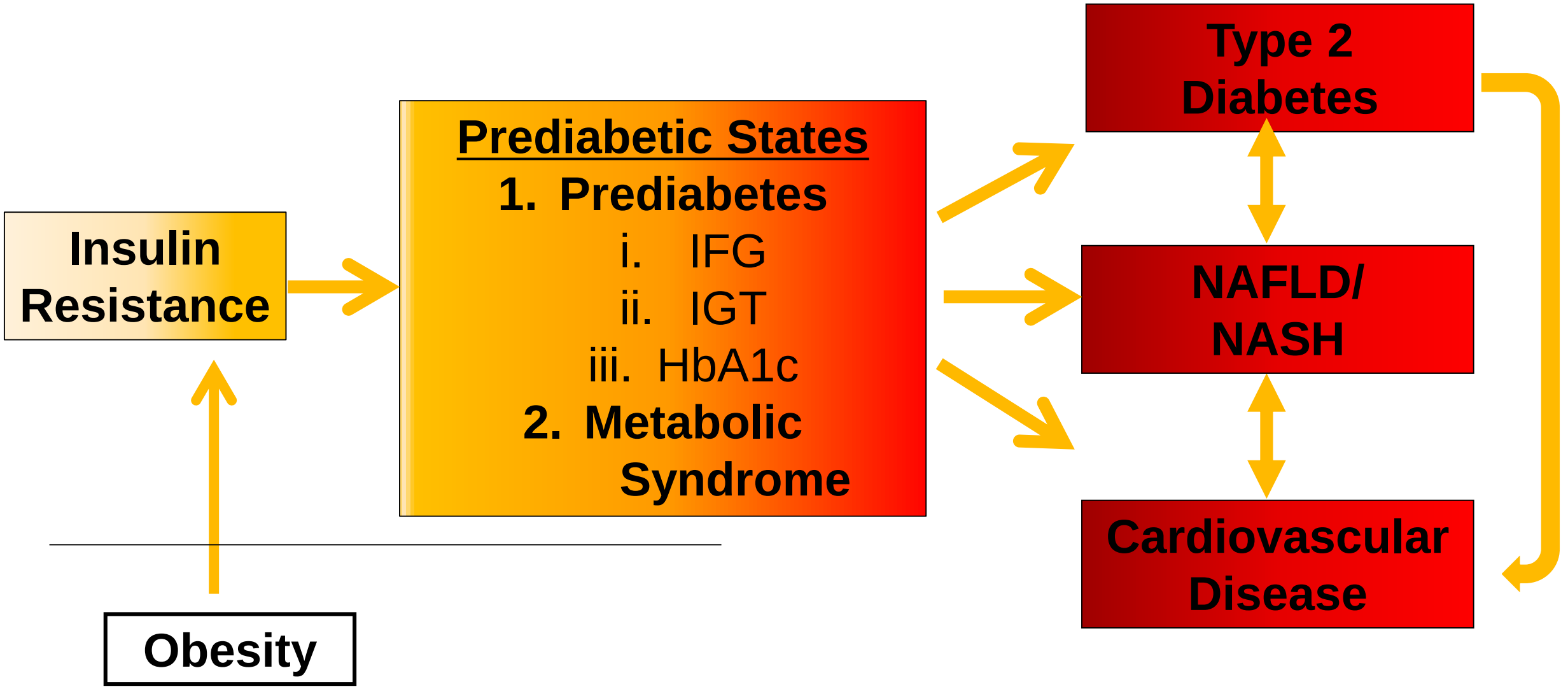
Men
>102 cm (40 in.)

Women
>88 cm (35 in.)

*World Health Organization defines overweight as BMI ≥25 kg/m^2 and obese as BMI ≥30 kg/m^2.

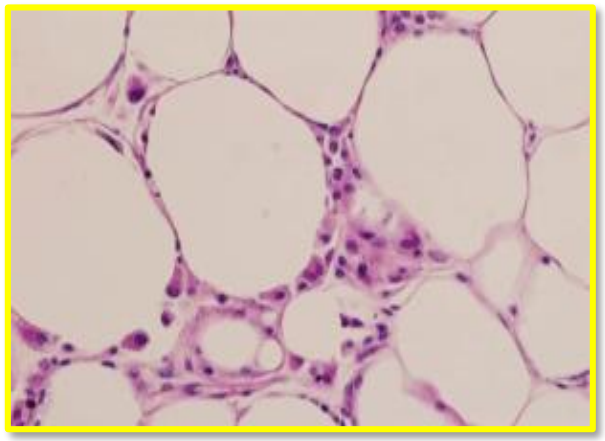
http://www.who.int/mediacentre/factsheets/fs311/en/. Accessed August 20, 2015.

The Spectrum of Cardiometabolic Disease



Abnormal Adipose Tissue Function in Obesity Pathogenesis of Cardiometabolic Disease

Adipose Tissue Inflammation



Ventral Adiposity

Dysregulated Secretion of Adipocyte Factors

Lipoproteins:
DYSLIPIDEMIA
- Increased large VLDL
- Increased small LDL
- Increased LDL particles
- Decreased large HDL

Blood Vessel:
ENDOTHELIAL DYSFUNCTION
- Vascular Reactivity
- Dysfibrinolysis
- Inflammation
- Foam Cell
- Hypertension

Muscle:
INSULIN RESISTANCE
- Glucose Intolerance

Secreted Adipocyte Factors

Insulin Resistance/Adipocyte Size

- Free Fatty Acids
- Leptin
- Adiponectin
- Resistin

Vascular Reactivity

- Free Fatty Acids
- Angiotensinogen (RAAS)
- Inflammation

Dysfibrinolysis

- PAI-1
- Platelet reactivity

Lipids/Lipoproteins

- Acylation Stimulation Protein
- Cholesterol Ester Transfer Protein
- Phospholipid Transfer Protein

Inflammation

- TNF alpha
- IL-1, IL-6, IL-8, IL-10
- MCP-1
- MIF

RAAS, renin–angiotensin–aldosterone system; TNF, tumor necrosis factor; IL, interleukin; MCP-1, monocyte chemotactic protein-1; MIF, macrophage migration inhibiting factor.

Metabolic Syndrome Trait Cluster

- Hyperinsulinemia
- Impaired glucose tolerance
- Obesity
- Increased visceral fat
- Hypertriglyceridemia/ low HDL
- Small, dense LDL
- Hypertension
- Positive family history
- Dysfibrinolysis (high PAI-1)
- Vascular reactivity/ endothelial dysfunction
- Inflammation
- Microalbuminuria
- Polycystic ovary syndrome
- NAFLD

HDL, high-density lipoprotein; LDL, low-density lipoprotein; PAI-1, plasminogen activator inhibitor-1; NAFLD, non-alcoholic fatty liver disease.

Environment

Genetics

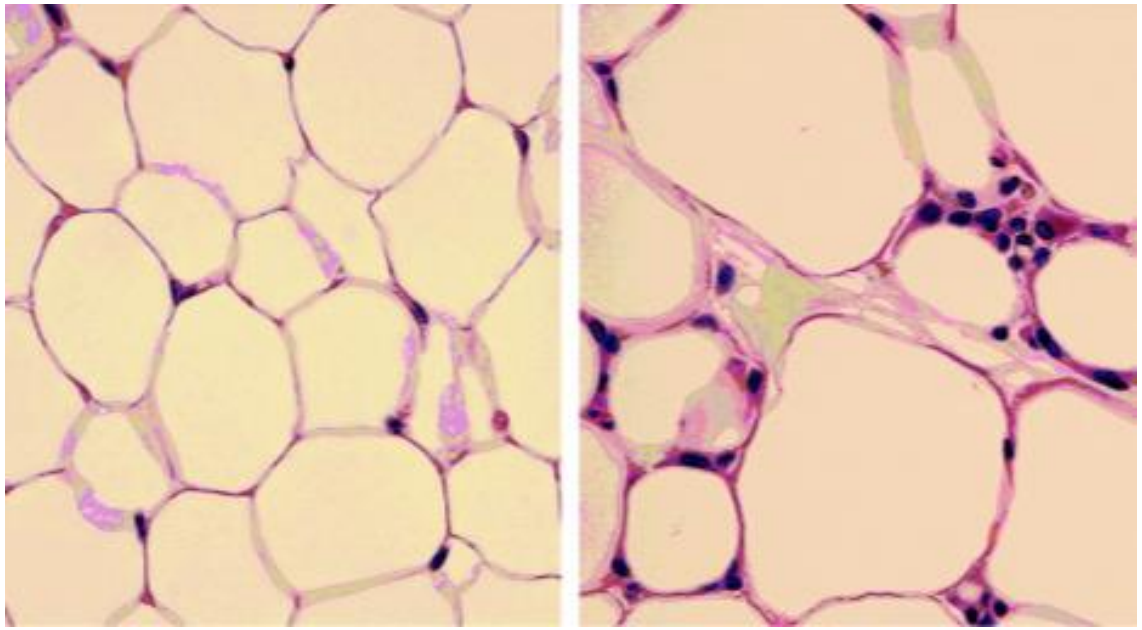
↑Energy Intake

↓Energy Expenditure

Excess fat storage

INSULIN SENSITIVE
increased fat mass

INSULIN RESISTANT
Inflammation in Fat



Osteo-arthritis

Sleep Apnea

Disability

GERD

Urinary Incontinence

Diabetes

Metabolic Syndrome

Prediabetes

NAFLD

HTN

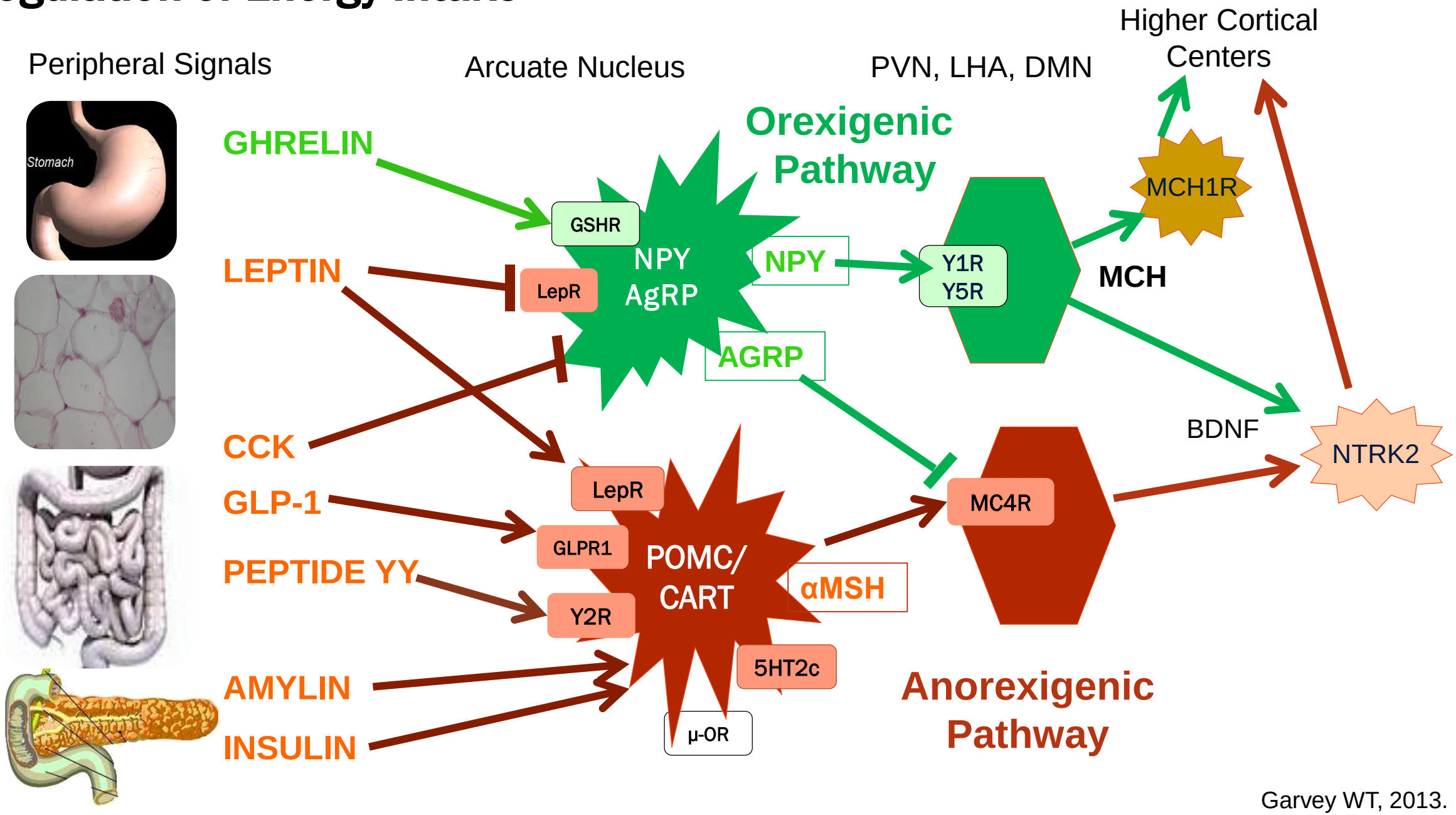
CVD

BIOMECHANICAL Complications

CARDIOMETABOLIC Complications

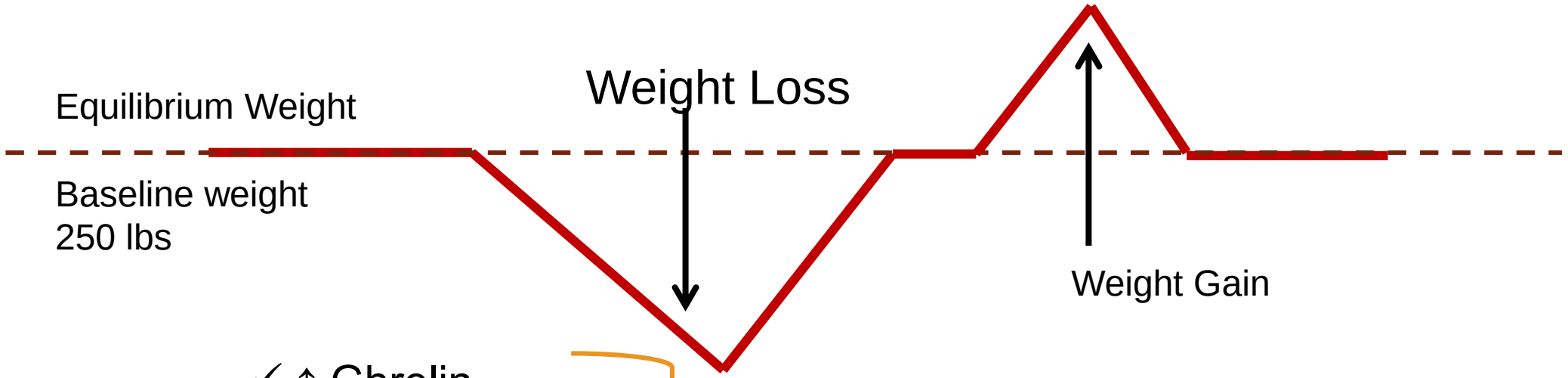
Adapted from Bray GA. *Obesity (Silver Spring)*. 2013;21:893-9.
Domenica M. Rubino, MD.

Regulation of Energy Intake



Garvey WT, 2013.

In Obesity, maladaptive responses protect against weight loss and maintain a high body weight



- ✓ ↑ Ghrelin
- ✓ ↓ Leptin, PYY, CCK, Amylin

→ Increased Appetite

- ✓ ↓ Resting energy expenditure

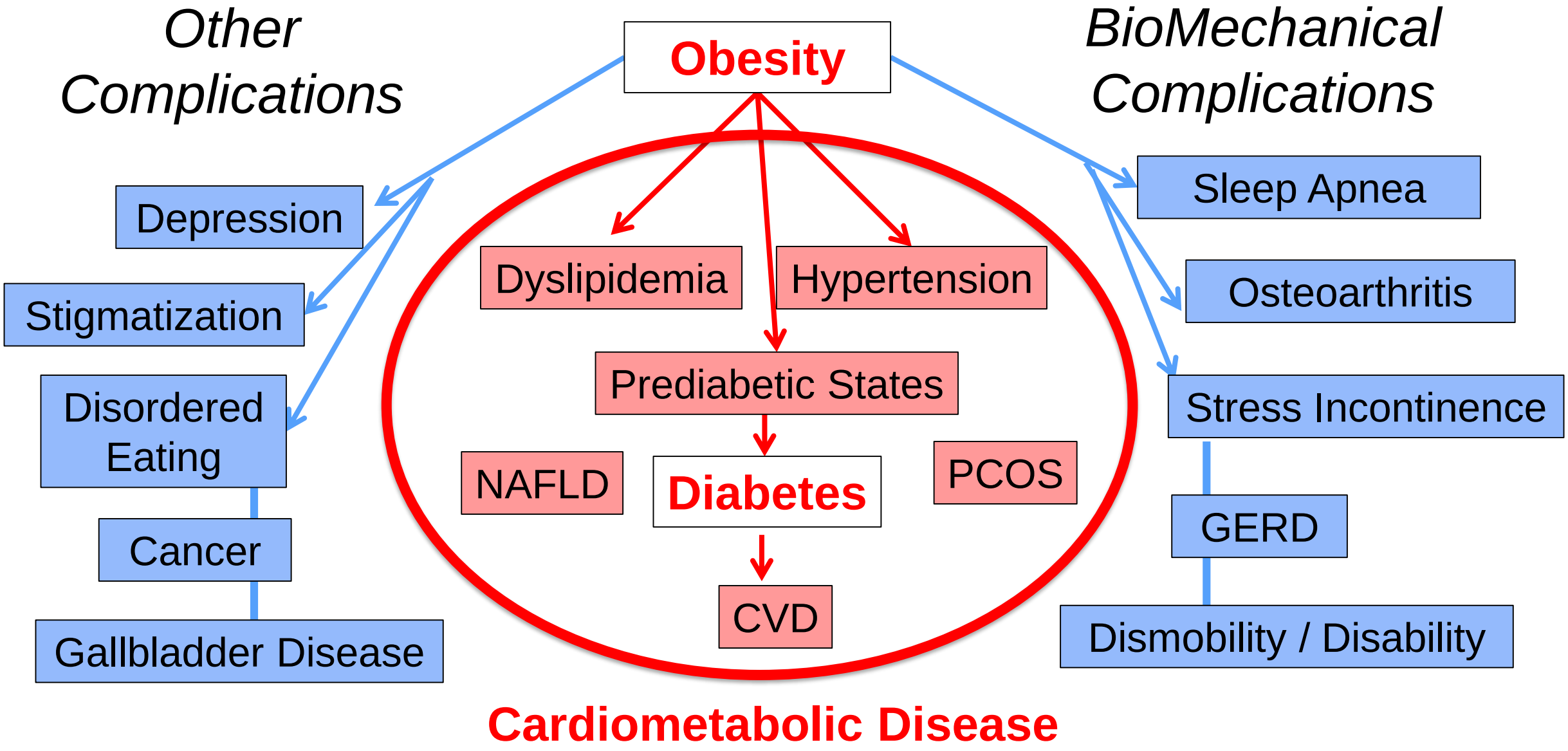
→ Decreased Energy Out

- ✓ ↑ Hunger
- ✓ ↑ Calorie-dense food preferences

→ Increased Energy In

Garvey WT, 2014

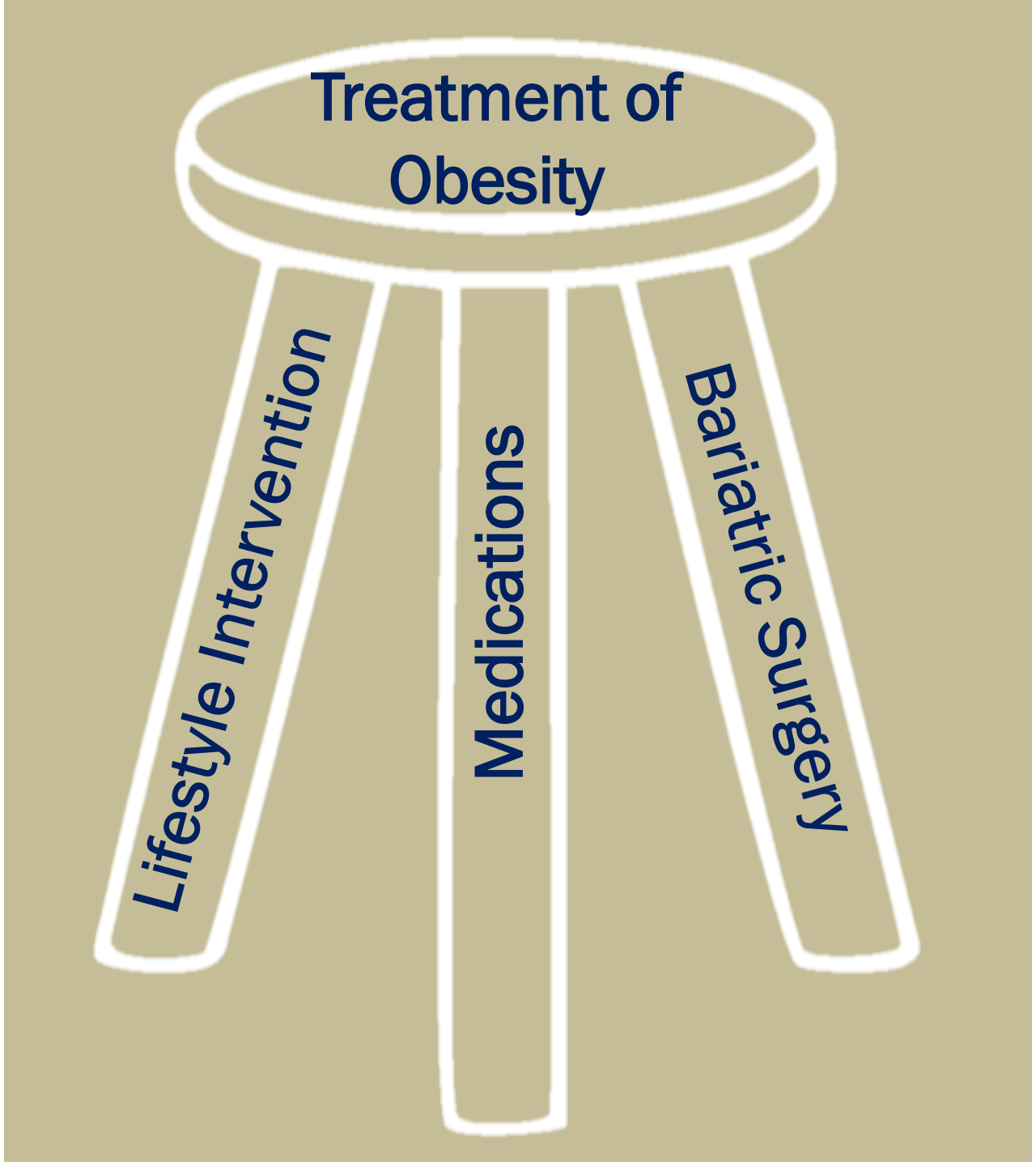
Medical Complications of Obesity



Daniel S, Soleymani T, Garvey WT. Curr Opin Endocrinol Diabetes Obes, 20:377-388, 2013

Obesity is a Disease in which Disordered Regulation of Caloric Intake Results in High Levels of Adiposity.
High Levels of Adiposity Impair Health via Weight-Related Complications.

Tools for Care of Patients with Obesity



Lifestyle Therapy for Obesity Management

- Healthy meal plan (low-fat, low-CHO, DASH, Mediterranean, vegetarian, etc)
  - Reduce energy intake by 500-1,000 kcal/d
  - Reduce portion size
  - Meal replacements
- Physical Activity
  - ≥150 min/wk (DPP)
  - Aerobic plus resistance exercise
  - BUT, anything is better than nothing
- Behavioral interventions: record food intake, physical activity, and weight; education, psychological factors, motivational interviewing

Diabetes Prevention Program Research Group. *N Engl J Med*. 2002;346:393-403. Look AHEAD Research Group. *Obesity*. 2006;14:737-752.

Garvey WT et al. AACE Obesity Guidelines. Endocrine Practice 22(Suppl 3):1-203, 2016

Intensification of Lifestyle Therapies to Achieve Weight Loss Goals

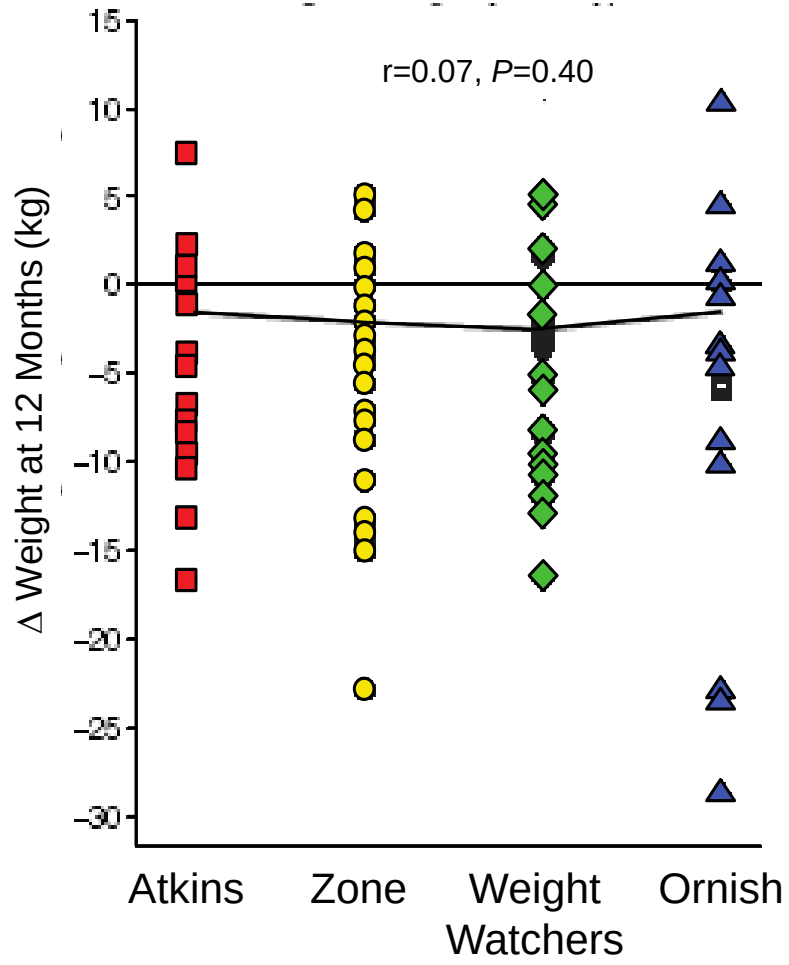
Lifestyle Therapy

- Simple advice to lose weight in doctor's office
- Internet programs or self-help books
- Dietitian
- Structured programs
- (Weight Watchers, YMCA, tele-
- communication)
- Multidisciplinary structured programs
- Physician-driven individualized structured programs

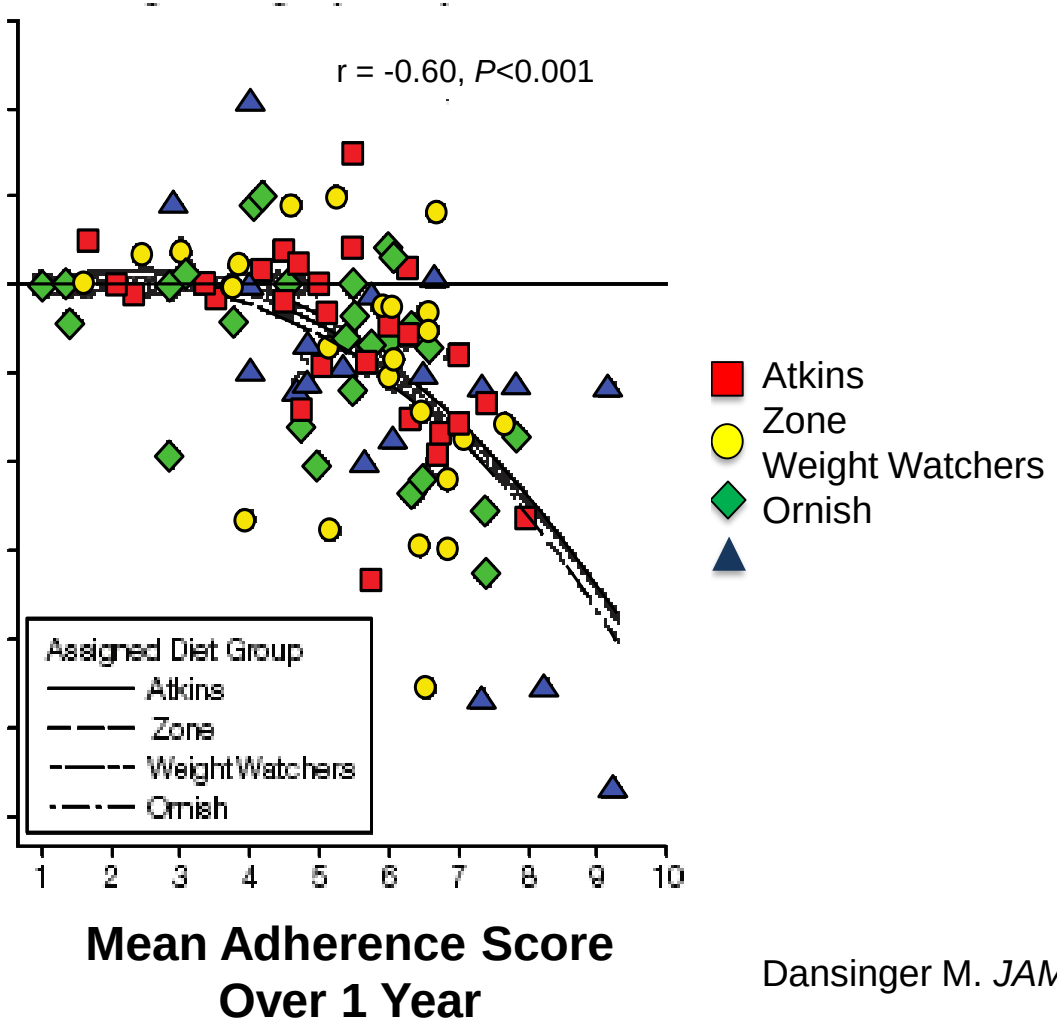
Impart skills and behavior change to induce and maintain weight loss

Adherence Is More Important Than Diet Type for Weight Loss Success

Weight Change by Diet Type



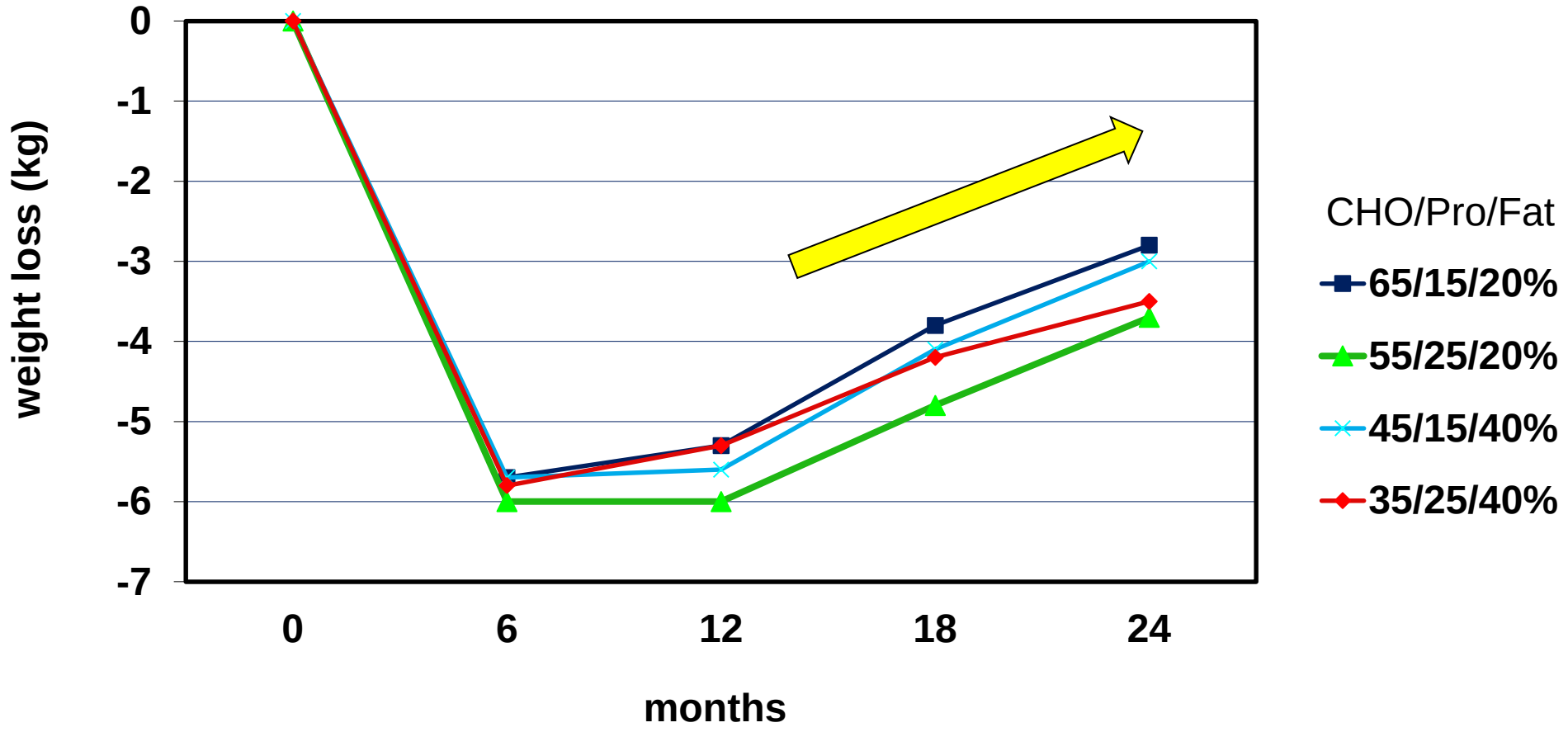
Weight Change by Dietary Adherence



Dansinger M. *JAMA*. 2005;293:43-53.

Remember the Pathophysiology of Obesity: mechanisms protecting against weight loss

It is difficult for patients to maintain their weight loss over time.



Sacks FS. et al. *NEJM* 2009;360(9) 859-873.

What do we know so far:

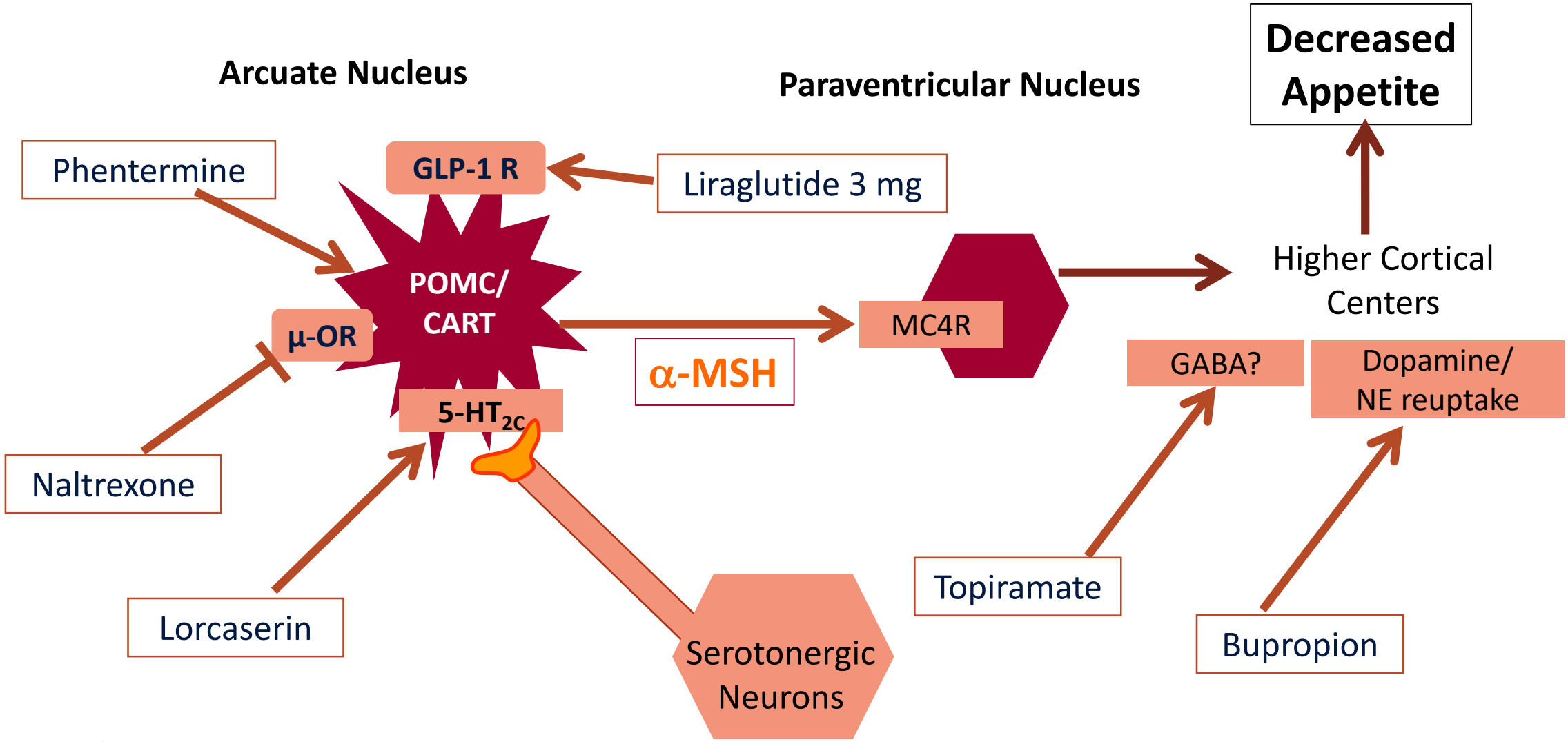
- It is difficult for patients to maintain weight loss.
  – ***Obesity protects obesity***
- They are fighting pathophysiological mechanisms at the core of obesity as a disease.
- Body weight is not a cognitive function.
- Patients need our help:
  - evidenced based approaches to medical care;
  - comprehensive, structured, individualized, lifestyle therapy programs;
  - health care professionals that get it:
  - ➡ medications that counteract pathophysiology.

Obesity Pharmacotherapy

Agents	Action	Approval
Previously available		
Phentermine	• Sympathomimetic	• 1959
Orlistat	• GI lipase inhibitor	• 1997
Recently Approved		
Phentermine/ Topiramate ER	• Sympathomimetic/Anticonvulsant (GABA receptor modulation?)	• Approved, Summer 2012
Lorcaserin	• 5-HT_{2C} serotonin receptor agonist	• Approved, Summer 2012
Naltrexone ER/ Bupropion ER	• Dopamine/noradrenaline reuptake inhibitor/Opioid receptor antagonist	• Approved, September 2014
Liraglutide 3 mg	• GLP-1 receptor agonist	• Approved, December 2014

US FDA. Drugs@FDA. http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA.

Actions of Recently Approved Weight-Loss Medications



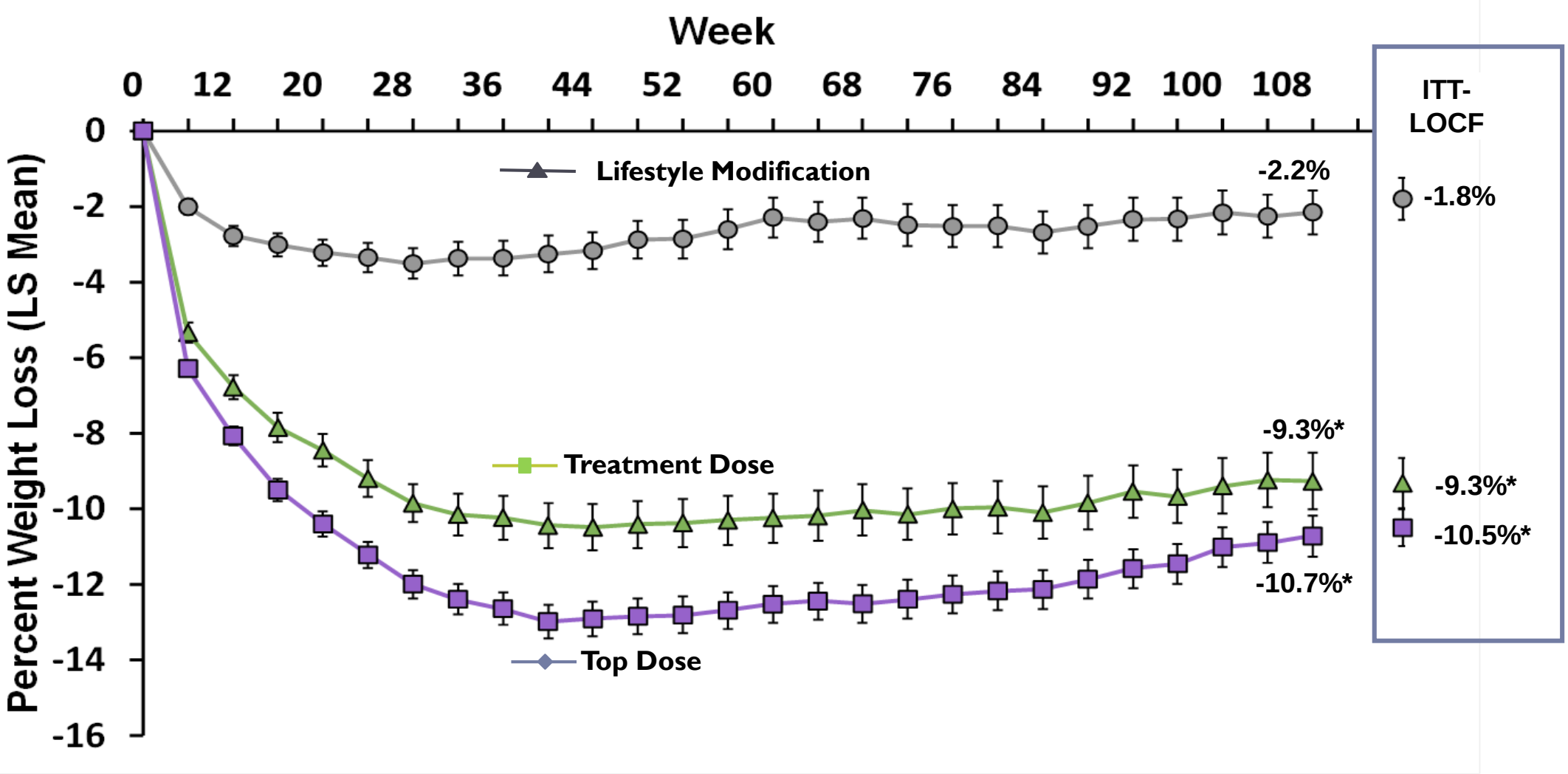
MC4R, melanocortin 4 receptor.
GABA, gamma-aminobutyric acid.
POMC/CART, pro-opiomelanocortin/cocaine- and-amphetamine-regulated transcript.

Courtesy of Dr. W. Timothy Garvey, 2014.

Important Aspects of Obesity Pharmacotherapy

1. Use as an adjunct to a lifestyle intervention program if BMI ≥30 or 27-29.9 with at leas one complication.
2. AACE, AHA/ACC/TOS, and OMA Obesity Guidelines all advise use of medications for patients who have sufficient health risk, not for cosmetic reasons.
3. Addition of a weight-loss medication consistently achieves greater weight loss than that achieved by the lifestyle intervention alone, and helps sustain weight loss for a longer period of time.
4. Therapeutic efficacy is lost once the medication is discontinued. Obesity is a life-long disease and requires long-term treatment and follow-up.
5. There is a large individual variation in the degree of weight loss with any intervention

Phentermine/Topiramate ER and the SEQUEL STUDY: Weight Loss Over 2 Years in Completers

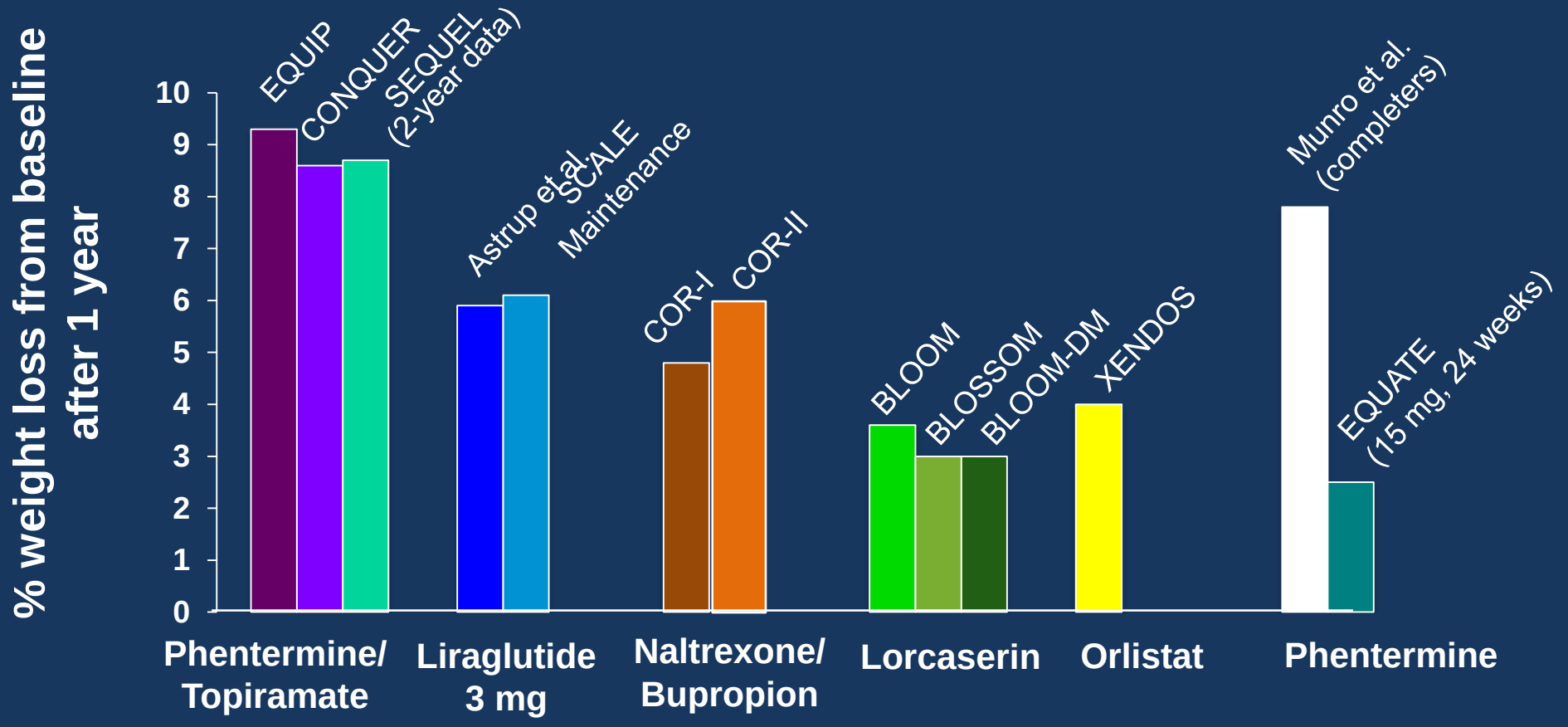


*P<0.0001 vs placebo

Garvey WT, et al. *Am J Clin Nutr*. 2012;95(2):297-308 2012

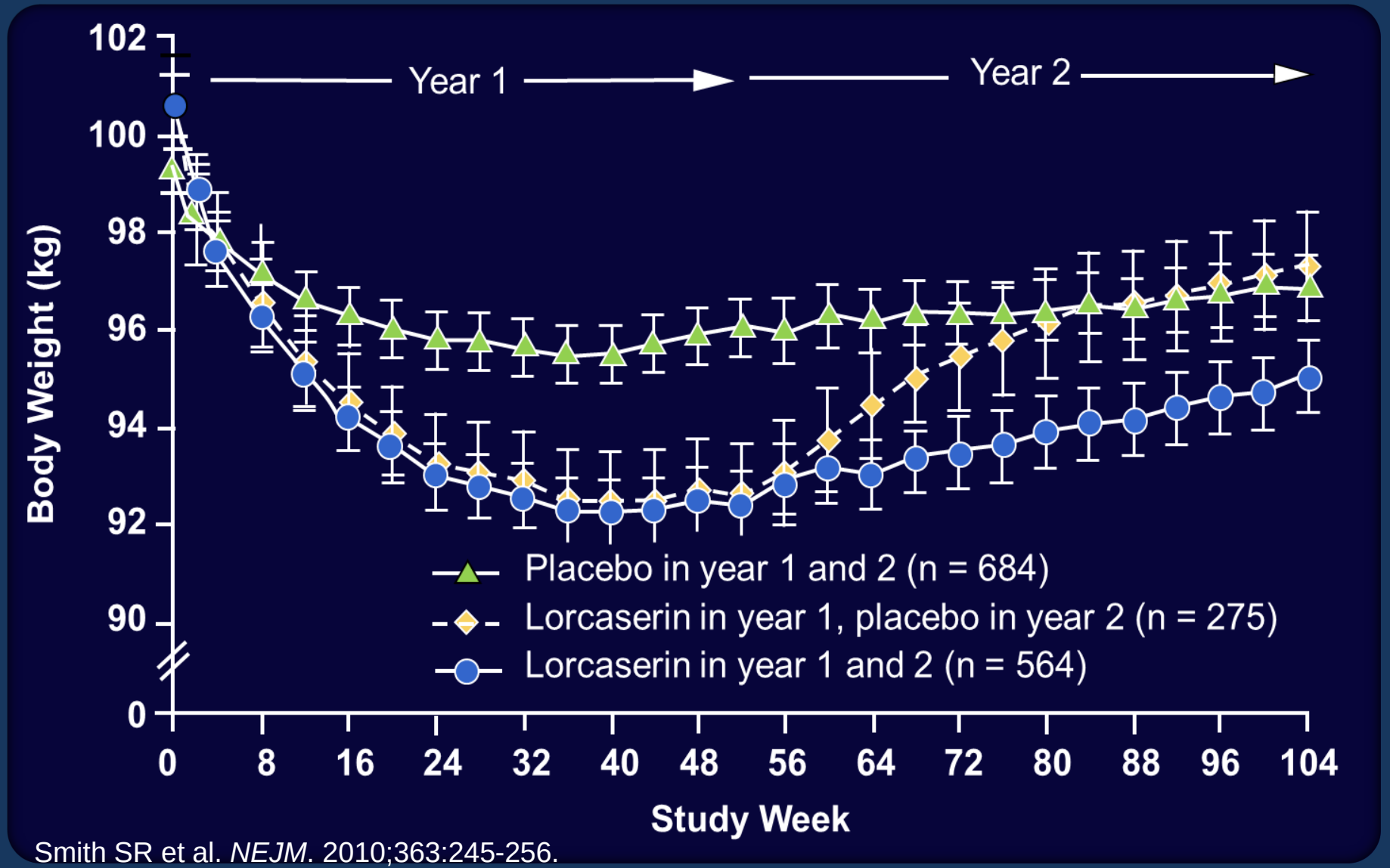
Comparative Efficacy of Weight-Loss Medications

All data placebo-subtracted, maximal dose, ITT-LOCF, 1 year, unless otherwise indicated



Garvey WT. *Endocr Pract*. 2013;19(5):864-874. Sep 6:1–31. Wadden TA et al. *Int J Obes (Lond)*. 2013;37(11):1443-1451.

Lorcaserin 10 mg bid: BLOOM Study Weight Change Over Two Years



Smith SR et al. *NEJM*. 2010;363:245-256.

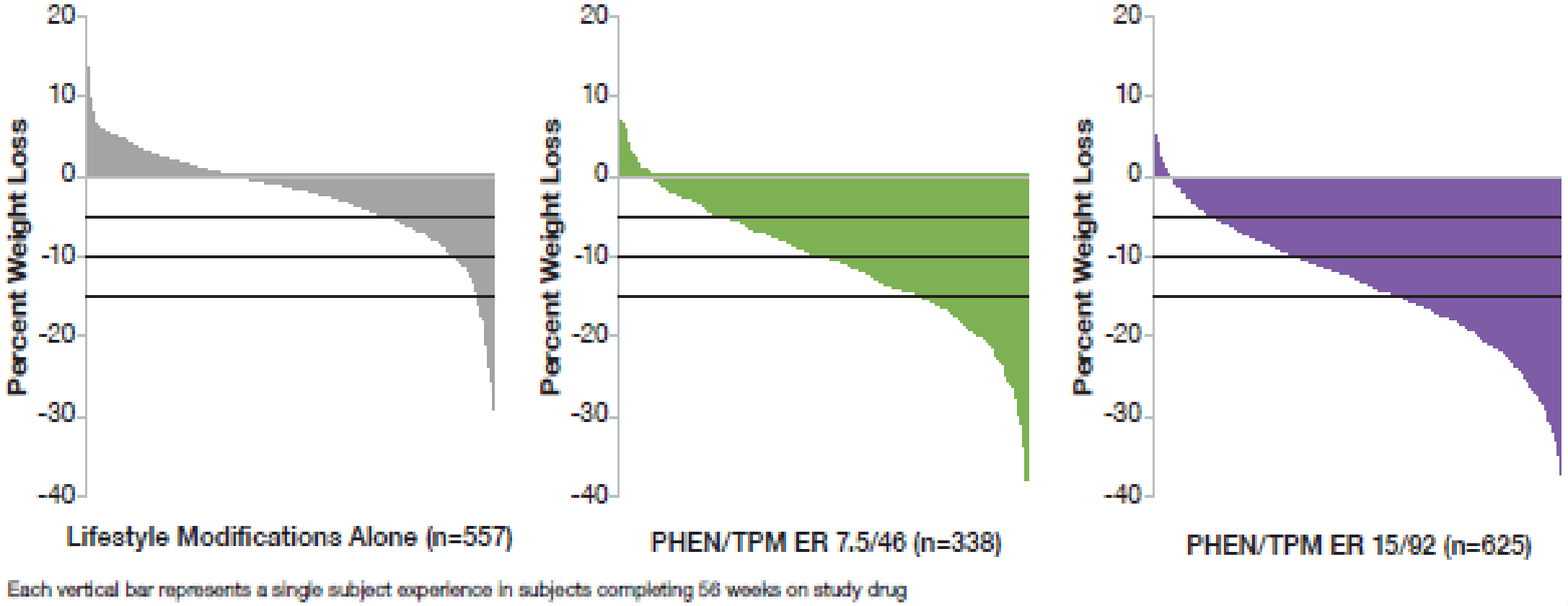
Effects of Obesity Medicines on Risk Factors:
Phentermine/Topiramate ER CONQUER Study

Variable		Phentermine/ Topiramate ER 7.5/46 mg	Placebo	*P* value
Waist (cm)	↓	-7.6	-2.4	<0.0001
Systolic BP (mm Hg)	↓	-4.7	-2.4	0.0008
Diastolic BP (mm Hg)		-3.4	-2.7	0.1281
Triglycerides (%)	↓	-8.6	4.7	<0.0001
LDL–C (%)		-3.7	-4.1	0.7391
HDL–C (%)	↑	5.2	1.2	<0.0001
CRP (mg/L)	↓	-2.49	-0.79	<0.0001
Adiponectin (µg/mL)	↑	1.40	0.33	<0.0001

Changes from baseline to week 56 in secondary endpoints

Garvey WT et al. Am J Clin Nutr. 2012;95(2):297-308.

There is a Variable Response to Weight Loss Therapy: It looks like this.



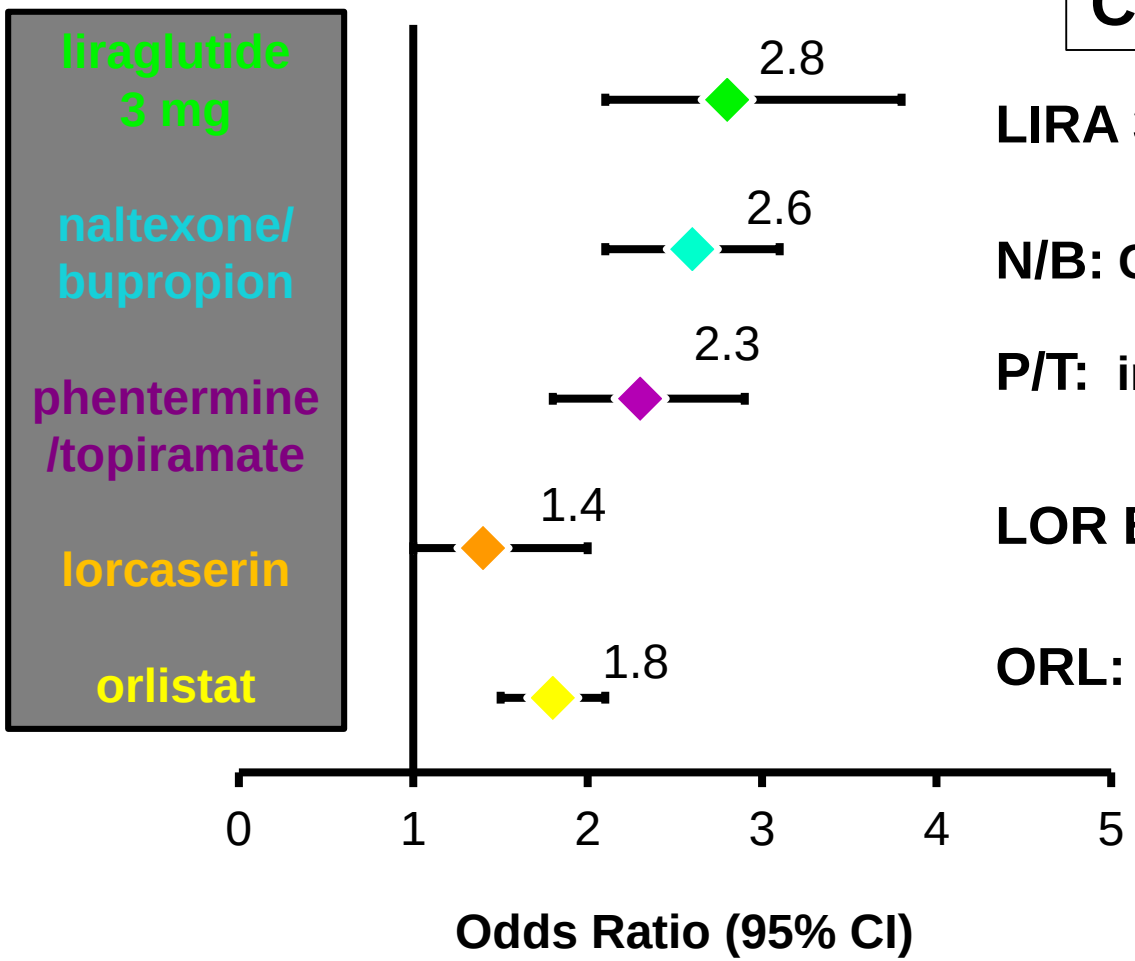
McCullough PA, et al. Poster AANP 2013.

FDA “Off-Ramp” for Obesity Pharmacotherapy

If patient has not lost at least 5 % of baseline weight by week 12 on the maintenance dose, then discontinue medication; need to alter therapy

- Lorcaserin: Begin treatment with full dose, 10 mg bid
- Naltrexone ER/bupropion ER: Begin one pill 8 mg/90 mg po q AM for week 1, then one bid for week 2, two q AM one q PM week 3, and 2 po bid week 4
- Phentermine/topiramate ER: one pill 3.75 mg/23 mg po q AM for 2 weeks, then treatment dose 7.5 mg/46 mg po q AM. If <3% weight loss at 12 weeks , proceed to top dose 15 mg/92 mg q AM
- Liraglutide 3 mg: Begin at 0.6 mg q day SQ for 1 week than increase by 0.6 mg q day each week until taking 3 mg q day

Direct Meta-Analysis: Likelihood of Discontinuation Due to Adverse Events[1]



Common Adverse Events[2-4,a]

LIRA 3.0 mg: hypoglycemia, GI AEs, headache

N/B: GI AEs, headache

P/T: insomnia, dry mouth, dizziness, distorted taste, parasthesia

LOR BID: hypoglycemia, headache, fatigue

ORL: abdominal discomfort, oily spotting/ stool, fecal urgency

[a] Selected common (defined as incidence > 5%) AEs are noted; refer to medication package inserts and cited references for complete information.

1. Khera R, et al. *JAMA*. 2016;315:2424-2434;
2. Drugs@FDA: FDA approved drug products. http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA; 3. Garvey WT, et al. *Endocr Pract*. 2016;22:842-884; 4. ADA. *Diabetes Care.* 2017;40(suppl 1):S57-S63.

Obesity Medications: Contraindications and Precautions[a]

- **Orlistat**
  - Chronic malabsorption syndrome
  - Consider fat soluble vitamins/medications
  - Cholestasis
- **Lorcaserin**
  - Concomitant SSRIs
- **Phentermine/Topiramate ER**
  - Glaucoma
  - Hyperthyroidism
  - During/within 14 days of MAOI use
  - Topiramate: fetal oral clefts (regular pregnancy testing)
- **Naltrexone ER/bupropion ER**
  - Uncontrolled hypertension
  - Seizure disorders; anorexia nervosa or bulimia; abrupt discontinuation of some drugs[b]
  - Use of other bupropion-containing products
  - Chronic opioid use (opioid withdrawal)
  - During/within 14 days of MAOI use
- **Liraglutide 3.0 mg**
  - MEN2, personal/family history of MTC (potential risk of thyroid C-cell tumors—rodent data[c])
  - Acute pancreatitis

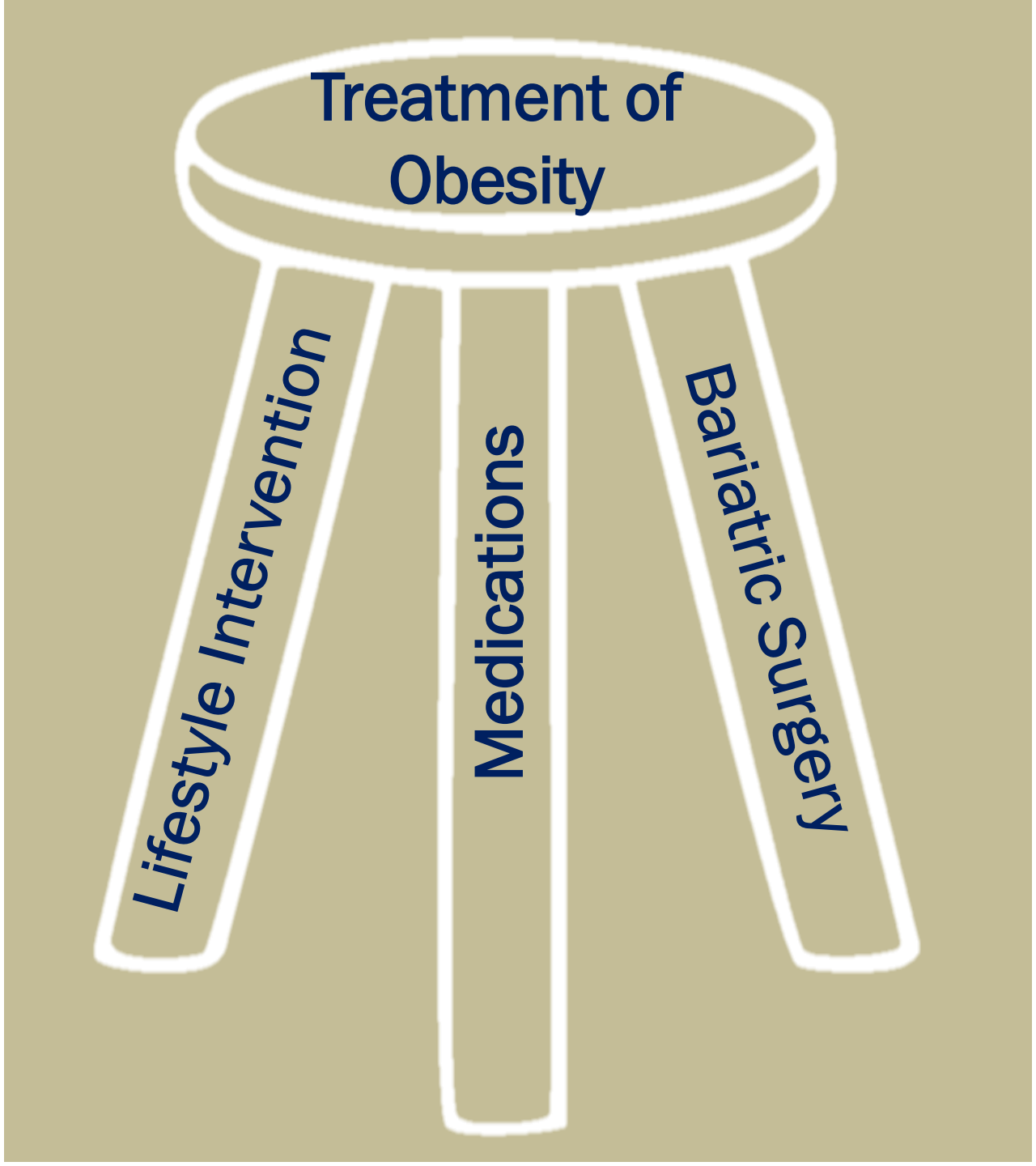
All are contraindicated in pregnancy and generally not recommended for women who are breastfeeding; caution on use of reliable contraception.

US FDA. Drugs@FDA. http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA.

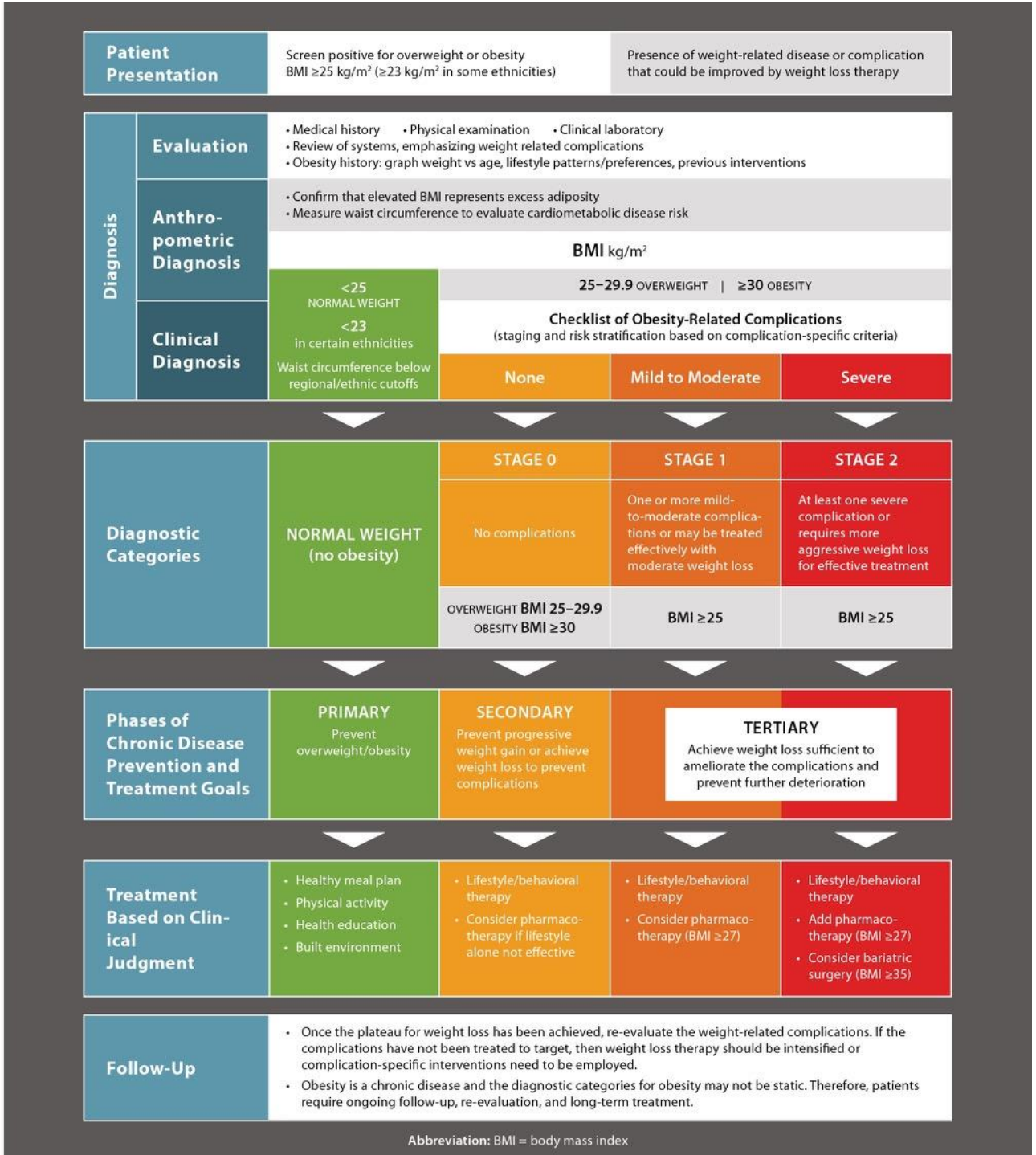
[a] For all agents, known hypersensitivity to agent or any component .
[b] Alcohol, benzodiazepines, barbiturates, antiepileptic drugs.
[c] Relevance in humans has not been determined.

Tools for Care of Patients with Obesity

- Balance efficacy, safety, and cost
- Optimize benefit: risk ratio
- Achieve best outcomes
- Cost-effectiveness of care



AACE/ACE ALGORITHM FOR THE MEDICAL CARE OF PATIENTS WITH OBESITY



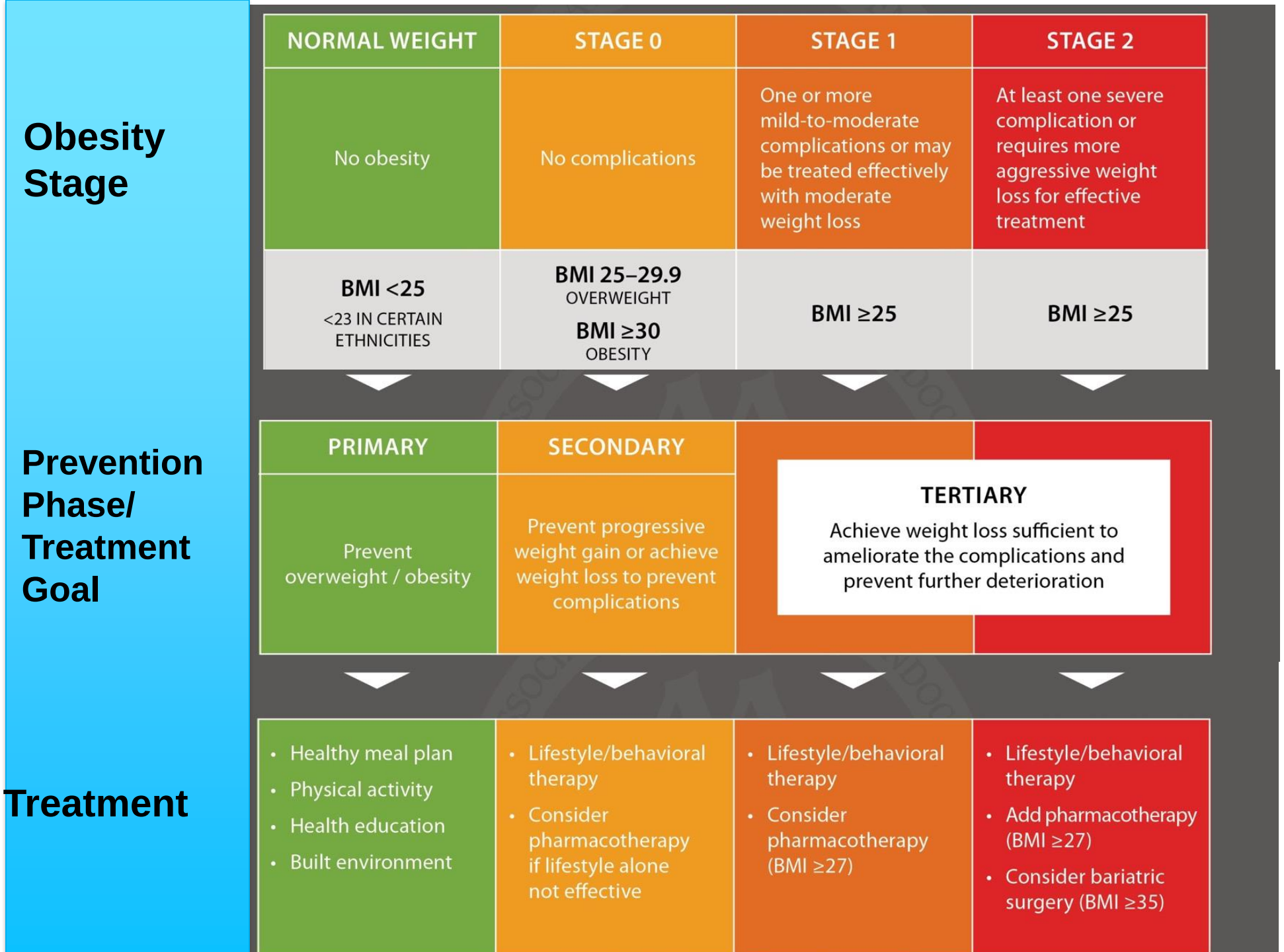
Garvey WT et al. Endocrine Practice 22(Suppl 3):1-203, 2016

2. Diagnosis: Clinical Component

EVALUATE FOR A CHECKLIST OF WEIGHT-RELATED COMPLICATIONS

Patients Present with Overweight or Obesity (Anthropometric Component)	Candidates for Weight Loss Therapy	Patients Present with Weight-Related Disease or Complication (Clinical Component)
Patients present with BMI ≥25 kg/m^2, or ≥23 kg/m^2 in certain ethnicities, and excess adiposity	Evaluate for weight-related complications →	Prediabetes
		Metabolic Syndrome
		Type 2 Diabetes
		Dyslipidemia
		Hypertension
		Cardiovascular Disease
		Nonalcoholic Fatty Liver Disease
		Polycystic Ovary Syndrome
		Female Infertility
		Male Hypogonadism
	← Evaluate for overweight or obesity	Obstructive Sleep Apnea
		Asthma/Reactive Airway Disease
		Osteoarthritis
		Urinary Stress Incontinence
		Gastroesophageal Reflux Disease
		Depression

Garvey WT et al. Endocrine Practice 22(Suppl 3):1-203, 2016



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3. Treatment Based on Clinical Judgment

WHEN TO INITIATE WEIGHT-LOSS MEDICATIONS IN PATIENTS WITH OVERWEIGHT/ OBESITY

INITIATE LIFESTYLE THERAPY

1. **No Complications.**
   Patients with overweight or obesity who have no clinically significant weight-related complications (secondary prevention)

2. **Mild to Moderate Complications.**
   - Patients with mild to moderate weight-related complications when lifestyle therapy is anticipated to achieve sufficient weight loss to ameliorate the complication (tertiary prevention)
   - Note: weight loss medications may also be indicated based on clinical judgment

INITIATE WEIGHT LOSS MEDICATION AS AN ADJUNCT TO LIFESTYLE THERAPY

1. **Failure on Lifestyle Therapy.**
   Add medication for patients who have progressive weight gain or who have not achieved clinical improvement in weight-related complications on lifestyle therapy alone.

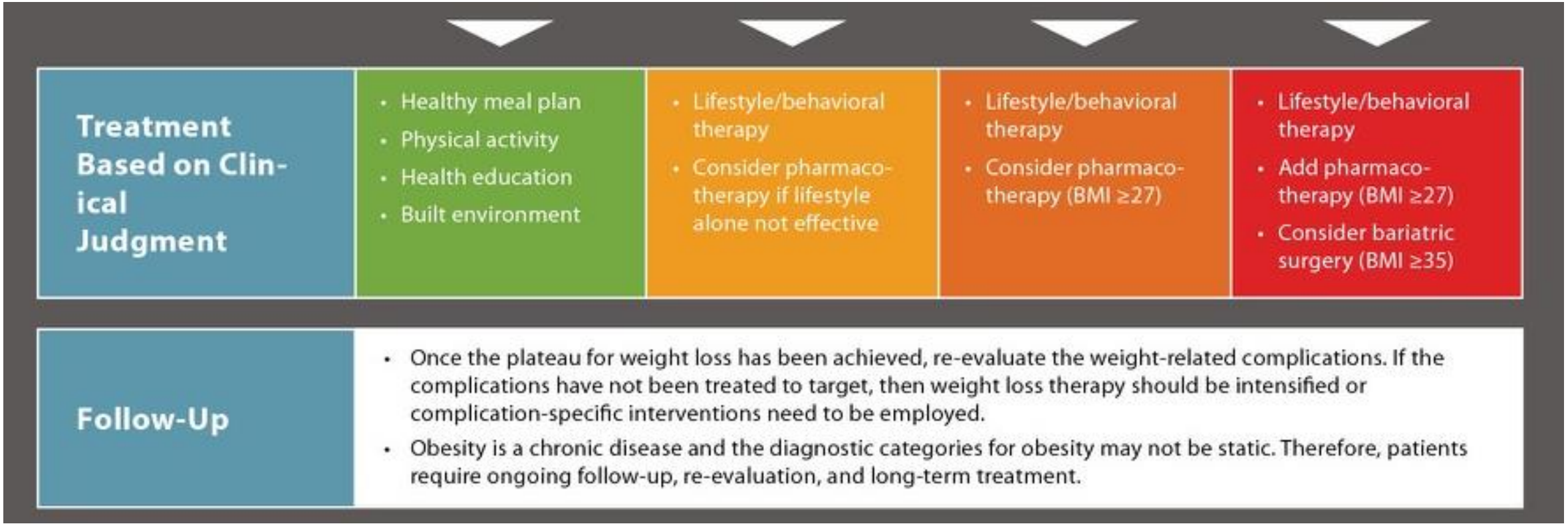
2. **Weight Regain on Lifestyle Therapy.**
   Add medication for patients with overweight (BMI 27–29.9 kg/m^2) or obesity who are experiencing weight regain following initial success on lifestyle therapy alone.

3. **Presence of Weight-Related Complications.**
   Initiate medication concurrent with lifestyle therapy for patients with overweight (BMI 27–29.9 kg/m^2) or obesity who have weight-related complications, particularly if severe, in order to achieve sufficient weight loss to ameliorate the complication (tertiary prevention).

Garvey WT et al. Endocrine Practice 22(Suppl 3):1-203, 2016

Follow-up and Goals of Therapy

- Are you at target for improvements in obesity complications?
- If not, intensify weight loss therapy and/or teat complications specifically
- Obesity is a life-long disease



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% Weight Loss Needed to Reduce Complications

COMPLICATION	% weight loss	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 at, 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%		Singh et al, 2013 Tutujian R, 2011
PCOS	5-15%	Lowers androgens, improves ovulation, increases insulin sensitivity	Panidis D et al, 2008 Norman et al, 2002 Moran et al, 2013

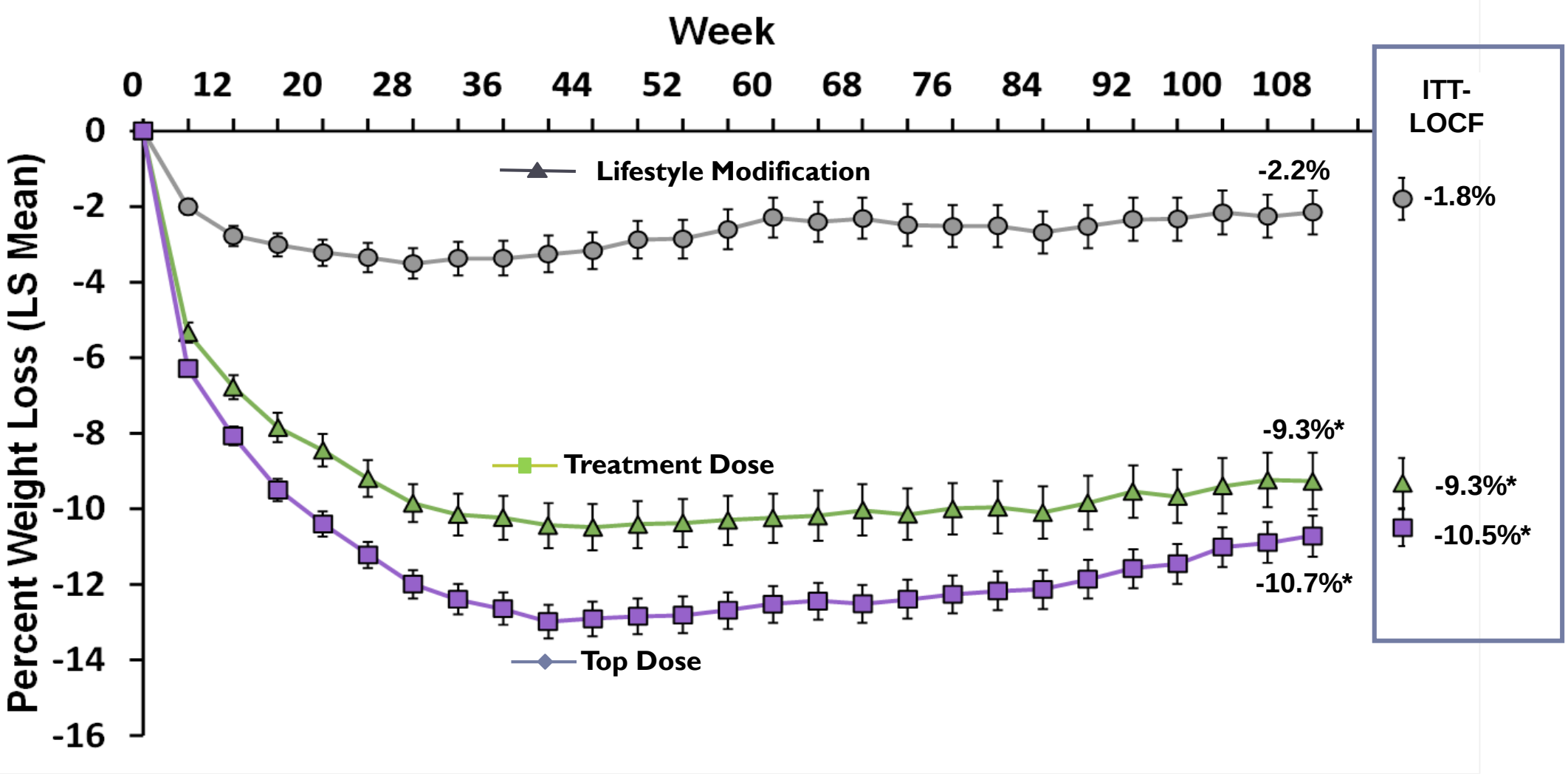
Application of AACE Obesity Guidelines

Complications-Centric Approach to Treatment of Patients with Obesity

- Preventing Diabetes in Patients with prediabetes or Metabolic Syndrome

- Patients with Type 2 Diabetes

Phentermine/Topiramate ER and the SEQUEL STUDY: Weight Loss Over 2 Years in Completers

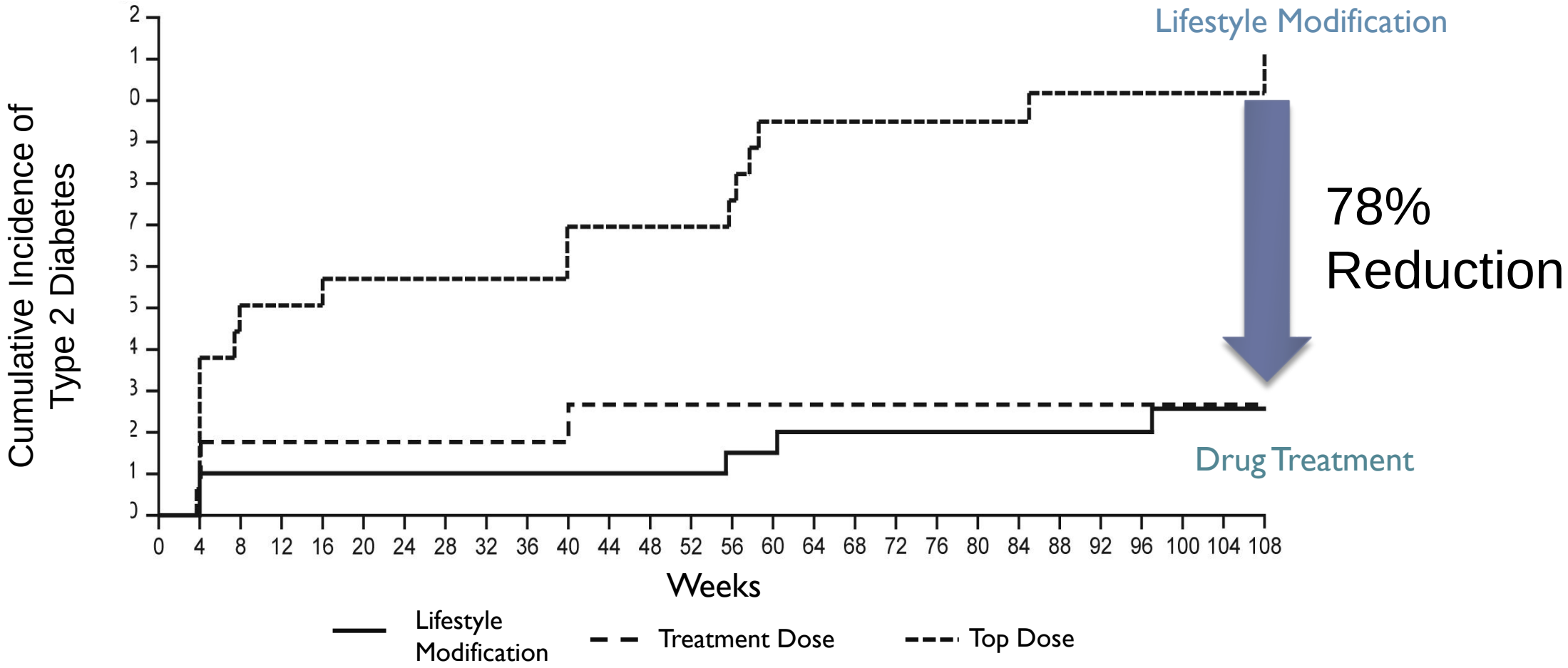


*P<0.0001 vs placebo

Garvey WT, et al. *Am J Clin Nutr*. 2012;95(2):297-308 2012

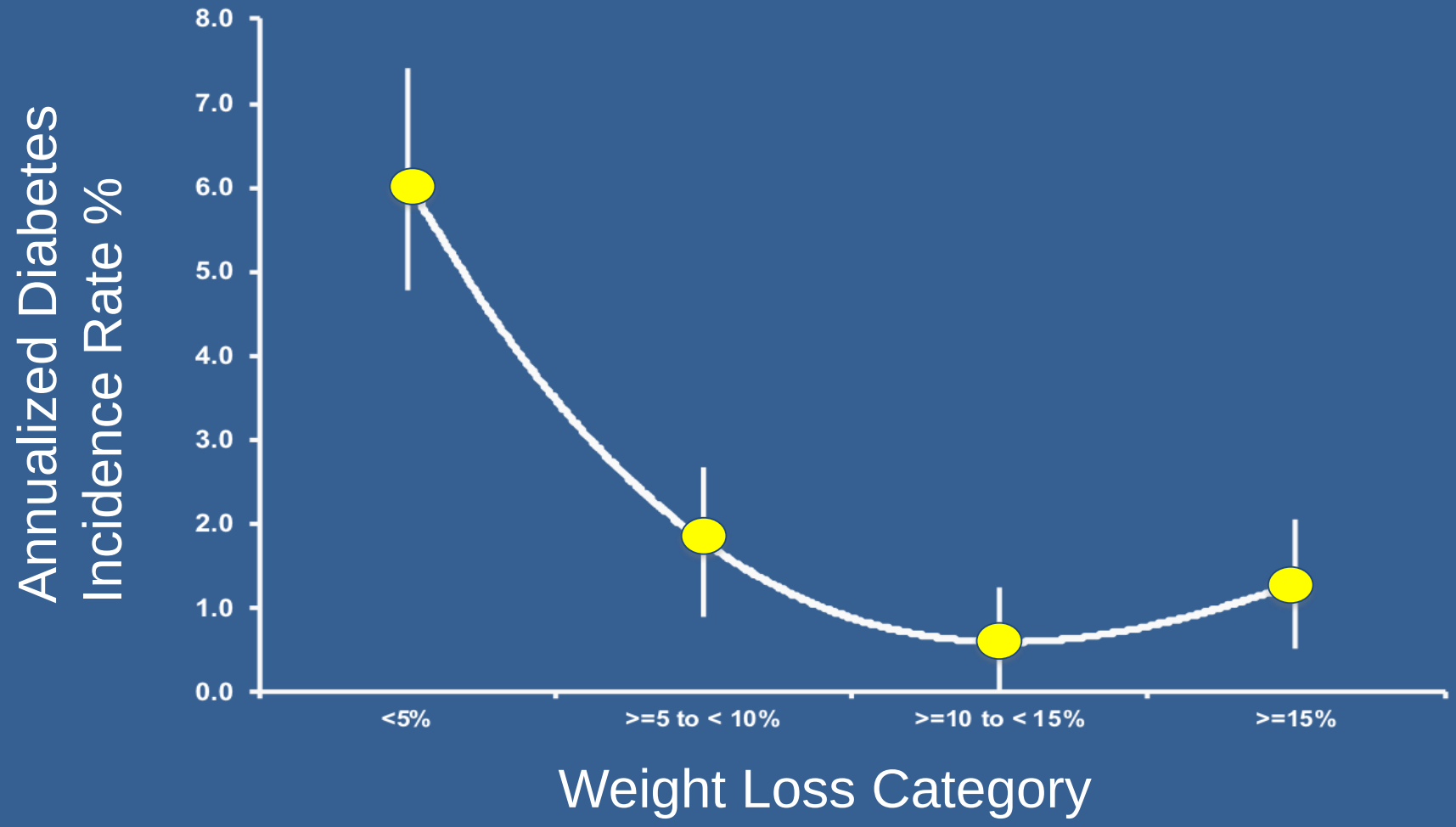
Prevention of Type 2 Diabetes in Patients with Prediabetes or Metabolic Syndrome at Baseline

Phentermine/Topiramate and the 2-Year SEQUEL STUDY



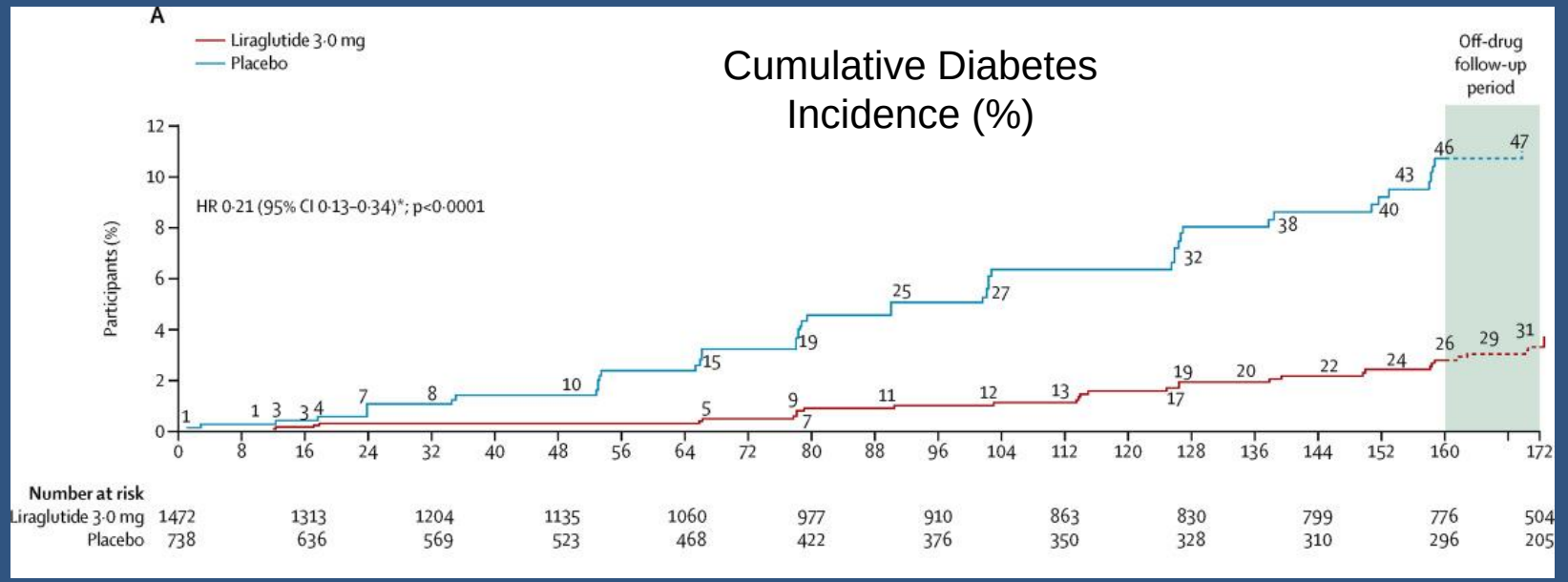
Garvey WT et al. *Diabetes Care*. 2014;37:912-921.

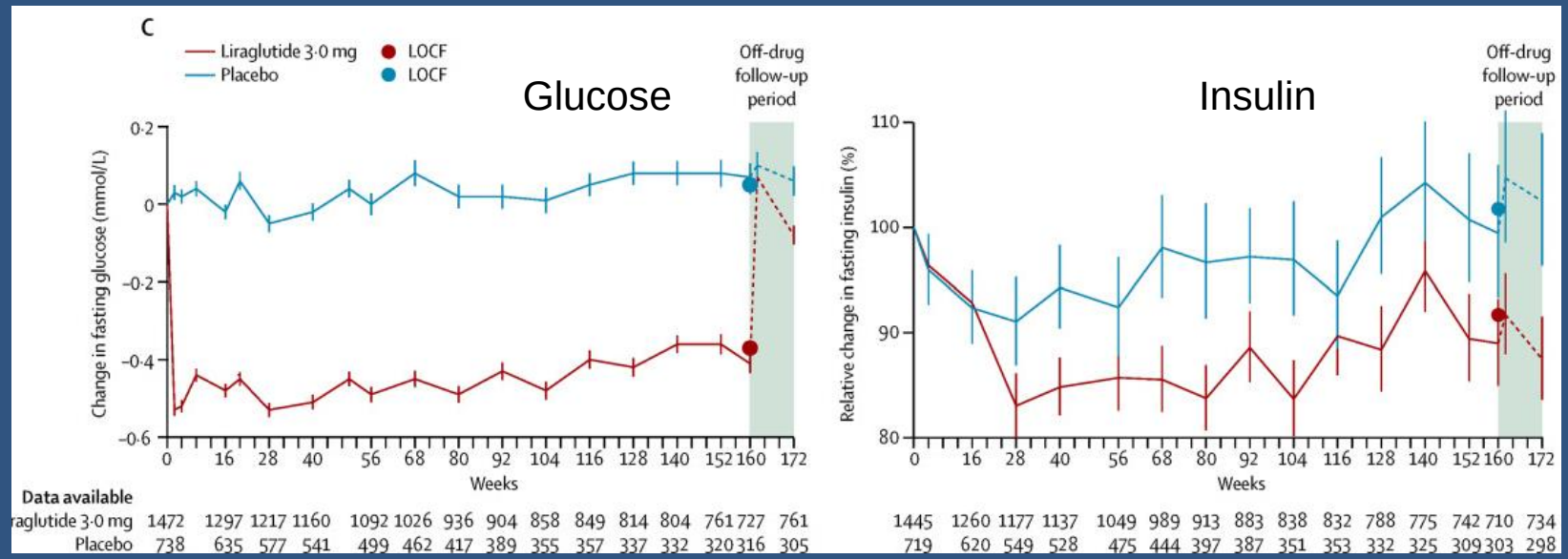
Dose-Response for Weight Loss and Diabetes Prevention due to Phentermine/Topiramate ER Treatment: SEQUEL



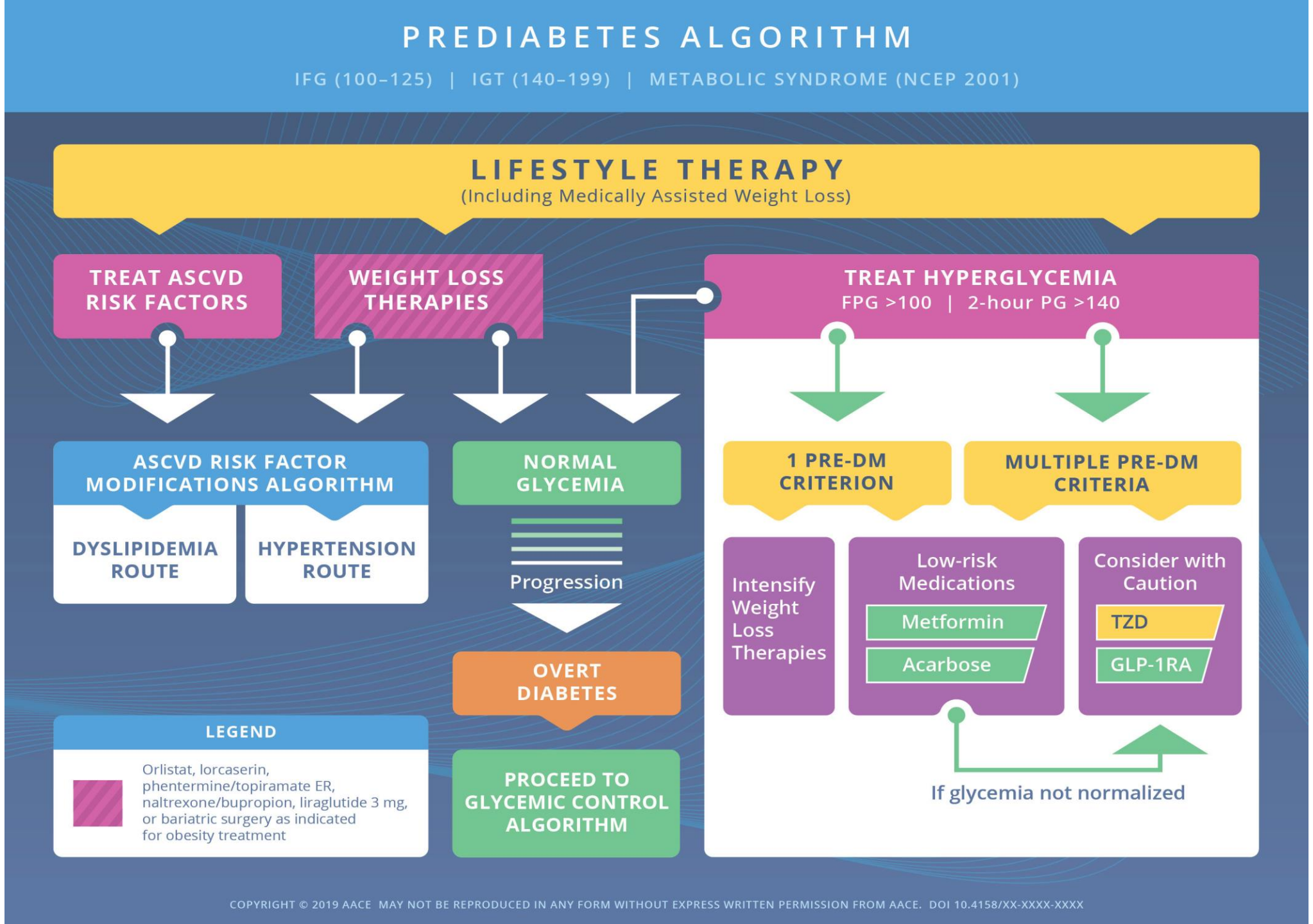
Garvey WT et al. *Diabetes Care*. 2014;37:912-921.

Treatment of Patients with Prediabetes with Liraglutide 3 mg/day





Le Roux CW et al. Lancet 389:1399, 2017



AACE Diabetes Algorithm 2019

Garber A et al. Endocr Pract 2019; 25(1):69-100

What if there was a treatment for T2D that:

1 Reduc…edications

2

3

4

5

6 …a

7

8

9

10 …can produce diabetes remission

This is the therapeutic profile of weight loss in T2D

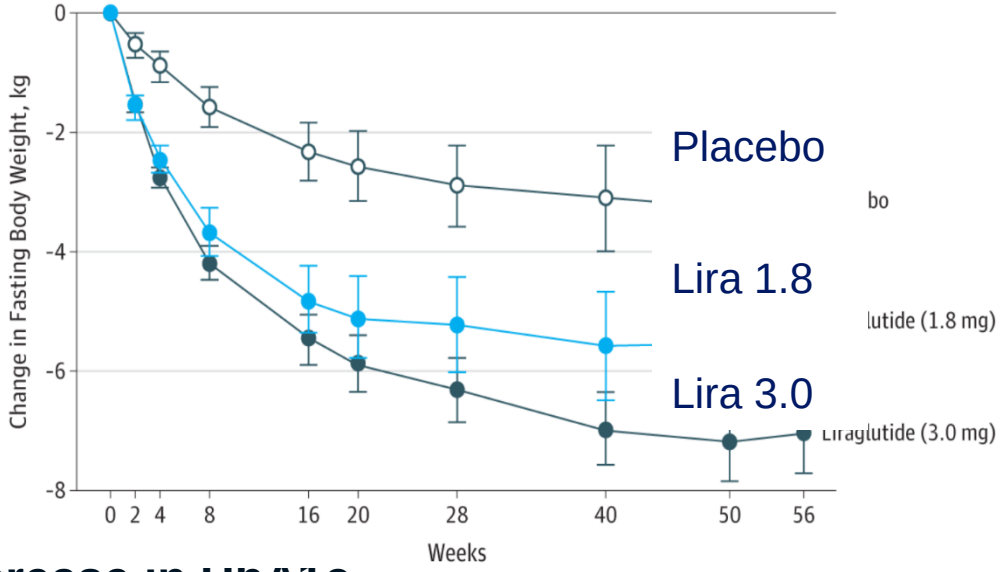
Look AHEAD study references. Phase 3 trials for weight loss meds

1. Look Ahead Research Group. *Diabetes Care* 2007;30:1374–83; 2. Look Ahead Research Group. *N Engl J Med* 2013;369:145–54;
3. Lean M et al. *Lancet* 2018;391:541–51; 4. Davies MJ *et al. JAMA* 2015;314:687–99

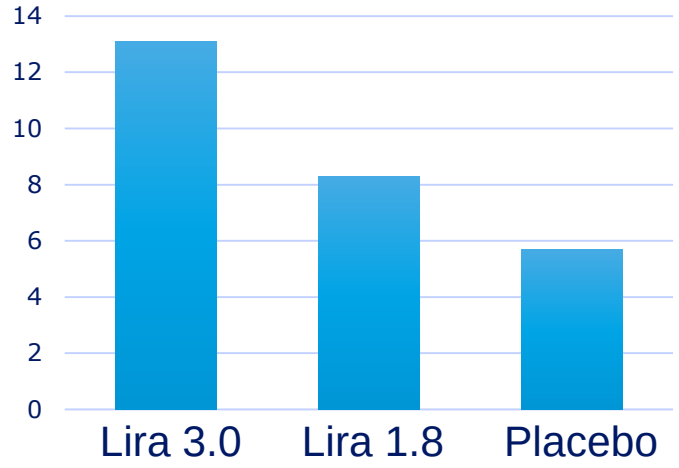
Treatment of Obesity with Liraglutide 3.0 mg in T2DM

SCALE Diabetes RCT Davies MJ, et al. JAMA 2015; 314(7):687-699

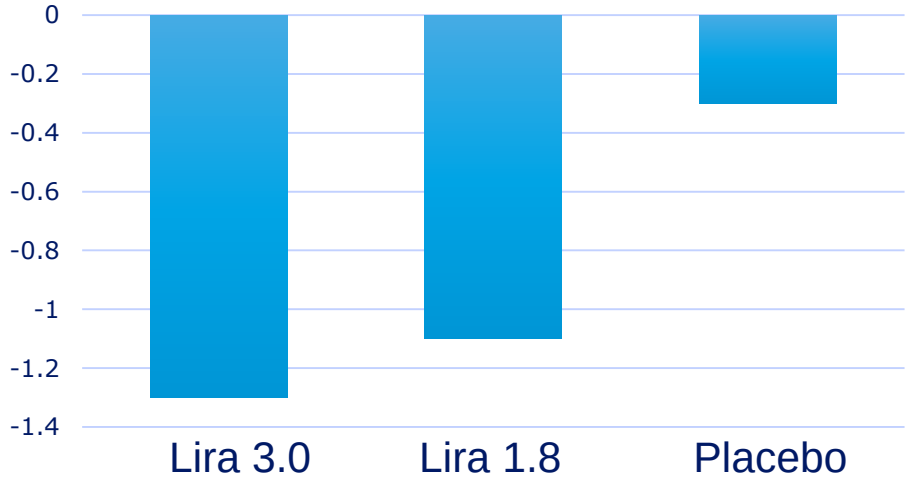
Decrease in % Body Weight



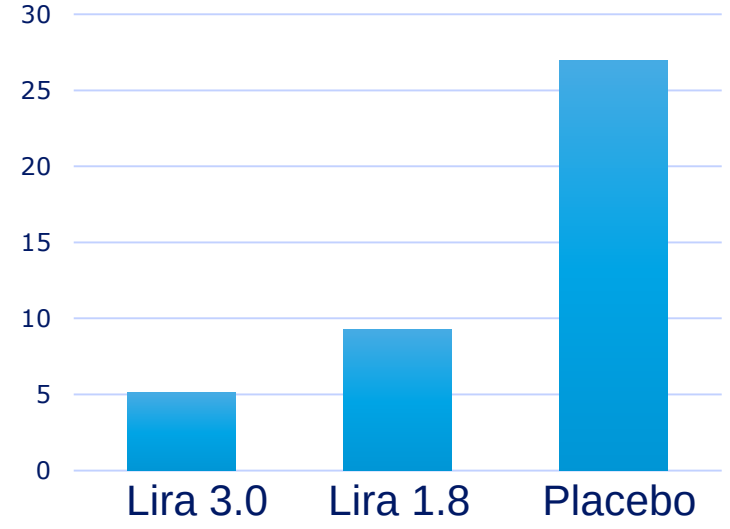
% With DECREASE Diabetes Meds



Decrease in HbA1c

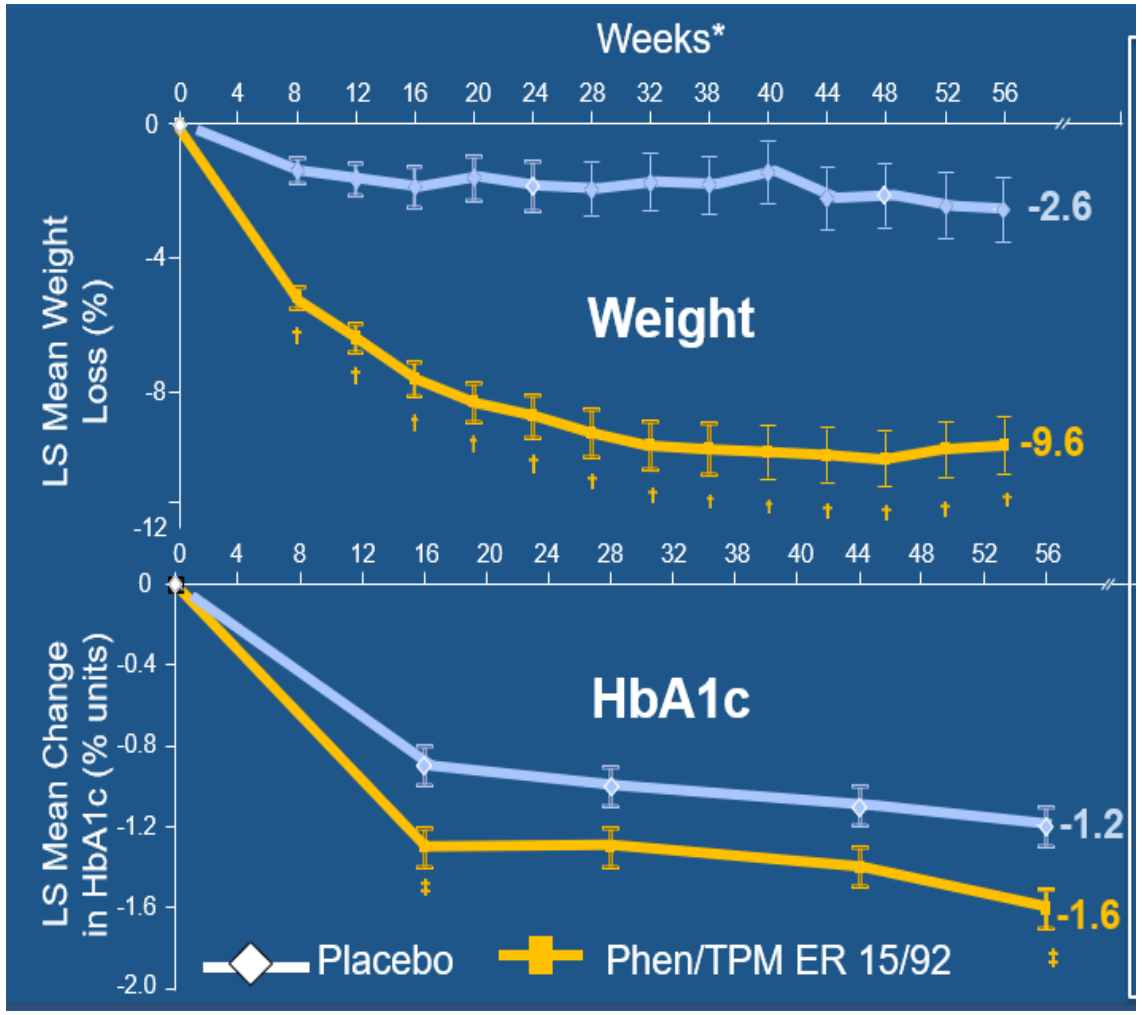


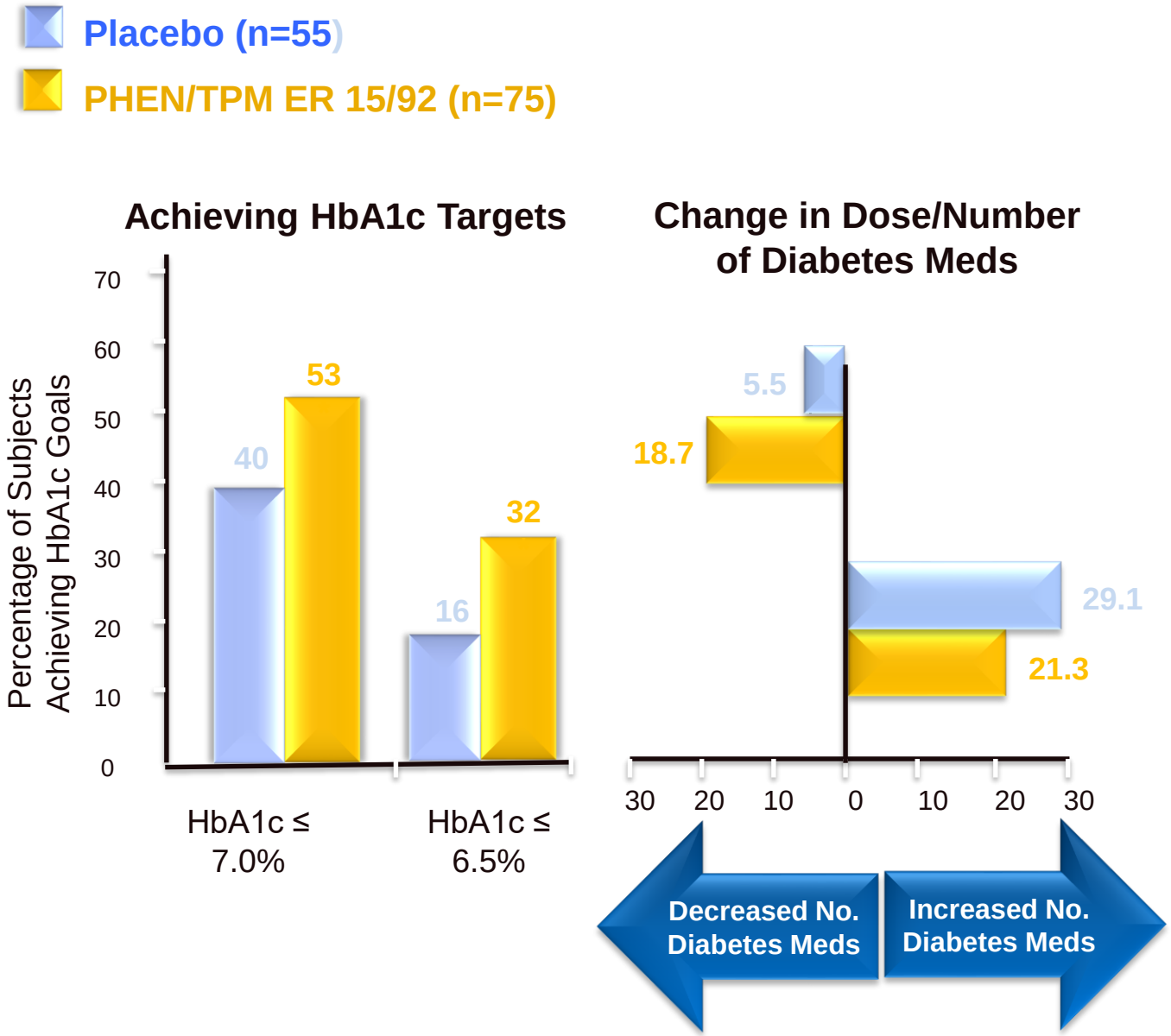
% With INCREASE Diabetes Meds

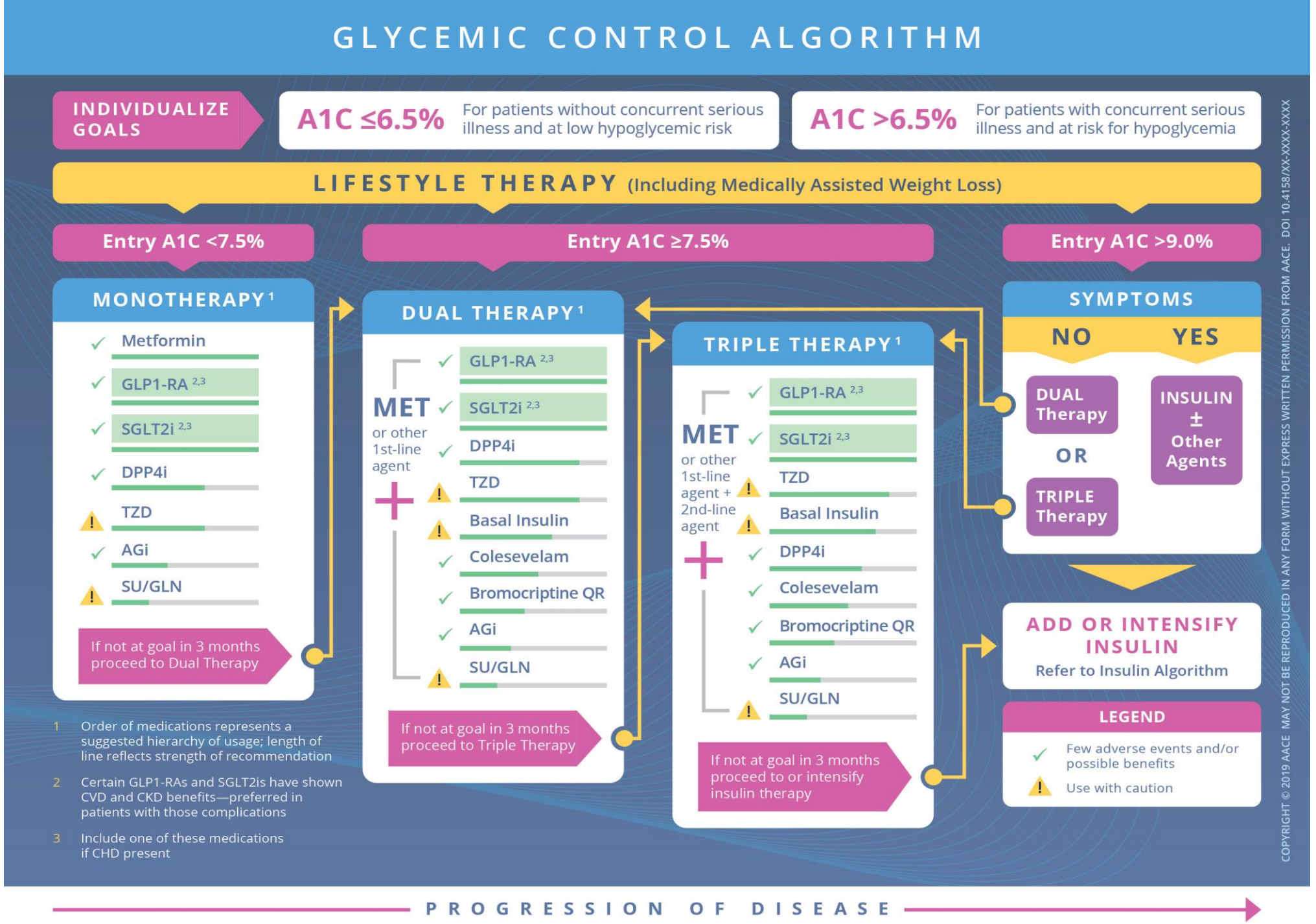


Treatment of Obesity with Phentermine/Topiramate ER in T2DM

Garvey WT, et al. Diabetes Care 2014; 37(12):3309-3316





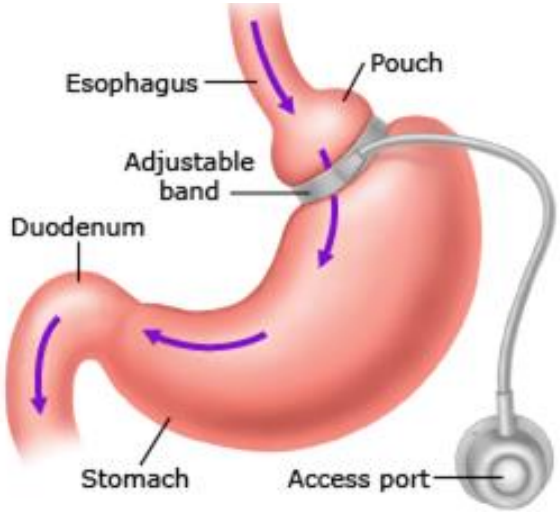


AACE Diabetes Algorithm 2019

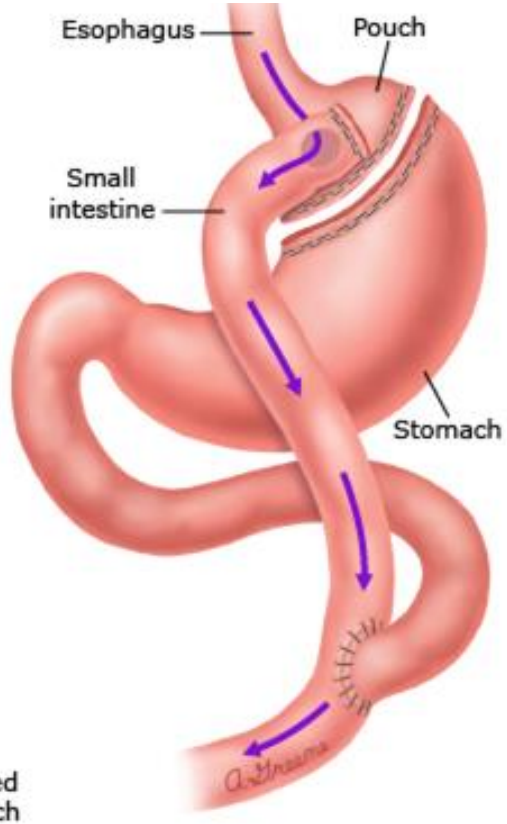
Garber A et al. Endocr Pract 2019; 25(1):69-100

Surgical Options

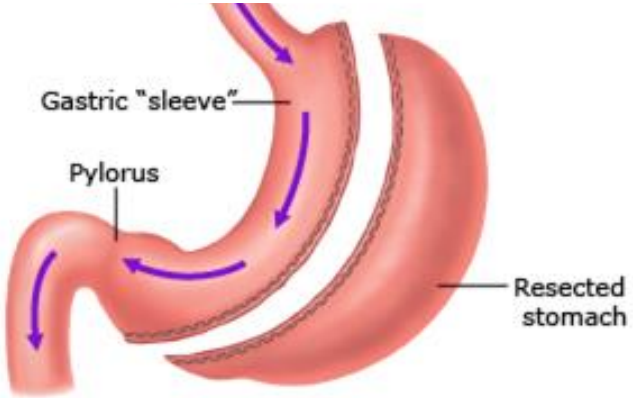
Gastric Banding



Roux-en-Y Gastric Bypass



Sleeve Gastrectomy



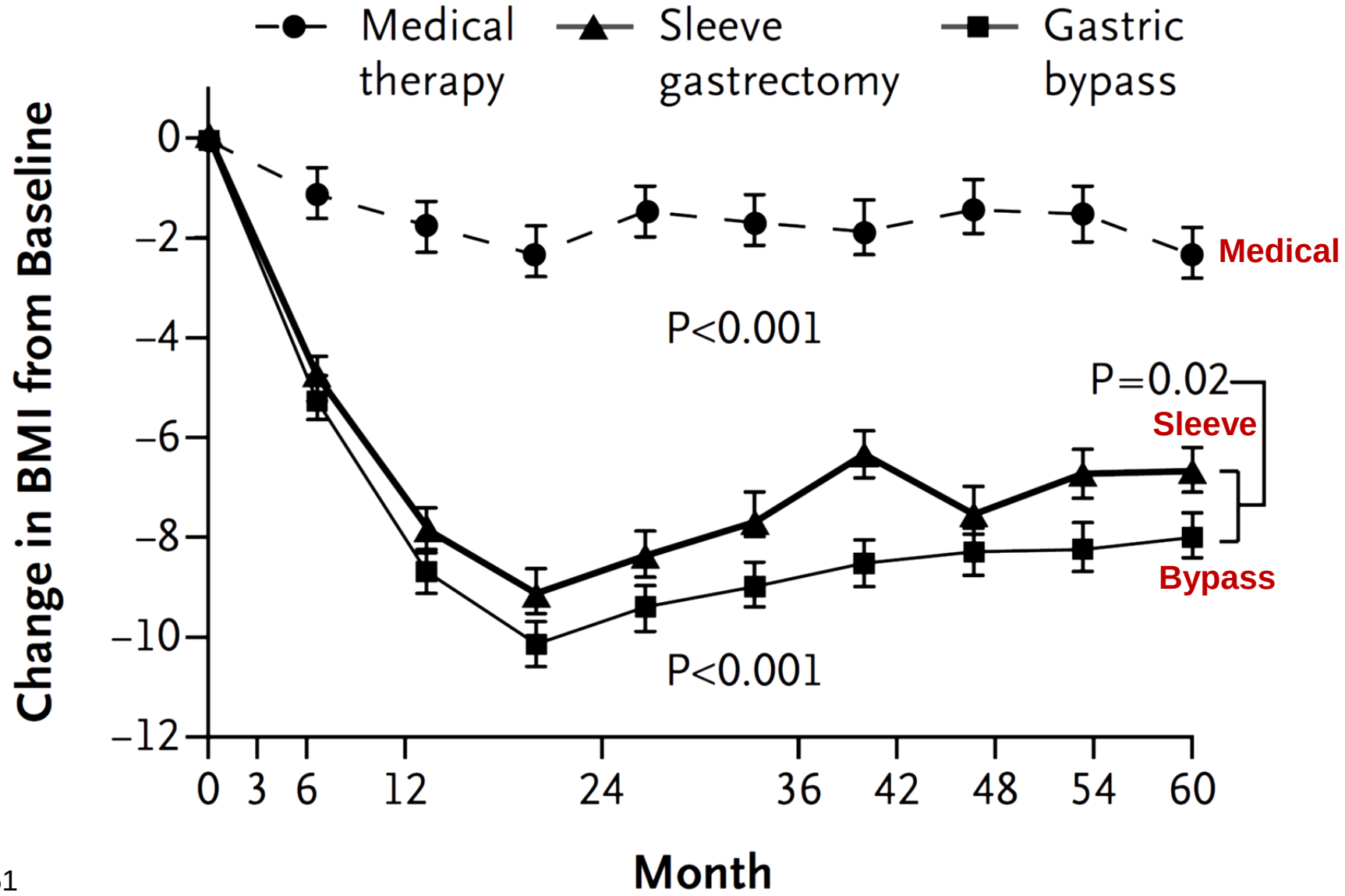
AACE/ASMBS/TOS Bariatric Surgery Guidelines 2013: *Indications*

- Patients with a BMI ≥40 kg/m^2 (Grade A)
- Patients with a BMI ≥35 kg/m^2 and 1 or more severe obesity-related co-morbidities, (Grade A)
- Patients with BMI 30-34.9 with therapeutic target of glycemic control in T2D (Grade C)

Endocr Pract 2013; 19(2):337-372

Bariatric Surgery and Long-term Weight Loss and Regain

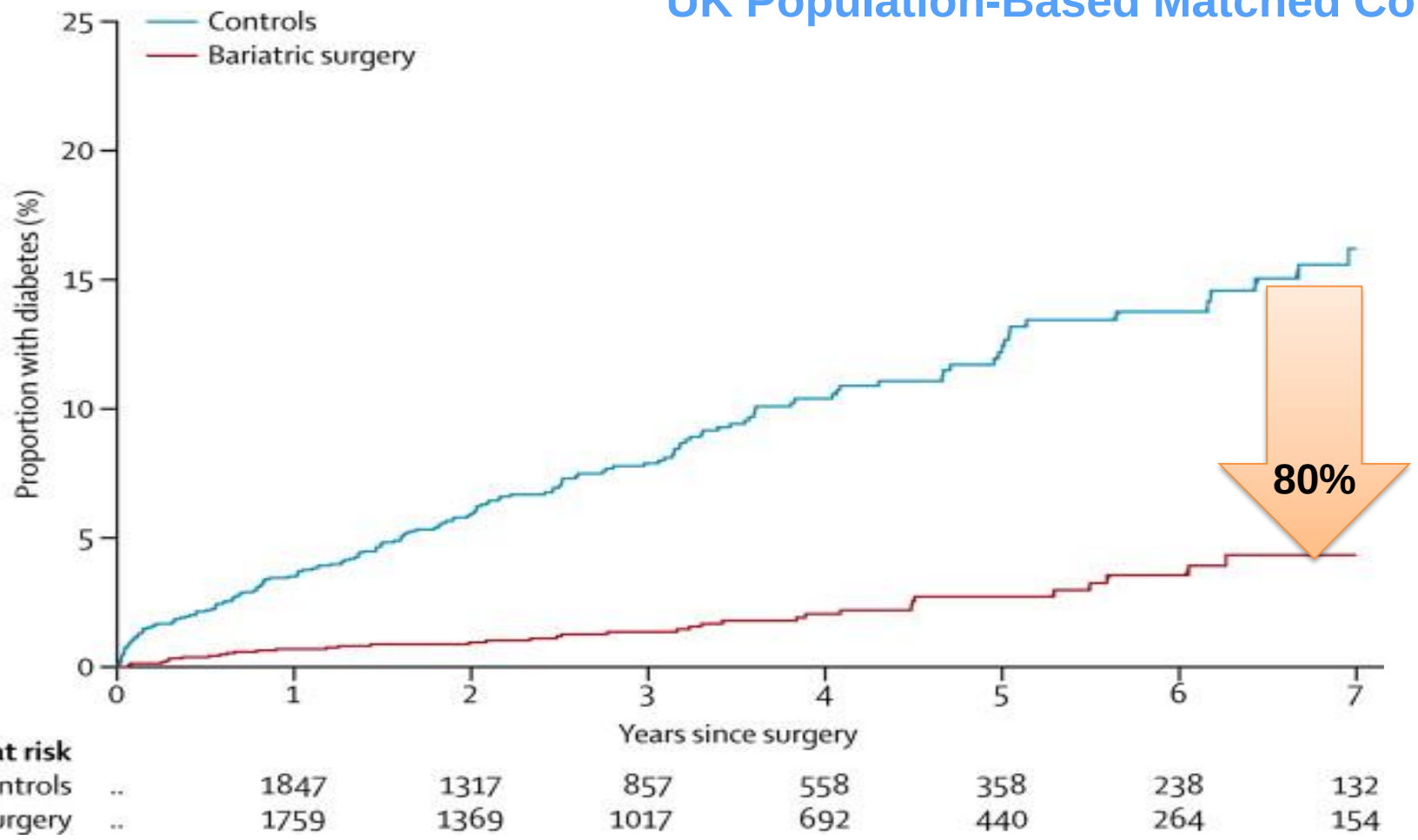
Stampede Study (n=150)



Schaurer PR et al.
NEJM 2017;376:641-651

Incidence of Diabetes After Bariatric Surgery

UK Population-Based Matched Cohort Study*

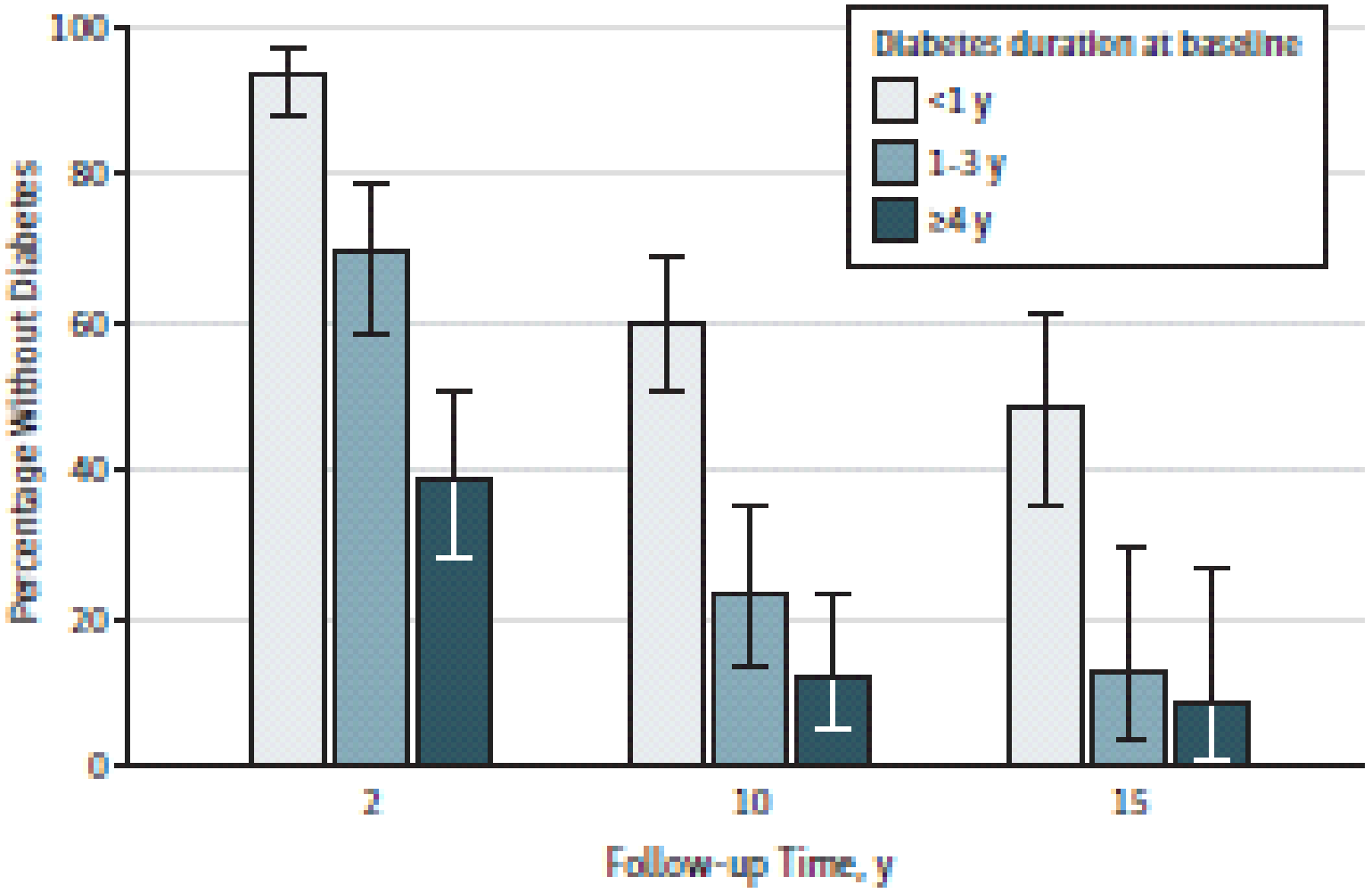


Number at risk								
Controls	..	1847	1317	857	558	358	238	132
Bariatric surgery	..	1759	1369	1017	692	440	264	154

*Matched for BMI, age, gender, index year, and A1C.

Booth H, et al. *Lancet Diabetes Endocrinol.* 2014;2:963-968.

Duration of T2DM Affects Rates of Diabetes Remission Following Bariatric Surgery



Sjostrom L et al JAMA 311:2297-2304, 2014

In Summary

1. AACE Obesity Guidelines are an evidenced based approach for diagnosis, staging, treatment decisions, goals of therapy, and follow-up.
2. Establishes a diagnostic approach that includes both an assessment of adiposity and impact on health as manifest by obesity complications.
3. Establishes treatment goals that do not simply reflect the amount of weight lost but the improvements in patient health.
4. Emphasizes a patient-centric approach for individualization of therapy to optimize effectiveness, patient safety, and the benefit/risk ratio.
5. Weight loss therapy in T2DM will
   - Reduce HbA1c while decreasing the need for diabetes medications
   - Reduce blood pressure and improve lipids
   - Improve quality of life, mobility, sleep apnea, and other weight-related complications
   - Can result in diabetes remission

Thank You