



Webinar 3:

Balancing Glycemic Management with Need to Address Overweight and Obesity in Patients with Type 2 Diabetes

Chair

Robert H. Eckel, MD, FAHA, FACC
Professor of Medicine, Emeritus

Division of Endocrinology, Metabolism and Diabetes

Division of Cardiology

S/P Charles A. Boettcher II Chair in Atherosclerosis

University of Colorado Anschutz Medical Campus

Denver, CO

Faculty

Sangeeta R. Kashyap, MD

Professor of Medicine

Cleveland Clinic Lerner College of
Medicine

Department of Endocrinology, Diabetes,
and Metabolism

Goals

- Identify key aspects of glycemic management in patients with diabetes and obesity
- Explain aspects of patient presentation and/or course that necessitate management options
- Formulate a management plan that includes steps/strategies supporting optimal glycemic management with weight loss benefits in diabetes

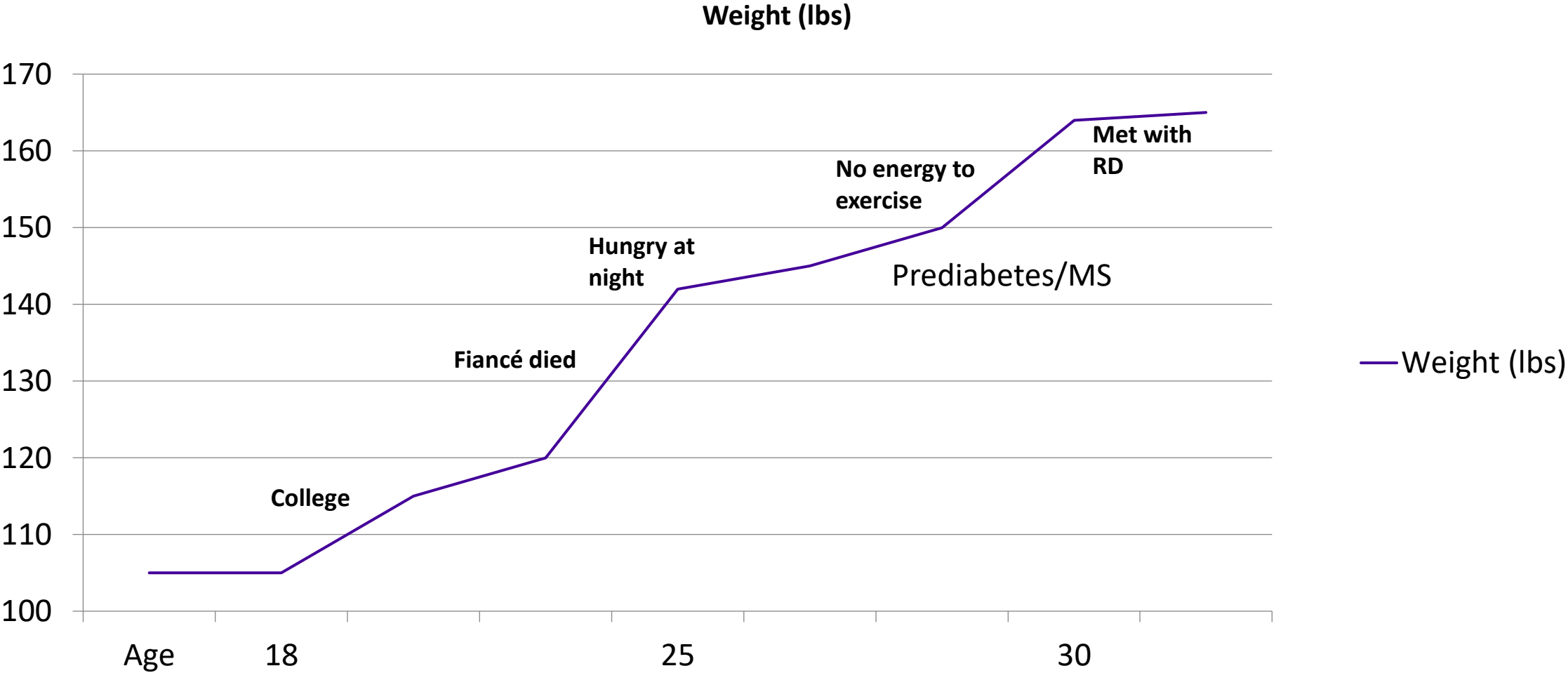
Mica, Age 30 yrs. (Initial Visit)

Patient seeks care for weight gain

- **Medical history:** Unremarkable
- **Medications:** None
- **Family history:**
 - Obesity-sister and mother
 - DM2-mother
- **Review of Systems:** + depressed mood
- **Exam:** Height 5'4", Weight 165 lbs, waist 35 in, BMI 28.3, BP 134/82 mm/Hg, otherwise unremarkable
- **Labs:** Fasting glucose 104 mg/dl, TC 189 mg/dL, HDL-C 36 mg/dL, Triglyceride 200 mg/dL



Graphing Weight



Approach for Mica

- **Engage support:**
 - Mica, her sister, and mother each prepare one meal per week for 3, with leftovers
- **Personalize:**
 - Dietary plan supports DASH program includes Mexican foods, with instruction on portion control, low fat substitutions, emphasis on vegetables and fruits, and use of meal replacements.
 - Physical activity plan includes walking dog in the evening and walking with family on “dinner nights”
- **Treat comorbidities:**
 - Mica is referred to a psychologist for depression and binge eating disorder
- Mica **lost 8% of her body weight** and maintained for several years until lost to follow-up

Mica, Age 42 returns for office visit for new onset DM

- Seeks care because she was told her blood sugar was elevated and required treatment
- Medical History:
 - Hypertension for 5 years; treated with enalapril 20 mg, atenolol 100 mg
 - Hypercholesterolemia for 5 years; treated with atorvastatin 40 mg daily
 - Depression; treated with paroxetine (Paxil) 20 mg daily
- ROS: Shortness of breath on exertion, daytime lethargy, low back pain
- Exam: Height 5'4", Weight 200 lbs, Waist 38 in, BMI 34.3, BP:142/90
- Lab: Fasting glucose 146 mg/dl, HbA1c 7.8%
- Lipids (mg/dL): Total Cholesterol 195 mg/dL, HDLc 42 mg/dL, LDLc 110 mg/dL, TG 196 mg/dL
- ALT 90 U/L, AST 24 U/L
- CBC, creatinine, and ECG normal
- No albuminuria and normal fundus exam. Sensation on feet intact with monofilament.

Initial Treatment Approach for Mica



Consultation with a dietitian, who instructed Mica on following a reduced-calorie Mediterranean Diet and exercising at the YMCA 150 min/week



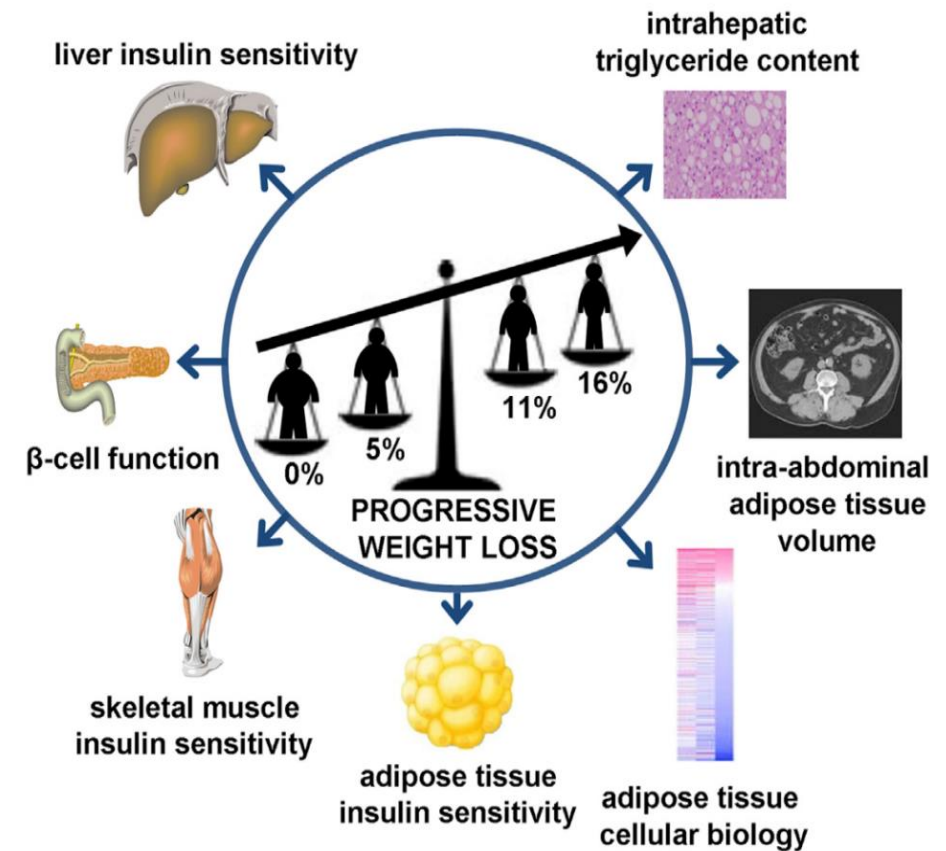
After 6 months, weight had not changed and her HbA1c is now 7.6% . Patient was placed on metformin but had intolerable GI side effects. Subsequently she was started on glyburide 2.5 mg day and sitagliptin 100mg daily.

Metabolic Benefits of Progressive Weight Loss on Diabetes Remission

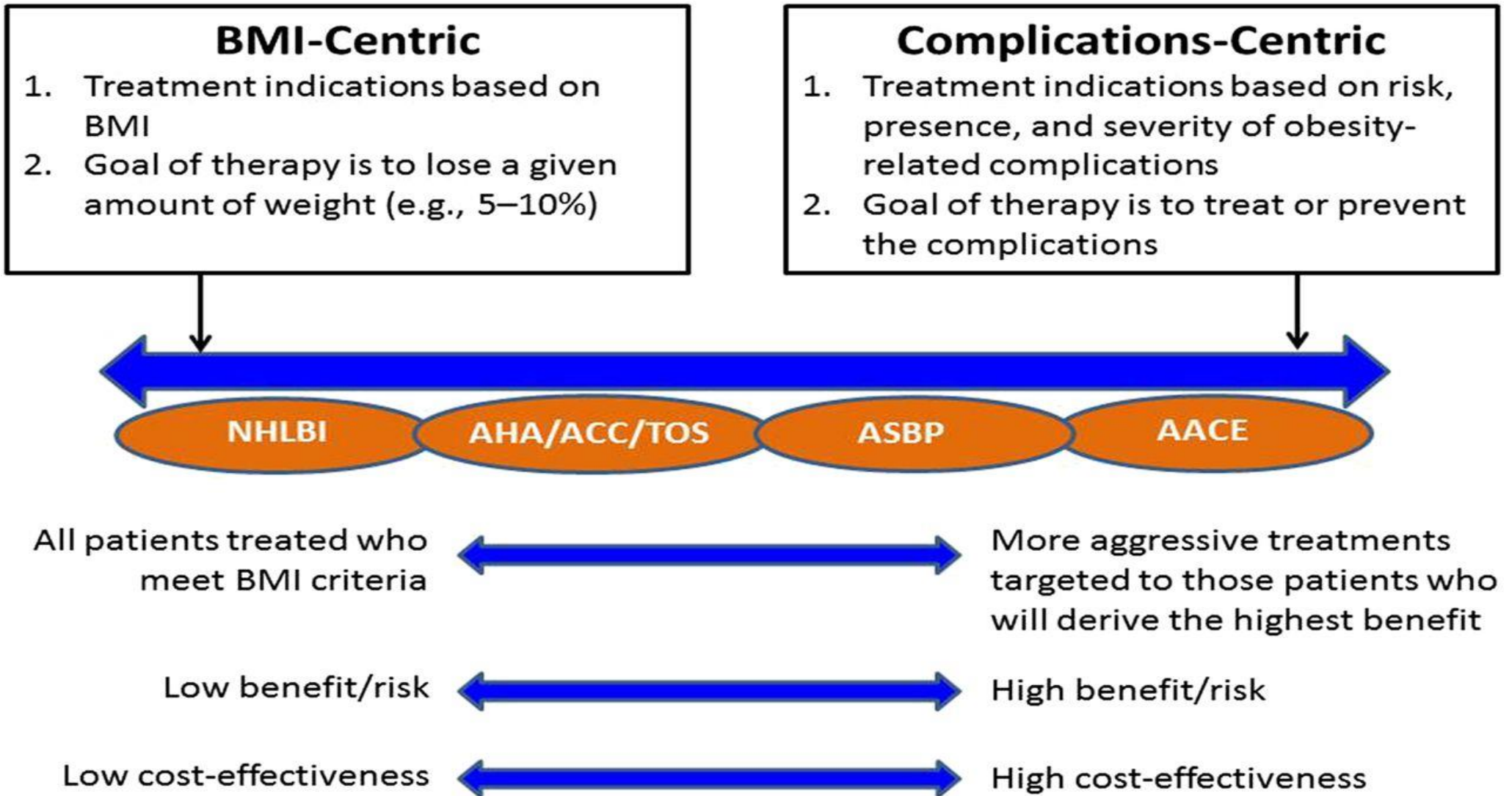
Moderate 5% weight loss improves multi-organ insulin sensitivity and b cell function

Additional weight loss of 11%–16% further increases insulin sensitivity in muscle

Progressive weight loss causes stepwise changes in adipose tissue biology



Metabolic Treatment of Diabetes: Two Areas of Focus



Incorporate agents that provide adequate **EFFICACY** to achieve and maintain glycemic goals

Higher glycemic efficacy therapy: GLP-1 RA; insulin; combination approaches (Table 9.2)

- Consider additional comorbidities, patient-centered treatment factors, and management needs in choice of therapy, as below:

MINIMIZE HYPOGLYCEMIA

No/low inherent risk of hypoglycemia:
DPP-4i, GLP-1 RA, SGLT2i, TZD

For SU or basal insulin, consider agents with
lower risk of hypoglycemia^{3,4}

IF A1C ABOVE TARGET

Incorporate additional agents based on
comorbidities, patient-centered treatment
factors, and management needs

MINIMIZE WEIGHT GAIN/ PROMOTE WEIGHT LOSS

PREFERABLY

GLP-1 RA with good efficacy for weight loss

OR

SGLT2i

IF A1C ABOVE TARGET

For patients on a GLP-1 RA, consider
incorporating SGLT2i and vice versa

- If GLP-1 RA not tolerated or indicated,
consider DPP-4i (weight neutral)

Incorporate additional agents based on
comorbidities, patient-centered treatment
factors, and management needs

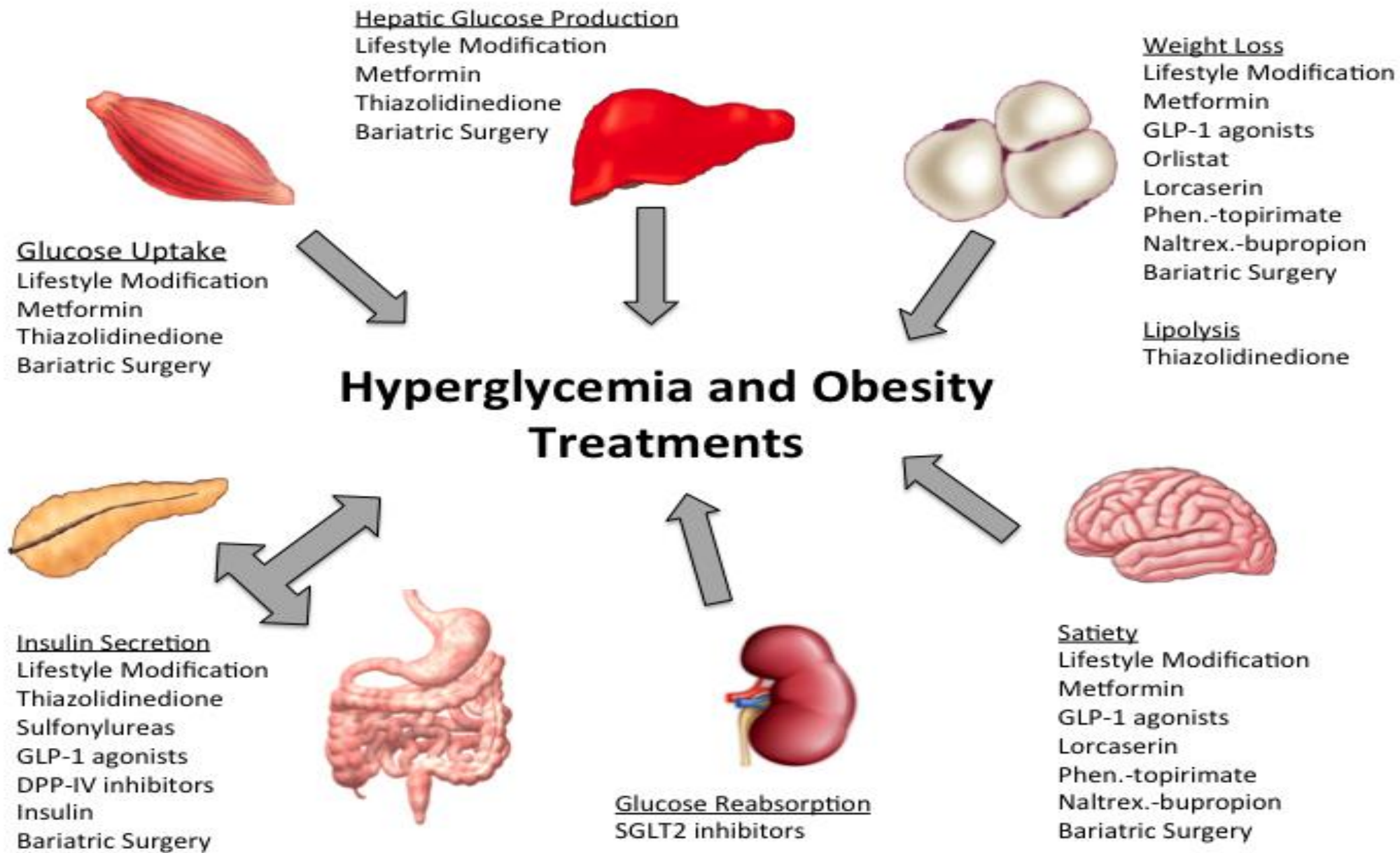
CONSIDER COST AND ACCESS

Available in generic form at lower cost:

- Certain insulins: consider insulin
available at the lowest acquisition cost
- SU
- TZD

IF A1C ABOVE TARGET

Incorporate additional agents based on
comorbidities, patient-centered treatment
factors, and management needs



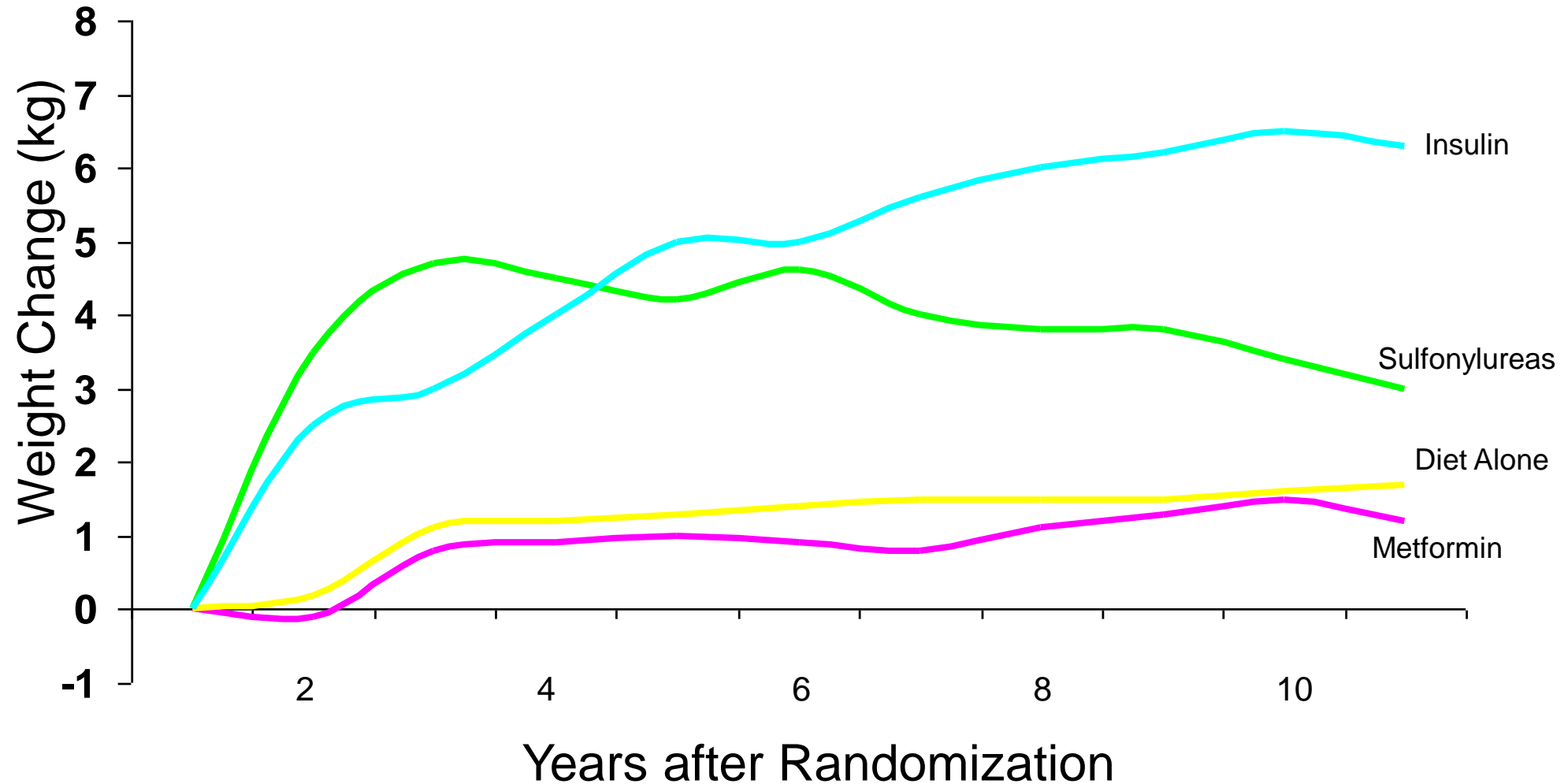
Iatrogenic Medications and Weight

Disease	Medication Class	Causing Weight Gain	Alternatives
Diabetes	insulin secretagogos and sensitizers	insulin, <u>sulfonylureas</u> , meglitinides, and TZDs	GLP-1 RA, SGLT2i, and amylin analogs
Hypertension	β-blockers, non-selective	propranolol, <u>metoprolol</u> , atenolol	ACEi, ARBs, calcium channel blockers selective β blockers (carvedilol, timolol)
Depression	tricyclics	amitriptyline, nortriptyline, and imipramine	trazadone, doxepin
	SSRIs, SNRIs, atypical	citalopram, <u>paroxetine</u> , mirtazapine	fluvoxamine, venlafaxine, duloxetine, fluoxetine, sertraline, and bupropion
Psychoses	Anti-psychotics	clozapine, quetiapine, olanzapine, and haloperidol	lurasidone, aripiprazole, and ziprasidone
	Mood stabilizers	lithium, valproic acid	lamotrigine, carbamazepine
Epilepsy		gabapentin, pregabalin, valproic	felbamate, topiramate, and zonisamide
Contraceptives		depot medroxyprogesterone	oral (progestin + estrogen), IUDs
Anti-Inflammatory	Glucocorticoids	prednisone, dexamethasone	NSAIDs, biologics
Anti-histamines	H1 anti-histamines	diphenhydramine, cetirizine	loratadine (does not cross BBB)

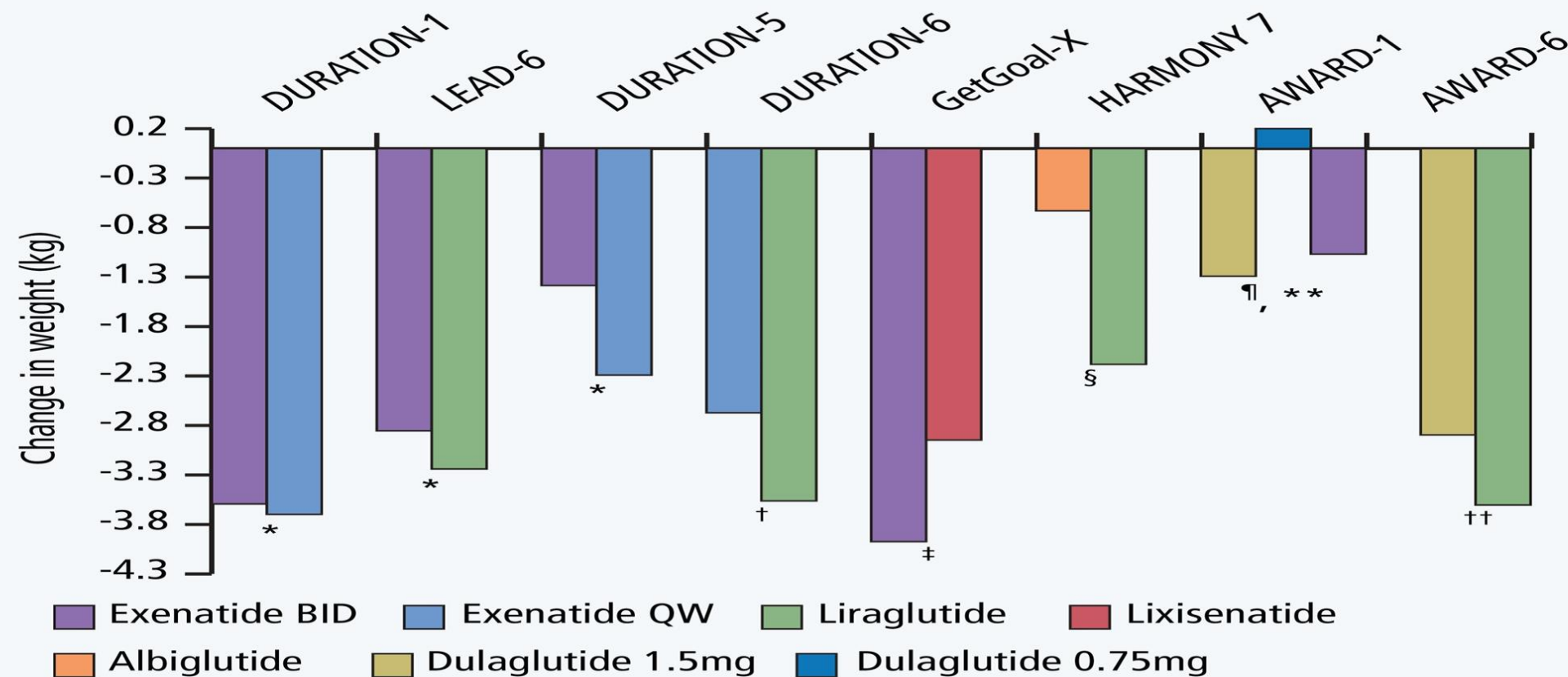
Wharton S et al. *Diabetes Metab Syndr Obes*. 2018;11:427–438.

Apovian C et al. *JCEM*.2015;100(2):342-362.

Change in Body Weight with Diabetes Medications



The role of GLP-1 receptor agonists as weight loss agents in patients with and without type 2 diabetes

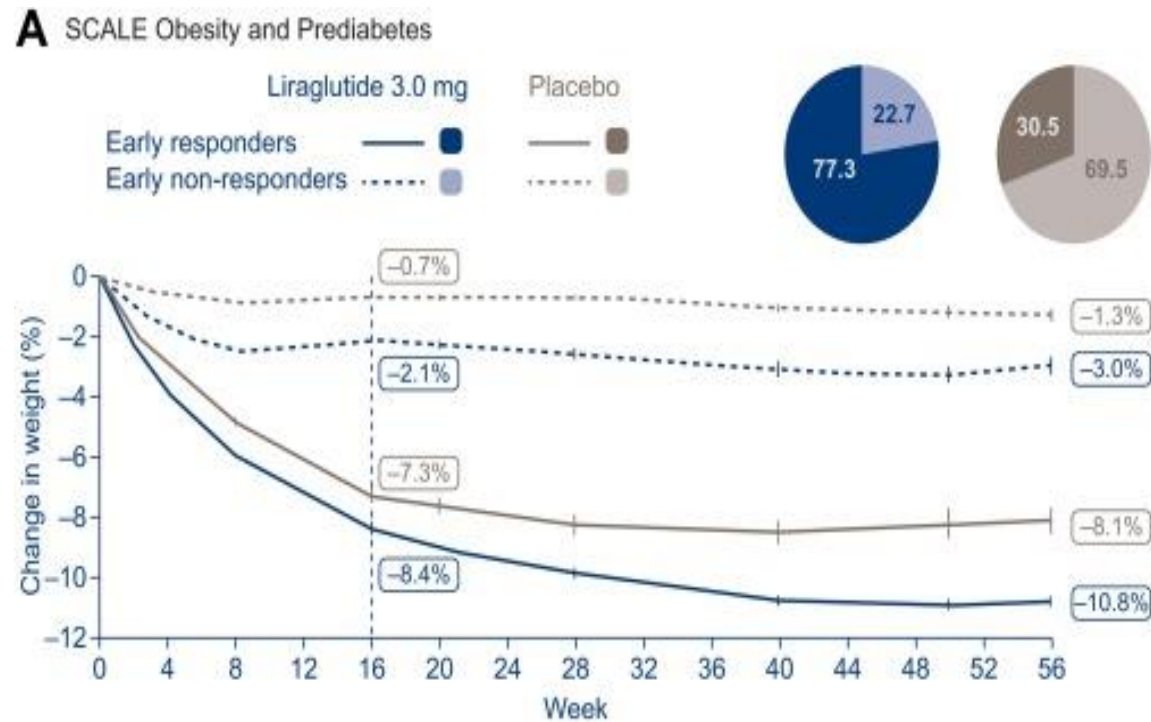


P-values are for statistical superiority (unless noted for non-inferiority); *p = not significant, †p=0.0005, ‡p-value not reported for weight difference of 1.02kg (95% confidence interval 0.456–1.581), §p<0.0001, ¶p<0.001 dulaglutide 0.75mg vs exenatide BID, **p = not significant between dulaglutide 1.5mg vs exenatide bid, ††p=0.011.

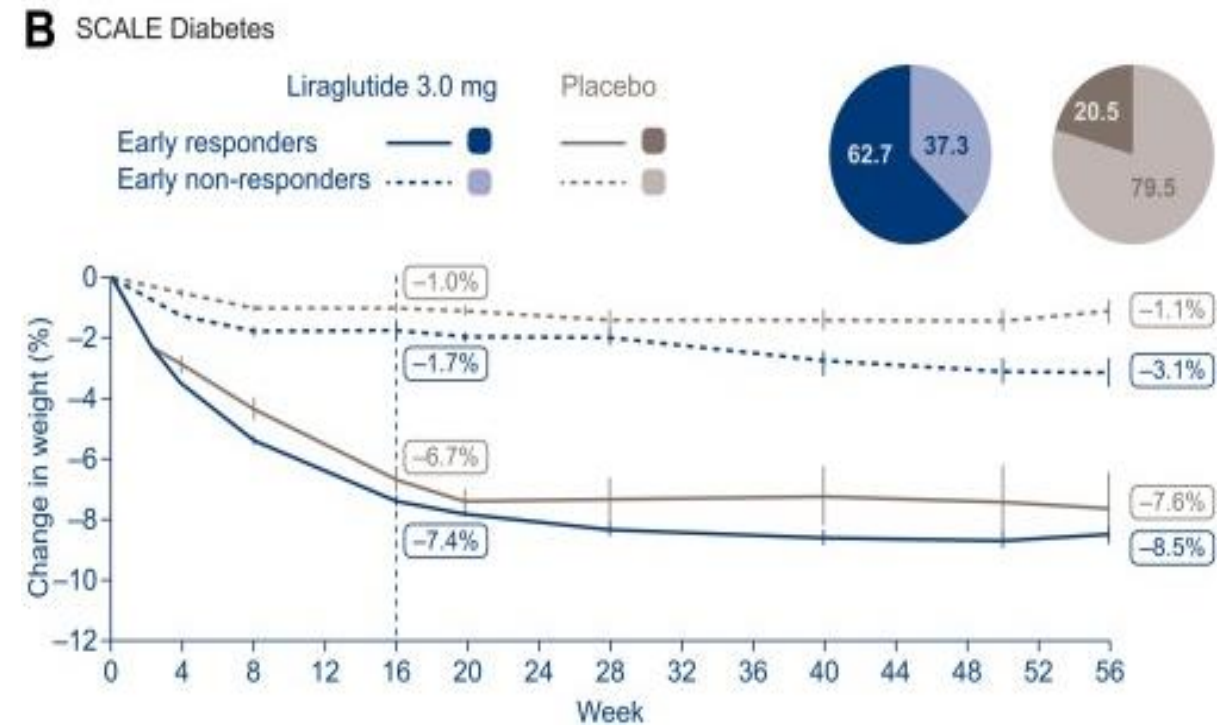
Early Response Predicts Long-term Efficacy

liraglutide 3 mg

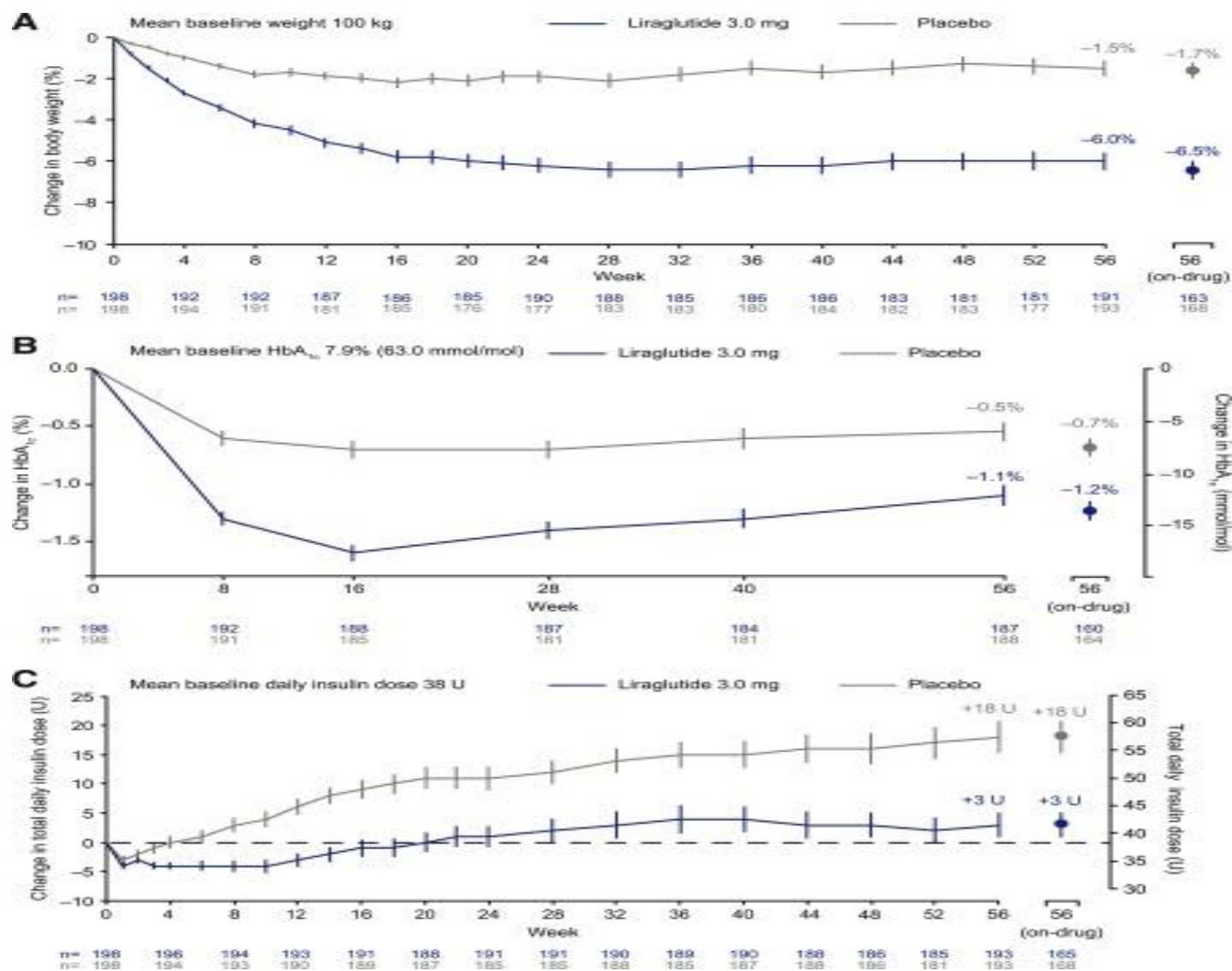
Non-Diabetes



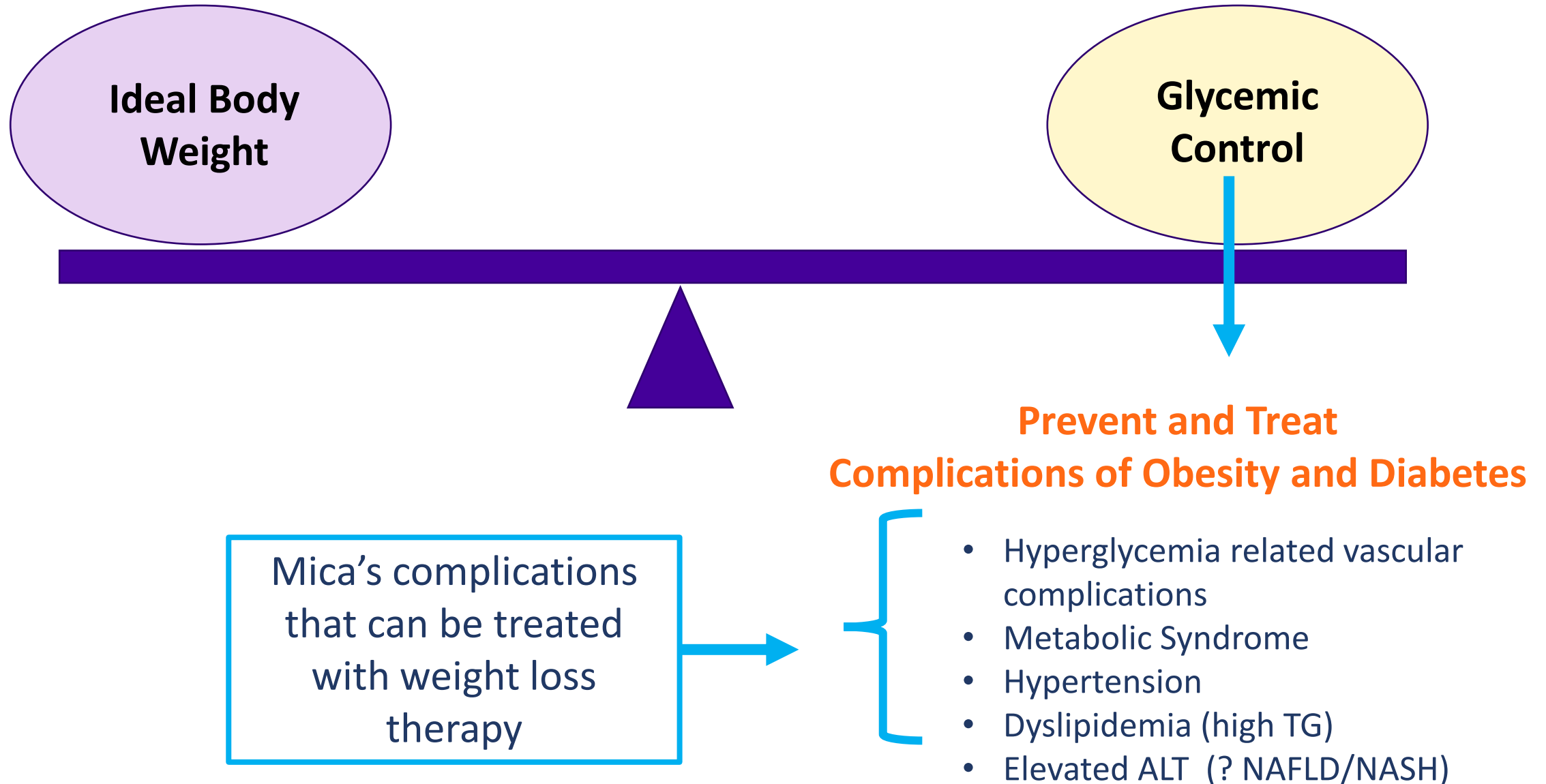
Diabetes



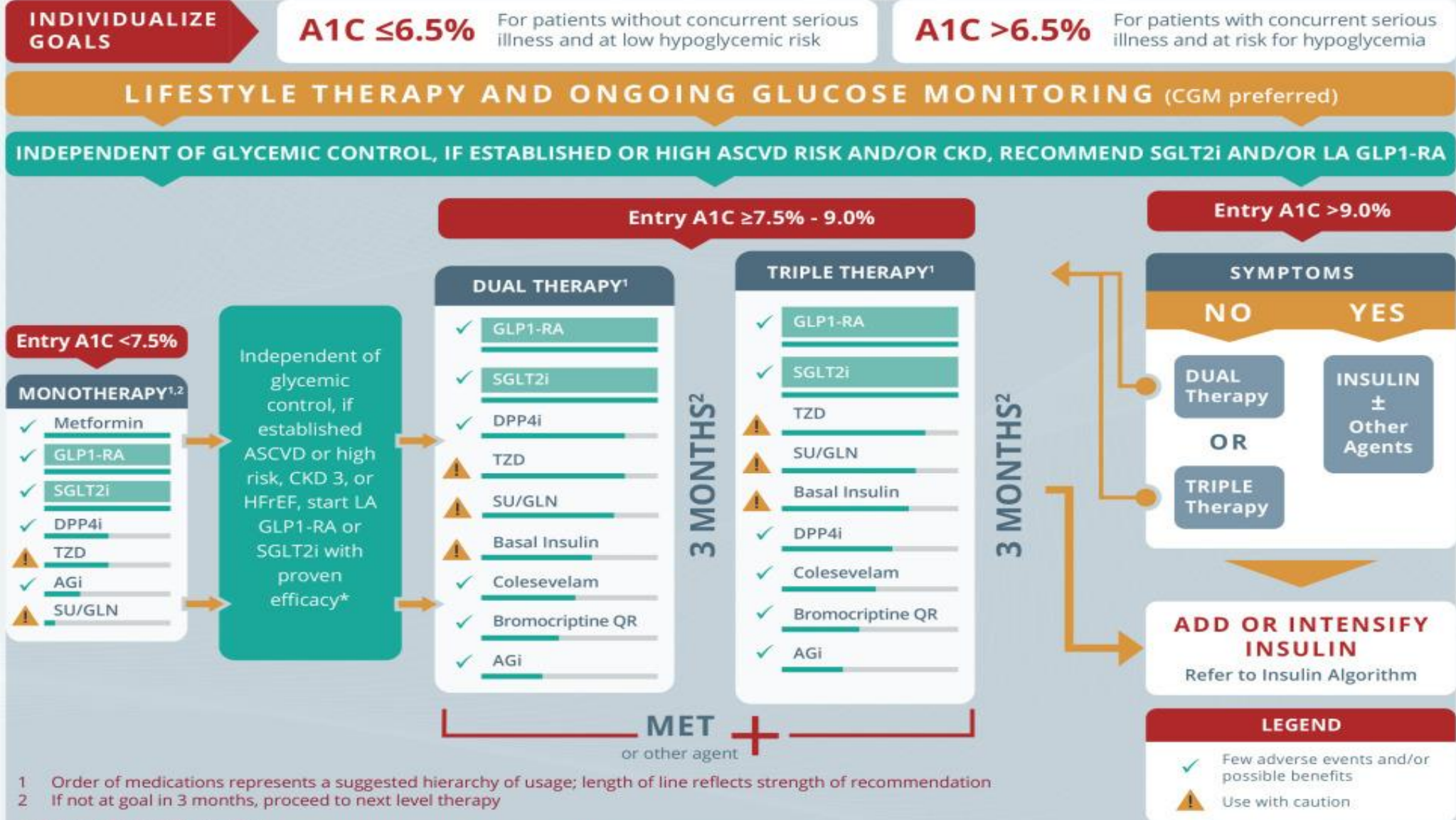
Liraglutide 3.0mg Added to Basal Insulin



Clinician and Patient: Harmonization of Treatment Goals



GLYCEMIC CONTROL ALGORITHM



Revised Treatment Approach for Mica

1. Discontinue DPP4 and glyburide for semaglutide starting at 0.25 mg/wk titrated to 2 mg/wk to achieve HbA1c < 7%. Consider adding SGLT2 inhibitor and basal insulin to GLP agonist as needed to maintain glycemic control.
2. Discontinue atenolol and substitute amlodipine 10 mg/day; discontinue paroxetine and substitute venlafaxine 150 mg daily.
3. She lost additional 6% at 3 months on new medication so it was continued resulting in 12% weight loss achieved at 1 year. Fasting glucose, blood pressure, triglycerides, ALT, and energy level all improved. She moves to San Francisco for better employment and to be near her sister and nieces for family support.