Treatment of Complicated Patients with Obesity

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OMA Advanced Certificate of Advanced Education in Obesity

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Disclosures

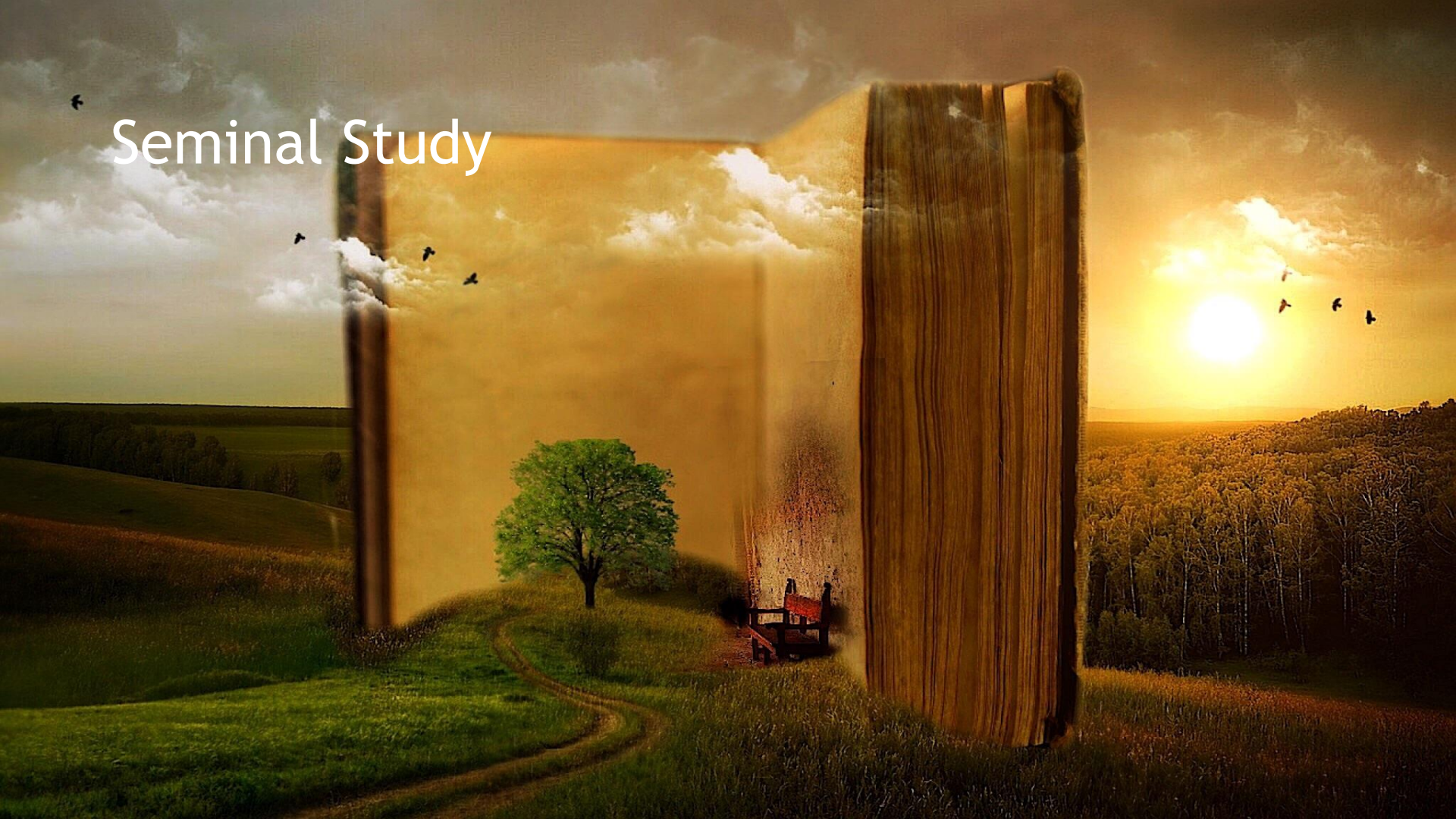
Company	Disease State/Topic	Role
Novo Nordisk	Obesity	Promotional speaker Advisory board
Acella	Thyroid	Advisory board Promotional speaker
Currax	Obesity	Advisory board Promotional speaker
Lilly	Obesity and Sleep apnea	Advisory Board Promotional speaker
BI	Obesity	Advisory Board
WW	Obesity	Advisory board

- All relevant financial relationships have been mitigated.

Objectives

- List the current identified complications of obesity
- Discuss the pathophysiology of obesity and how it causes various complications
- Review the treatment of obesity and how this effects complications
- Identify evidence-based guidelines for pharmacologic management of chronic disease of obesity and how the medication impacts the complications

Seminal Study



Complications of Obesity

T-P-3166: A systematic review and evaluation of current evidence reveals 236 obesity-associated disorders (ObAD)

Michele M. Yuen[1,2], Rebecca L. Earle[1], Nitya Kadambi[1], Joseph Brancale[1], David T. Lui[2], Scott I. Kahan[3], Lee M. Kaplan[1]

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Background

The breadth of comorbid conditions associated with obesity has not been comprehensively described. Using a systematic approach, we performed an extensive, systematic review of the literature to evaluate the extent of obesity-associated disorders (ObAD).

Aims

- To assess the **relationship between the severity of obesity**, using *body mass index (BMI) categories* and *waist circumference (WC)* as measures, **and the risk of having the ObAD** (manuscript in preparation)
- To assess the **population-attributable risk** of obesity in the major ObAD (manuscript in preparation)
- To assess the **benefit of weight loss** (to be addressed in Part 2 of this study)
- To evaluate the **strength of evidence** of the association between obesity and each ObAD using a modified **Grading of Recommendations Assessment, Development & Evaluation (GRADE)** approach

Methods I

Generated list of candidate ObAD based on *a priori* knowledge

↓

Searched PubMed using MeSH terms with Boolean logic
Example: comorbidity/epidemiology[MAJR] AND obesity/epidemiology[MeSH]

↓

Applied filters: "Human", "English", "Adults:19+years"

↓

Narrowed or broadened search by adding or removing MeSH terms

- 1 or more articles reporting an OR, RR or HR → Characterized strength of association by a modified **GRADE** approach
- No report of OR, RR or HR → Removed from final ObAD list

Methods II

Modified Grading of Recommendations Assessment, Development & Evaluation (GRADE)

Consider study design

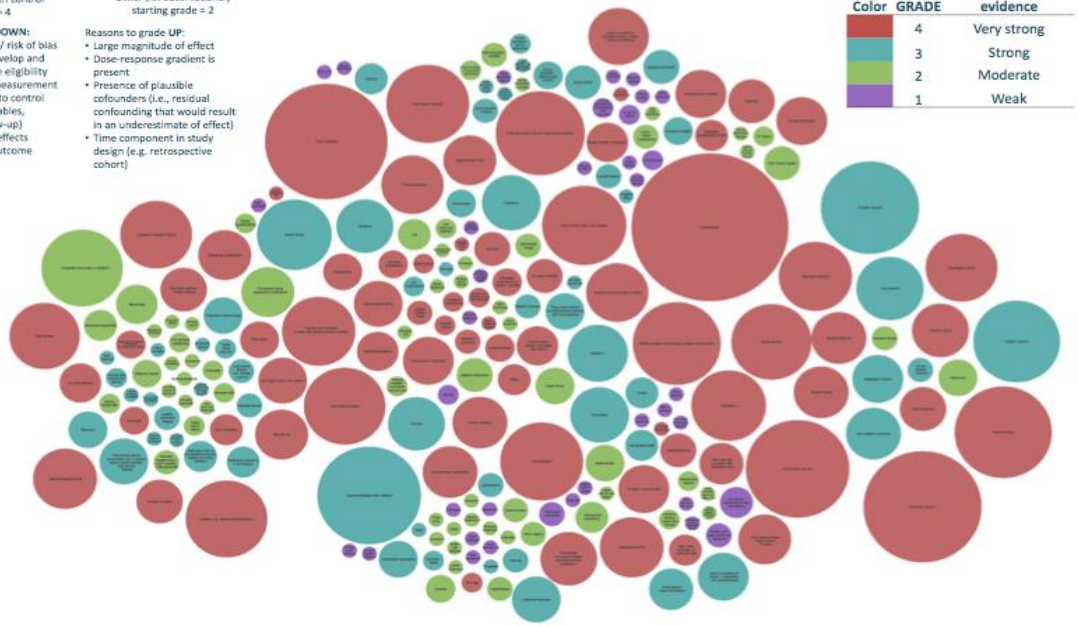
- Randomized control Prospective cohort with control starting grade = 4
- Other (ie. observational) starting grade = 2

Reasons to grade **DOWN:**
- Study limitations / risk of bias (e.g. failure to develop and apply appropriate eligibility criteria, flawed measurement methods, failure to control confounding variables, incomplete follow-up)
- Inconsistency of effects
- Indirectness of outcome
- Imprecision

Reasons to grade **UP:**
- Large magnitude of effect
- Dose-response gradient is present
- Presence of plausible cofounders (i.e., residual confounding that would result in an underestimate of effect)
- Time component in study design (e.g. retrospective cohort)

Figure: Strength of evidence for each of the 236 ObAD

- ObAD are clustered by discipline and organ system affected (if applicable)
- Size of the dot represents number of article retrieved for the individual ObAD.
- Color of the dot represents the highest GRADE of retrieved articles



Results

- 236 ObAD were identified
- Strongest associations (≥50-100 relevant, high-quality articles each) were observed for **cardiovascular disorders, cancers, selected infections, obstetric conditions**
- Moderate associative evidence (10-50 articles each) was found for **GI, renal, orthopedic, psychiatric and dental** disorders
- Weak evidence (<10 qualifying articles) was identified for **hematological, pulmonary, neurological, rheumatological, ENT, surgical and ophthalmological** ObAD
- Weakest evidence (10-50 cross-sectional studies) was found for **quality of life** disturbances **and dermatological** ObAD

Conclusions and Implications

- Obesity is linked to over 200 discrete disorders
- This number is far greater than previously reported
- The diseases that obesity is linked to comprise 35% of non-fatal global burden of disease and 38% of causes of global causes of death based on data from 2015 (retrieved from http://www.healthdata.org/gbd)
- This methodology provides a framework for further study to more precisely define these clinical relationships and to explore their pathophysiological basis and health policy implications.

Contacts

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Yeun, M., et al. (2016, November). A systematic review and evaluation of current evidence reveals 236 obesity-associated disorders (ObAD). Poster session presented at Obesity Week 2016, New Orleans, LA. Used with permission

All Cause Mortality

- Adults with obesity
  - Die 3.7 years earlier from all causes
  - Die 1.6 years earlier from CVD
  - Most at risk adults aged 45 years to 64 years with obesity
    - Die up to 12.8 years earlier than those who are at normal weight
- Most, if not all, of these sequela could be reduced with relatively moderate weight loss of just 5%-10%
  - Stage 2 and 3 obesity were both associated with significantly higher all-cause mortality
  - Overweight was associated with significantly lower all-cause mortality

Flegel, K., et al. (2013). JAMA*, 309*(1): 71-82.
Flegal, K., et al. (2007). JAMA *298*(17): 2028-2037.

Common Complications that Respond with the Treatment of Obesity

- Hypertension
- Diabetes Type 2
- Dyslipidemia
- MASLD
- Depression

Hypertension

Case 1

James is a 44-year-old

- PMH: hypertension, hyperlipidemia
- Medication: lisinopril 20mg
- VS today
  - 5’10” 230# BMI 33kg/m^2
  - 128/62 HR 72 RR 16
- Class 2, Stage 2

Photo courtesy of World Obesity Federation

Hypertension

- Obesity connection
  - Excessive reactive oxygen species production
  - abnormal RAAS, especially aldosterone
  - pro-inflammatory signaling
    - monocytes promote the inflammatory response changing the vascular endothelium
    - MCP-1 is elevated and a possible target for treatment
  - reduced nitric oxide bioavailability and activity

Han, T. & Lean, M. *Journal of the Royal Society of Medicine Cardiovascular Disease, 5*, 1-13.

Hypertension

- Obesity connection
  - PVAT – layer of adipose tissue around blood vessels
    - Normal adiposity – primarily anticontractile enhancing NO bioavailability within endothelium
    - Obesity – reduction in NOS expression in vascular tissues + increase in inflammation (TNF) = increase in oxidative stress and more inflammation so increase in contractile state of vascular bed
  - Leptin elevation increases SNS activation in CNS as well as receptors in peripheral endothelium and smooth muscle vasculature – further promotion of inflammation = development of arterial wall stiffening

Han, T. & Lean, M. *Journal of the Royal Society of Medicine Cardiovascular Disease, 5*, 1-13.

Clinical Implications

- Weight loss can partially or completely reverse the vascular consequence of obesity even after they occur
- AACE, 2016
  - Lifestyle interventions for 5-15% weight reduction to achieve BP reduction

Garvey, W., et al. (2016). *Endocrinology Practice, 22*(3), 1-203.

Clinical Implications

- AACE, 2016
  - AOMS should be considered
    - orlistat, lorcaserin, phentermine/topiramate ER and liraglutide 3mg monitor HR and BP closely with phentermine/topiramate ER and liraglutide 3mg
    - naltrexone ER/bupropion ER avoided if others can be used as no expectation of BP reduction and contraindicated in uncontrolled HTN
  - Bariatric surgery considered: Roux-en-Y or sleeve gastrectomy recommended

Garvey, W., et al. (2016). *Endocrinology Practice, 22*(3), 1-203.

Clinical Implications

- Other medications
  - ACE-I, ARBS first line for HTN if weight loss is not effective with above
  - Combination therapy add Calcium Channel blocker (beta-blockers and thiazide diuretics may be considered but can have adverse effects on metabolism, beta blockers and alpha blockers promote weight gain)
- Aldosterone antagonists for resistant hypertension

Poddar, M., Chetty, Y., & Chetty, V. (2017). How does obesity affect the endocrine system? A narrative review. *Clinical Obesity, 7*:136-144.
Garvey, W., et al. (2016). *Endocrinology Practice, 22*(3), 1-203.

Case 1 - Treatment plan

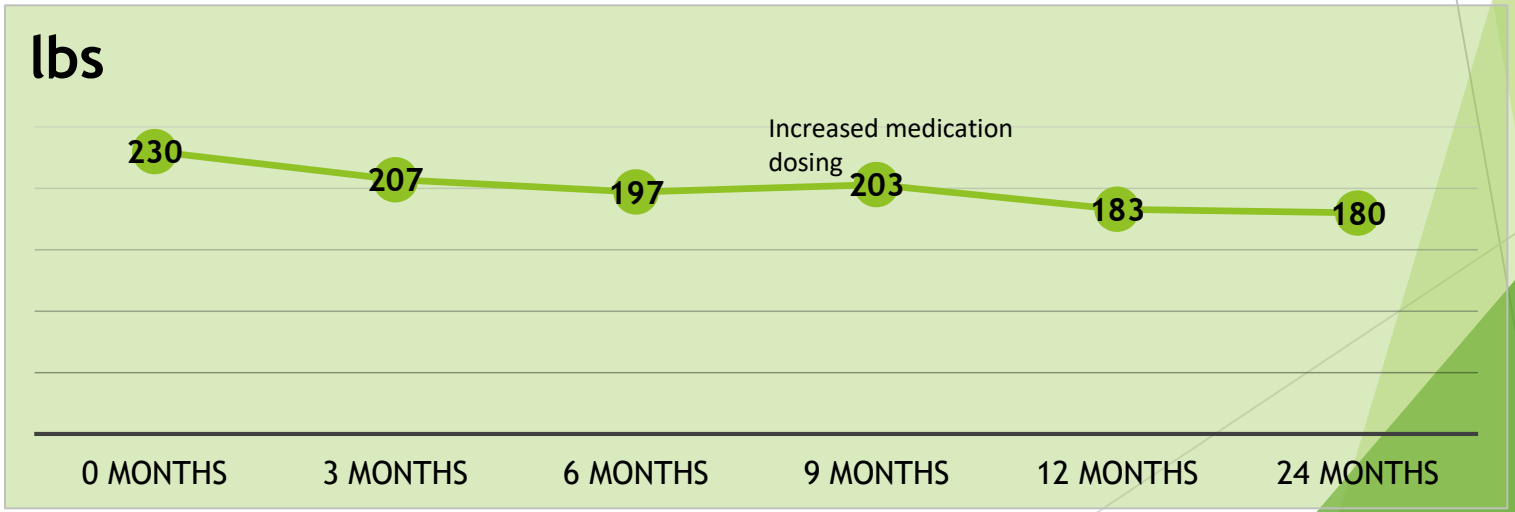
- Dietary Options
  - James selects Mediterranean eating plan
- PA
  - walking 10 minutes after lunch and dinner to work up to 40 minutes a day
- Begins Intensive Lifestyle Intervention program
  - Group meetings every other week

Photo courtesy of World Obesity Federation

Case 1 - Treatment plan

- Medication
  - BP controlled with ACE-I
  - Shared decision-making: starts phentermine/topiramate
    - 7.5mg/46mg until 9 months then increased to 11.25mg/69 mg

Photo courtesy of World Obesity Federation



T2DM and Depression

Case 2

Amanda is a 28-year-old

- PMH: T2DM (fairly-new diagnosis), depression
- Medication: metformin 2000 ER every day, citalopram 40 mg every day
- VS today
  - 5’6” 225# BMI 36.31kg/m^2
  - 112/62 HR 80 RR 16
  - PHQ9 11
- Labs HgBA1C 8.2
- Class 2, Stage 2

Photo courtesy of World Obesity Federation

IR/Prediabetes/DM

- Obesity Connection
  - Adipose tissue overwhelmed with FFAs - leads to fatty acid deposition in muscle, liver and pancreatic beta cells
  - Leads to decreased insulin sensitivity to glucose and insulin resistance
  - Leptin from adipocytes – releases aldosterone causing increase in SNS – increasing angiotension II
  - Hyperaldosterone leads to insulin resistance
    - IR – prediabetes – DM… Continuum

Poddar, et al. (2017). *Clinical Obesity, 7*:136-144.

Insulin resistance

- Obesity Connection
  - Dysfunctional insulin resistant adipocytes
    - Diminished ability to store lipids
    - Redistribution of fat to the intra-abdominal compartment
    - Accumulation of lipid in muscle and hepatocytes
    - Cornerstone factor affecting insulin insensitivity is the release of NEFAs

Al-Goblan, et al. (2014). *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, *7*, 587–591.

Diabetes

- Diabesity
- Endothelial dysfunction worsens
- β-cells can no longer compensate
- Hyperglycemia results
- Studies of interest
  - Nurses' Health Study - 2014 (275,000 participants) and Health Professionals Follow-up Study (2014)
  - Findings: individuals who gained 5-9.9 kg as young adults have 1.5-to-3-fold risk for DM, CVD, and HTN – increased risk with larger weight gain

Kodama, S., et al. *Obesity Reviews 15*(3): 202-14

Clinical Implications

- Study of Interest: Diabetes Prevention Program
  - Findings Subjects achieved approximately 6% mean weight loss at 2 years and 4% weight loss at 4 years in the lifestyle intervention arm, and, in post-hoc analysis, a progressive 16% reduction in T2DM risk was seen with every kilogram of weight loss
  - These combined data suggest that 10% weight loss will reduce the risk of future T2DM by ~80%
- IFG may relate to impaired liver functioning “hepatic insulin resistance” ? r/t ectopic fat deposits

https://www.niddk.nih.gov/about-niddk/research-areas/diabetes/diabetes-prevention-program-dpp last accessed 1/12/2021

Clinical Implications - Prediabetes

- Reduced calorie, healthy meal plan and physical activity with aerobic and resistance – prevention of progression to DM
- AACE:
  - AOM recommendation:
    - orlistat, phentermine/topiramate ER, or liraglutide 3mg for pts at risk of DM + ILI to obtain 10% weight loss
  - DM medication to add, if above not successful: metformin, acarbose, or thiazolidinediones

Clinical Implications - DM

- Treat with ILI for 5-15% weight loss OR MORE to achieve lowering of A1C
- AOMs considered in all patients with T2DM regardless of length of disease (AACE, 2016)
  - phentermine/topiramate ER – 10% weight loss at one year with 0.4% decrease in A1C in mild T2DM, 1.6% in more severe, long standing T2DM
  - All AOM's are appropriate
- Utilize weight neutral or weight loss causing DM meds, if possible
- Bariatric surgery – Roux-en-Y, sleeve gastrectomy, or biliopancreatic diversion

Garvey, W., et al. (2016). *Endocrinology Practice, 22*(3), 1-203.

Psychiatric Implications

- Obesity connection:
  - Obesity causes systemic inflammation and dysregulation of the HPA axis, and these are factors in depression
  - Additionally, obesity can lead to social stigmatization with society bias, body dissatisfaction, diminished self-esteem and stress in society
  - Poor eating, disability and pain associated with obesity can increase the risk of depression and anxiety

Garvey, W., et al. (2016). *Endocrinology Practice, 22*(3), 1-203.

Clinical Implications

- Weight loss has demonstrated an improvement in depression symptoms
- Monitor patients closely for mood disorders and suicidal ideation
- AACE, 2016:
  - orlistat, liraglutide 3mg and phentermine/topiramate ER at initiation and low dose may be considered for patients with depression – lorcaserin and naltrexone ER/bupropion ER used with caution or avoided if pt taking an antidepressant
  - Caution with obesity and anxiety and the use of maximal dose of phentermine/topiramate ER
  - metformin may be beneficial for patients with psychotic disorders taking antipsychotics
- Consider use of non obesigenic medications for depression and anxiety

Garvey, W., et al. (2016). *Endocrinology Practice, 22*(3), 1-203.

Case 2 - Treatment plan

- Dietary Options
  - Amanda selects low carbohydrate – well qualified ketogenic eating plan
- PA
  - Walking increasing steps to 10,000 a day + Pilates 2 x week
- Begins ILI program
  - Group meetings every other week

Photo courtesy of World Obesity Federation

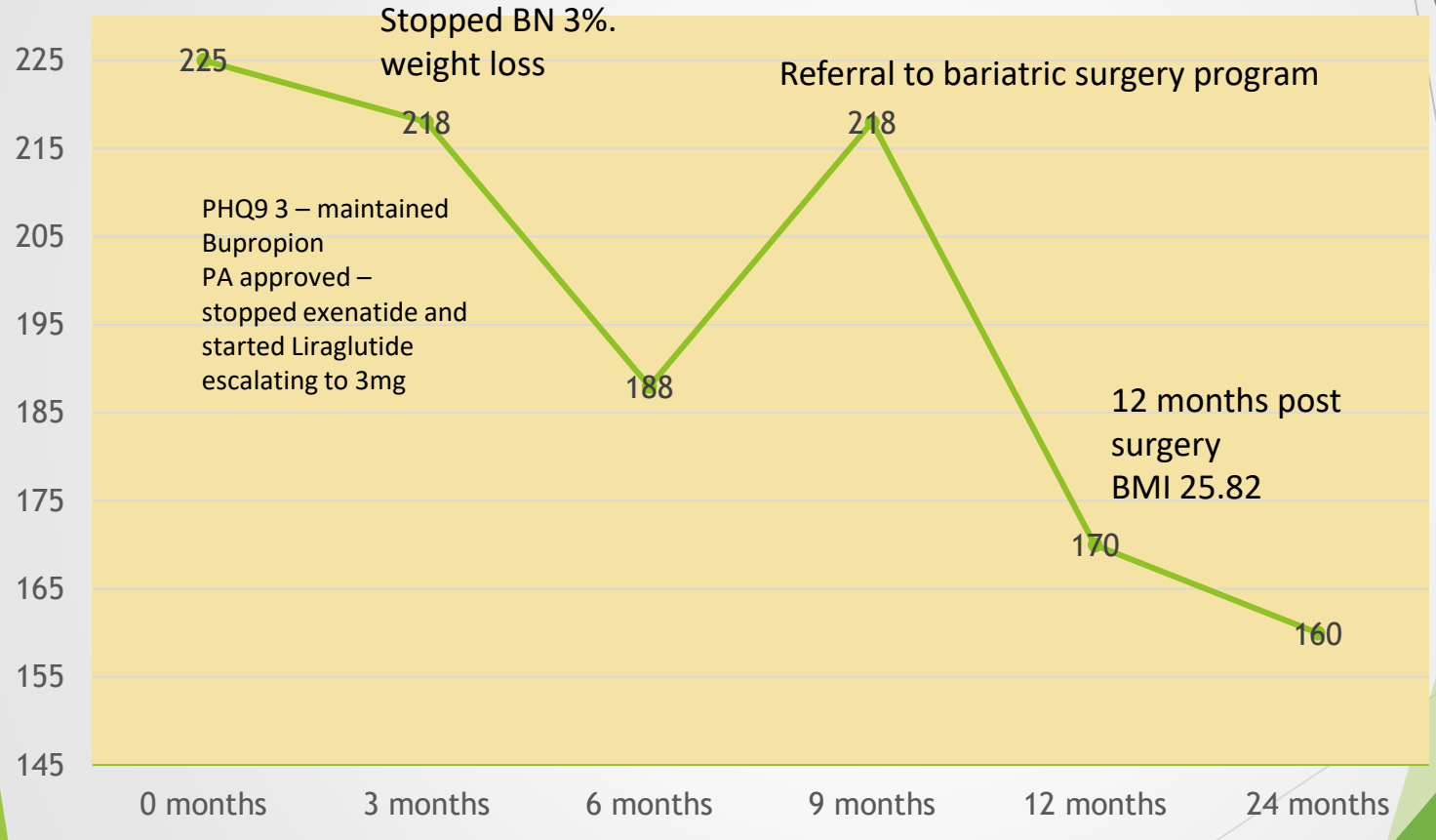
Case 2 - Treatment plan

- Medication
  - Consider changing citalopram d/t possible obesogenic
    - More weight neutral: bupropion, fluoxetine, vortioxetine
  - Shared decision-making: wants to start liraglutide 3mg, prior authorization requests other medications first
    - T2DM not controlled – add exenatide
    - Obesity – add bupropion/naltrexone

Photo courtesy of World Obesity Federation

Case 2 - Treatment plan

Photo courtesy of World Obesity Federation



Dyslipidemia and MASLD

Case 3

Miguel is a 20-year-old

- PMH: Hyperlipidemia, NAFLD
- Medication: Algae Omega-3 850mg
- VS today
  - 5’11” 222# BMI 30.96 kg/m^2
  - BP 124/86 HR90 RR 20
- Labs
  - TC 210mg/dL, LDL 120mg/dL Non-HDL 145 mg/dL, HDL 43mg/dL, Triglycerides 248 mg/dL, CHOL/HDLC ratio 4.2
  - AST 61 units/L. Alt 72 units/L
  - Platelet count 219 x 10-3/mL
  - HSI Score 40.4
- Class 2, Stage 1

Permission to use personal photo

Dyslipidemia

- Obesity connection:
  - Hypothesis – high CHO consumption drives hepatic VLDL production
  - Insulin resistance also elevates triglycerides
  - HDL becomes dysfunctional due to the inflammation and oxidative stress – the ability to cause cholesterol efflux lowers – HDL clearance occurs faster than production
  - Down regulation of Apo-A occurs

Han, T. & Lean, M. *Journal of the Royal Society of Medicine Cardiovascular Disease, 5*, 1-13.

Dyslipidemia

- Obesity connection:
  - FFAs from adipose tissue increases the amount of VLDL – leading to more TG
  - Relationship between BMI and circulating lipids is complex
  - Insulin and leptin are secreted in direct proportion, and adiponectin in negative proportion, to the size of the adipose mass

Han, T. & Lean, M. *Journal of the Royal Society of Medicine Cardiovascular Disease, 5*, 1-13.

Clinical Implications

- Lifestyle therapy
  - Physical activity, meal plan with reduced calories, minimizing sugar and refined CHO, avoiding trans fats and limits ETOH
  - PUFAs decrease TG
- 5 to 10% weight loss or more as needed to achieve therapeutic targets
- AOMS with life-style therapy
- Medications for hyperlipidemia if above unsuccessful (AACE)

Garvey, W., et al. (2016). *Endocrinology Practice*, *22*(3), 1-203.

Clinical Implications

- Study of interest: POUNDS LOST (2009)
  - 811 “free-living overweight or obese adults”
  - Findings:
    - Weight loss after six months and two years similar all four diets
    - Craving, fullness, hunger, and diet satisfaction similar
    - All diets improved risk factors for CV disease at 6 months and 2 years (reduced levels of TG, LDL, lowered BP, and increased HDL)
    - Heart-healthy, reduced-calorie diets, regardless of which macronutrients they emphasize, can help achieve and maintain weight loss with CV outcomes

Sacks FM, et al. N Engl J Med. 2009 Feb 26;360(9):859-73.

Liver

- MASLD (NAFLD) affects 60-80% of patients with DM + obesity and 100% of people with severe obesity
  - Pathophysiology of NAFLD includes genetic, dietary, metabolic and hormonal factors
  - Ectopic fat accumulation combined with low-grade chronic inflammation in an organ not able to accumulate fat
  - Hepatocytes become vulnerable to lipid oxidation, impaired apoptosis, and cytokine activity

Eslam M, et al. 2020 May;158(7):1999-2014.

Liver

- Obesity connection
  - Visceral adipose tissue produces FFA and diverse adipokines
    - Increased: TNF-a, resistin, interleukin-6
    - Decreased adiponectin
  - Increases ectopic fat accumulation and inflammation – including in the liver

Vizuete J, et al. J Clin Transl Hepatol 2017;5(1):67–75

Clinical Implications

- MASLD treatment as directed at obesity
  - Lifestyle modifications
    - 7% weight loss of baseline – significant improvements in steatosis and lobular inflammation
    - 9% body weight loss showed histologic improvement (may require as high as 40%)
  - Bariatric surgery
    - Some patients experience complete resolution of MASH
  - Medication: orlistat, liraglutide

Garvey, W., et al. (2016). *Endocrinology Practice*, *22*(3), 1-203.

Clinical Implications

- MASLD treatment is directed at obesity
  - Supplements
    - PIVENS study demonstrated Vitamin E improved steatohepatitis, enzyme levels and inflammation
    - Curcumin – showed decreased BMI, HgBA1C
    - Flavonoids – positive effect on lipid metabolism, insulin resistance, inflammation and oxidative stress
  - Eating plan
    - Mediterranean-type effect on hepatic steatosis independent of weight loss

Sanyal, A. J., et al. *The New England Journal of Medicine*, *362*(18), 1675–1685.

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Case 3

Miguel is a 20-year-old

- PMH: Hyperlipidemia, NALFD
- Medication: Algae Omega-3 850mg
- VS today
  - 5'11" 222# BMI 30.96 kg/m^2
  - BP 124/86 HR90 RR 20
- Labs
  - TC 210mg/dL, LDL 120mg/dL Non-HDL 145 mg/dL, HDL 43mg/dL, Triglycerides 248 mg/dL, CHOL/HDLC ratio 4.2
  - AST 61 units/L. Alt 72 units/L
  - Platelet count 219 x 10-3/mL
  - HSI Score 40.4
- Class 2, Stage 2

- Dietary Options
  - Miguel selects Whole Food Plant Based due to animal rights concern
- PA
  - Plays baseball 5 times a week and is in a strength training program
- Begins ILI program
  - Individual meetings every other week with provider

Case 3 - Treatment plan

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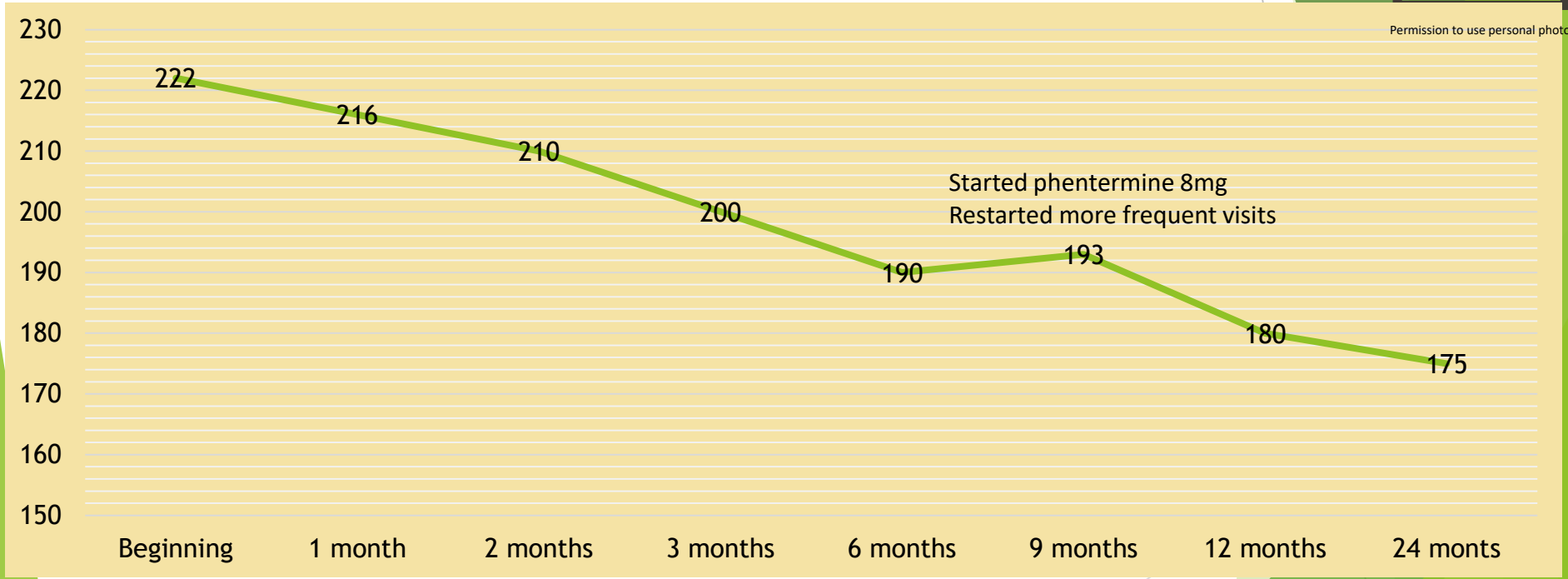


Multiple Complications and Comorbidities

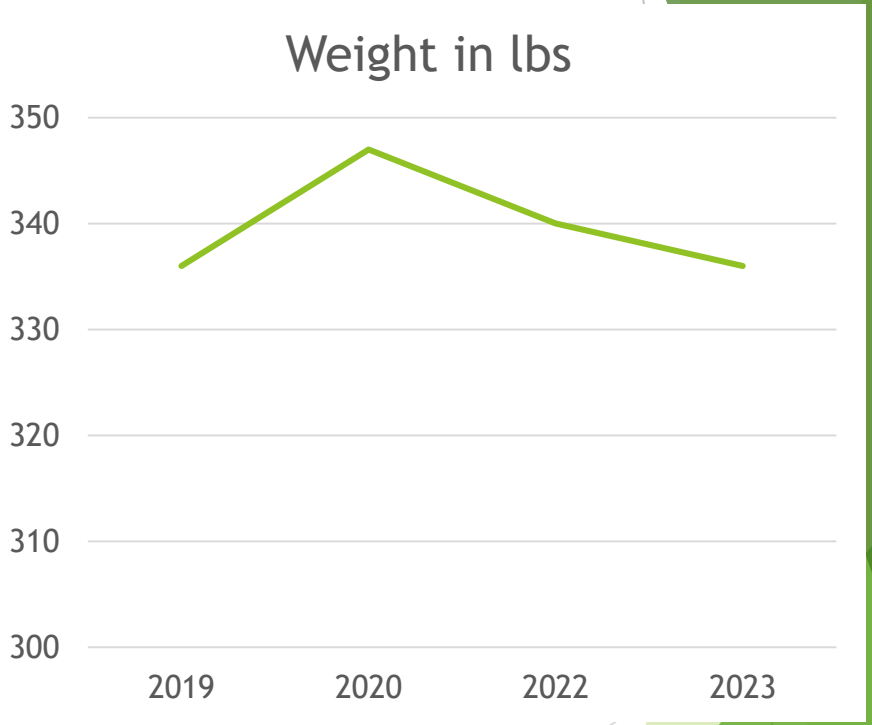
Case 4

- Jose is 59-year-old man
- Diagnosis
  - Diabetes at age 35 (FH of T2DM in mother and older sister)
    - Treatment working out at the gym 3-5 times a week
  - Obesity class 3 (BMI 44)
  - Hypertension
  - Mixed dyslipidemia
  - CAD – MI at age 48
- CKD Stage 3a
- Peripheral neuropathy
- Sleep Apnea
- MASLD
- Venous insufficiency

Case adapted from Ricardo Correa with permission presented at Clinical Pathways in T2D Care, Fellows Scholar Program 2024

Case 4

- Physical exam
  - Acanthosis nigricans on neck
  - Whitish stretch marks on abdomen
  - Bilateral edema on legs
  - Reddish brown patches with shiny skin both lower extremities

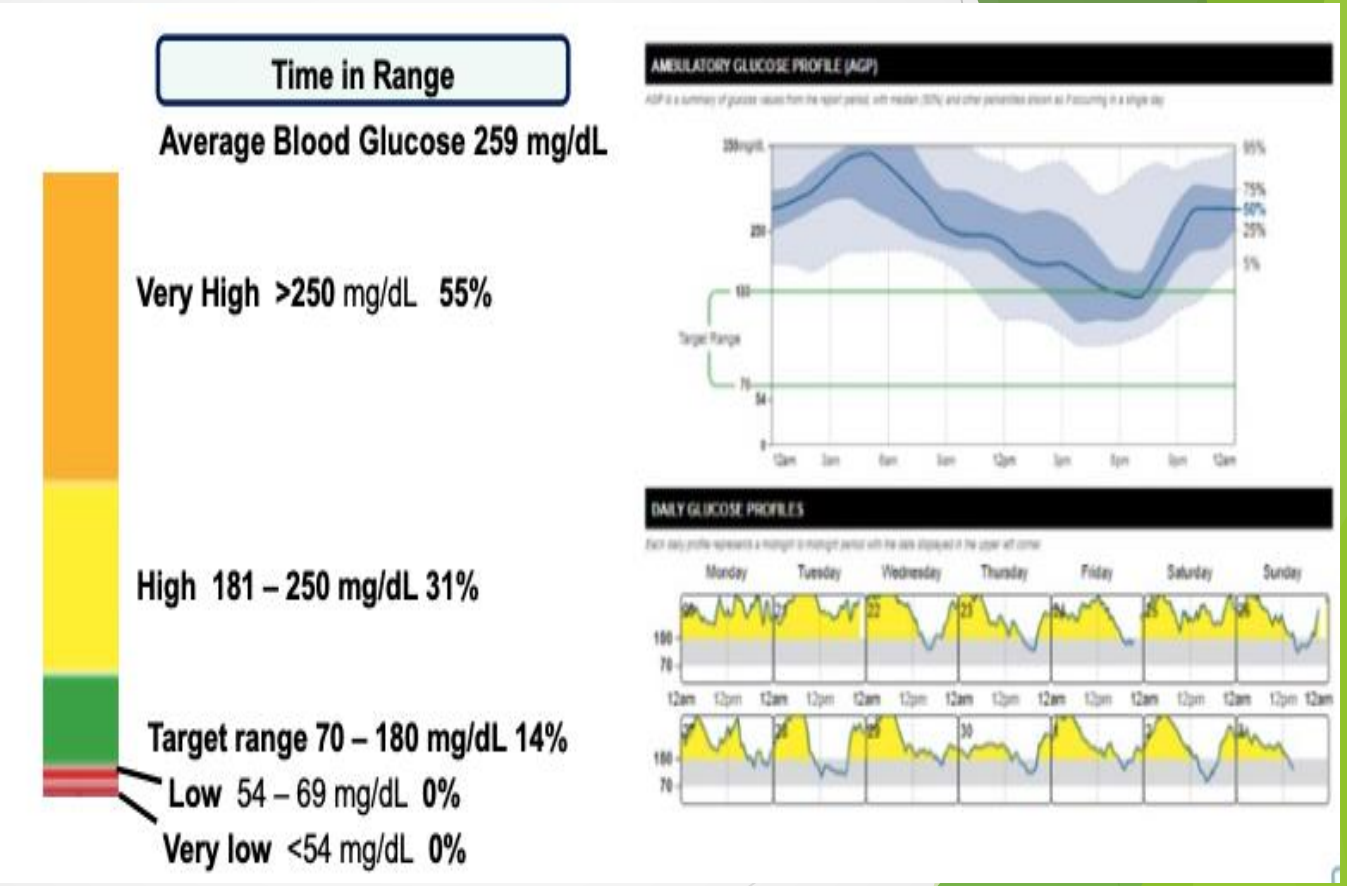


Case 4

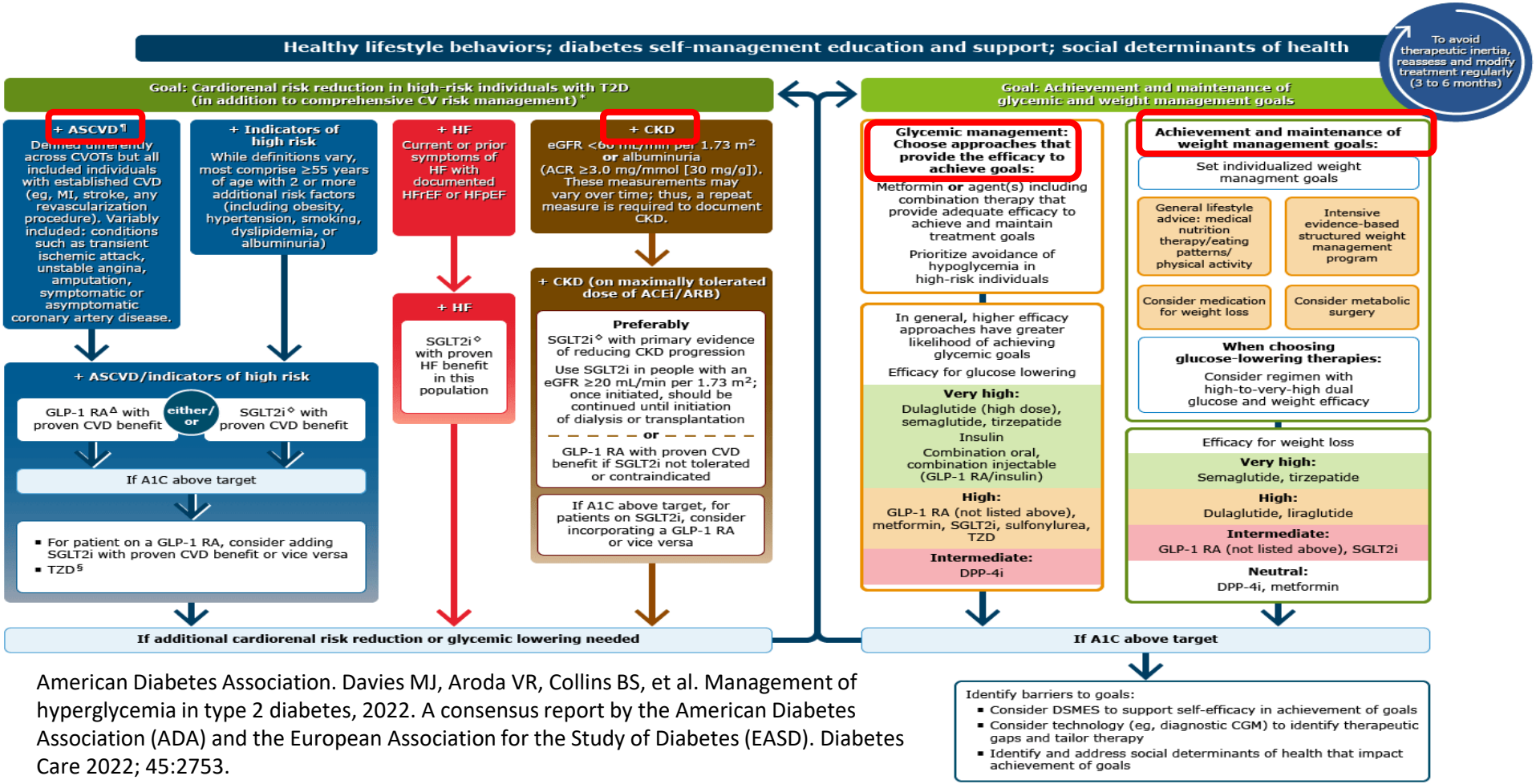
- Diabetes
  - U-300 insulin glargine 100 unites daily
  - Insulin lispro 4 units with meals + sliding scale
  - Glipizide 10 mg BID
  - Empagliflozin 10 mg QD
    - Previously on metformin – GI intolerant
    - Exenatide SQ stopped with insulin
- HTN
  - Lisinopril 40mg/d
- dyslipidemia
  - rosuvastatin 40 mg qd
- peripheral neuropathy
  - gabapentin 600 mg tid
- post MI
  - ACE-I (on for HTN)
  - Carvedilol 12.5 mg bid
  - Clopidogrel 75mg/d
  - Nitroglycerin 0.4mg tablets SL prn
- venous insufficiency with stasis
  - compression stockings
  - tacrolimus ointment 0.1% applied prn for itching
- CKD
  - ACE-1 (on for HTN)
  - Chlorthalidone 25mg qd

Case 4

- HgB A1C 9.5%
  - What to do???



Case 4



American Diabetes Association. Davies MJ, Aroda VR, Collins BS, et al. Management of hyperglycemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care 2022; 45:2753.

Case 4

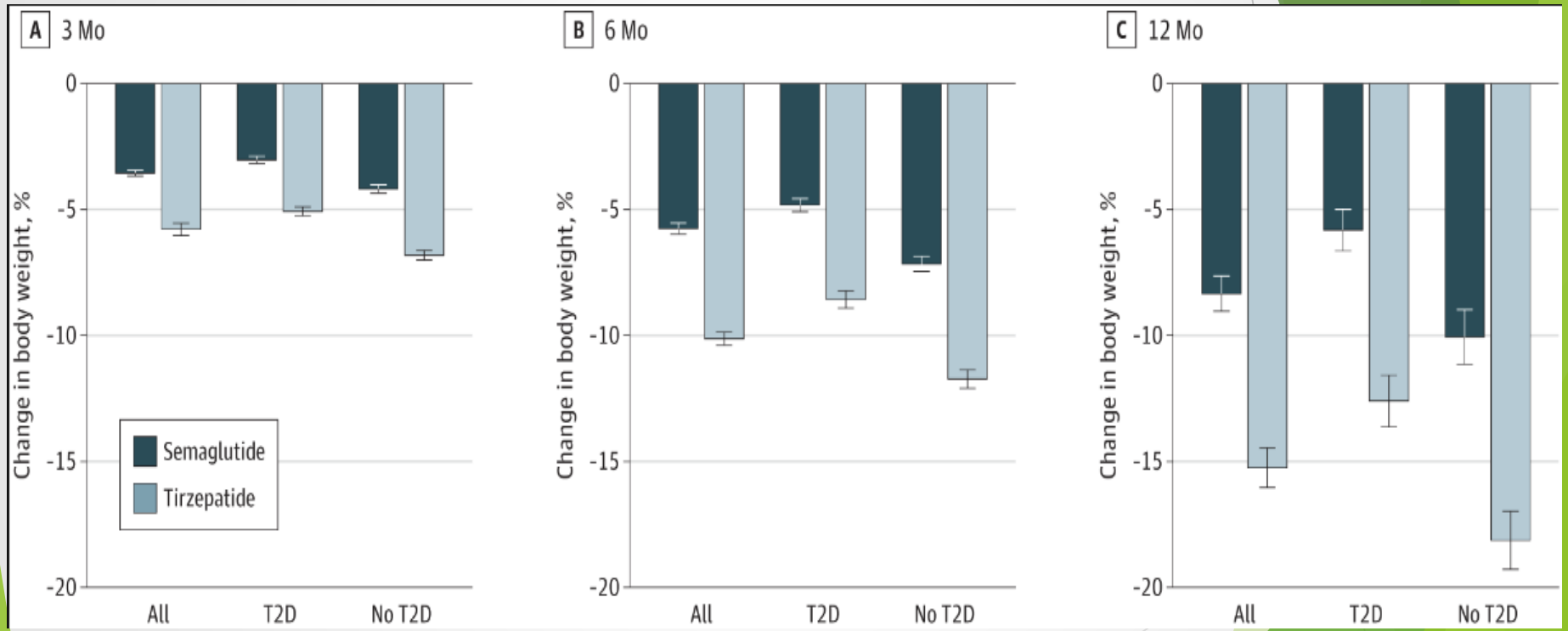
Chronic Kidney Disease
EGF < 60 mL/min

Prefer. SGLT2i associated with reduced progression of CKD
Or GLP1RA with CV benefit proven if SGLT2i not tolerated/contraindicated

- canagliflozin
- dapagliflozin
- empagliflozin
- semaglutide SQ
- dulaglutide
- liraglutide

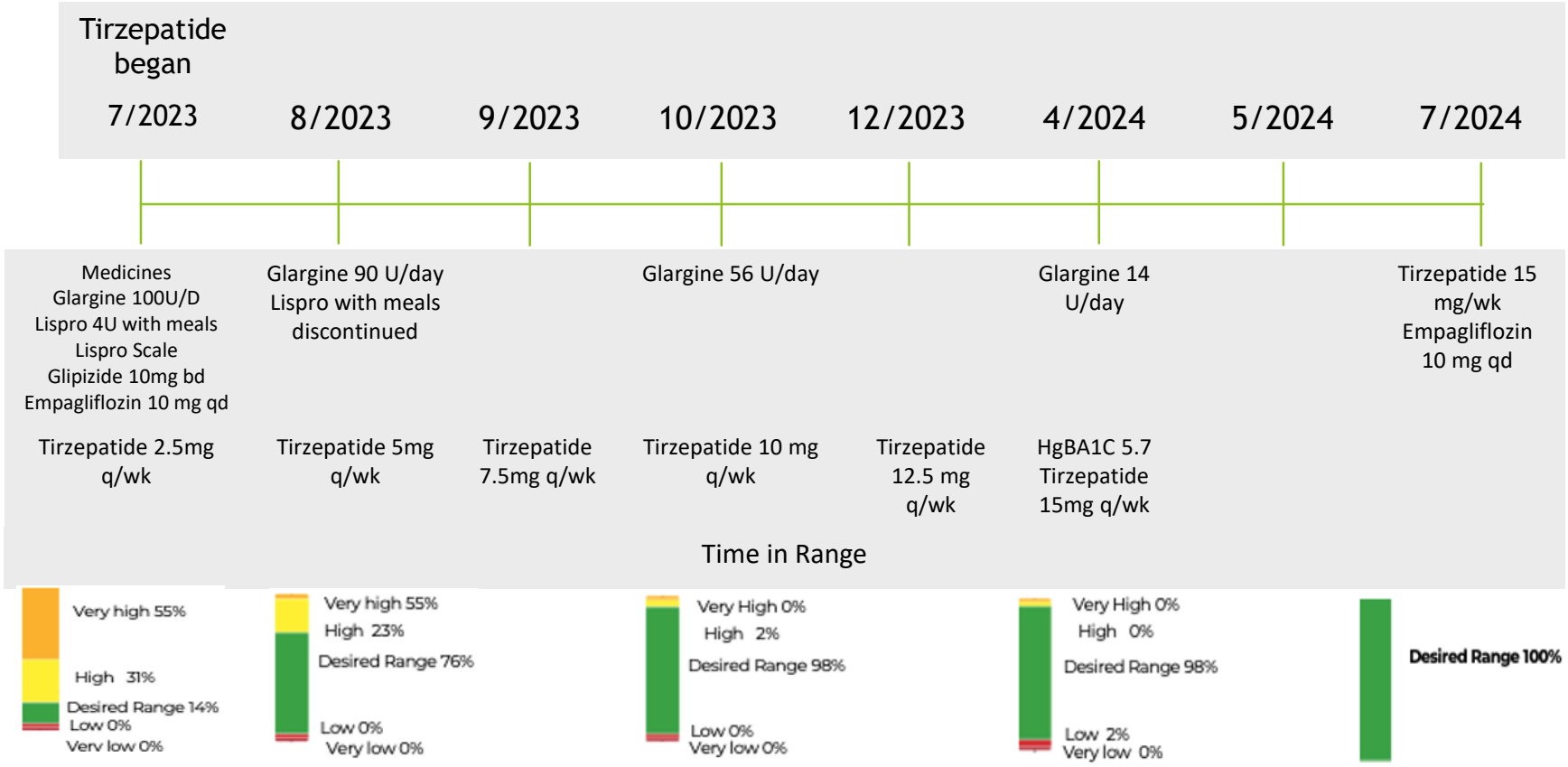
If HgBA1C is above the target, for patients already treated with SGLT2i, consider incorporating GLP1RA

Case 4 Weight Loss with GLP-1 RA/GLP1-RA GIP

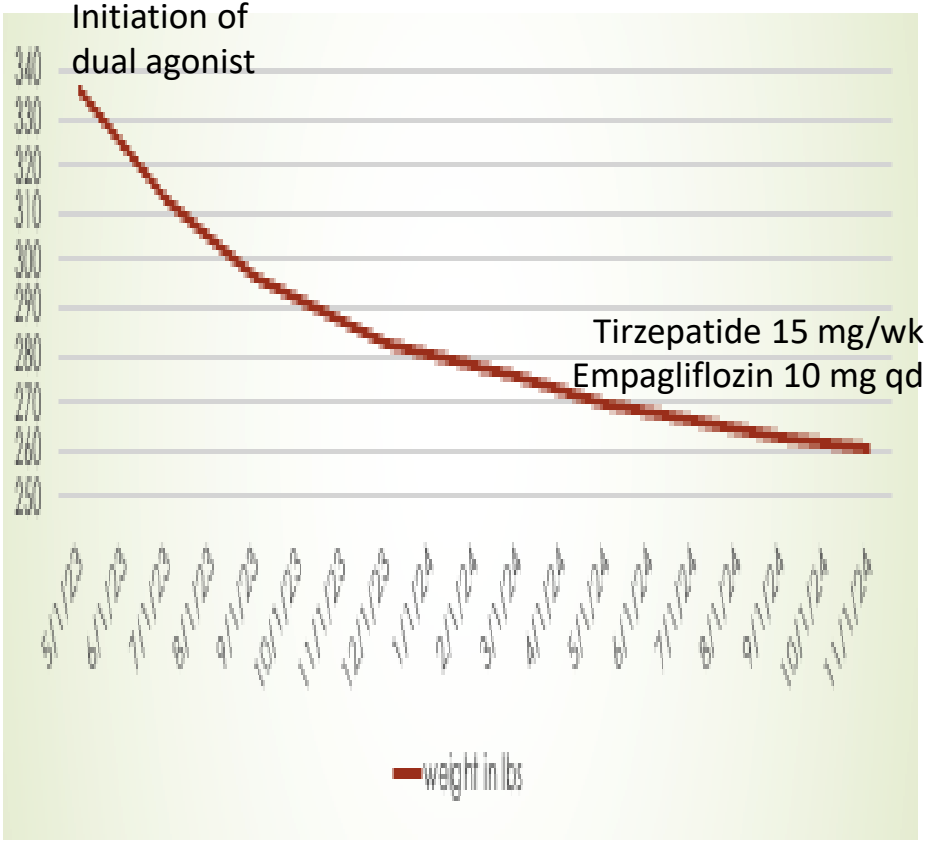


Rodriguez PJ, Goodwin Cartwright BM, Gratzl S, et al. Semaglutide vs Tirzepatide for Weight Loss in Adults With Overweight or Obesity. *JAMA Intern Med.* 2024;184(9):1056–1064. doi:10.1001/jamainternmed.2024.2525 Open Access Figure 3

Case 4 Changes in Treatment and Glucose Levels



Case 4 – Weight Graph



- Diabetes
  - Tirzepatide 15mg/wk
  - Empagliflozin 10 mg QD
- HTN
  - resolved
- dyslipidemia
  - resolved
- peripheral neuropathy
  - D/C gabapentin
- post MI
  - Lisinopril 40mg/d
  - Carvedilol 12.5 mg bid
  - Clopidogrel 75mg/d
  - Nitroglycerin 0.4mg tablets SL prn
- venous insufficiency with stasis
  - compression stockings
- CKD
  - ACE-1 (on for post MI)
  - Chlorthalidone 25mg qd

Process for Medication Decision Making

Considerations for Selecting an AOM

Reimbursement/cost

e**X**cluded for contraindications or side effects (check allergies to medications)

Additional reason to use an AOM: Complications or patient history

Off-label options – if not able to use on label medication

Medication selection with patient: Shared decision making

Meet Ellen

Image: © Obesity Action Coalition

- Social history: ETOH 1 x week, married with two teenagers at home, works outside the house as a nurse
- FH: father, mother, sister with HTN, diabetes, and all are “heavy”, no history of thyroid cancer
- Personal: no history of alcohol or drug abuse, no personal history of pancreatitis
- Obesity history: has been “heavy” since teenager but 40 weight gain over the past 4 years
  - has never seen a provider for weight/obesity treatment
  - Has tried lots of OTC remedies – ex raspberry ketones
- Eating – tries to be careful most days, craves sweets at night
- Activity – nothing specific right now

Ellen: Medical History

- Medical history:
  - Hypertension
  - Obstructive sleep apnea (OSA) - on BiPAP
  - Gastroesophageal reflux disease (GERD)
  - Depression
- Stage 2 obesity

- Medications:
  - Lisinopril 20mg once daily
  - Omeprazole OTC once daily
  - Vortioxetine 20mg/day
  - Multivitamin once daily
- Pregnancy prevention: IUD
- Allergies:
  - NKDA

	Yes	No
Has your NP or provider said that you have a heart condition OR high blood pressure	X	
Do you feel pain in your chest at rest, during your daily activities of living OR when you do physical activity		X
Do you lose balance because of dizziness OR have you lost consciousness in the last 12 months? (answer no if your dizziness was associated with over-breathing – including during vigorous exercise)		X
Have you ever been diagnosed with another chronic medical condition (other than heart disease or high blood pressure)? Please list condition(s) here _____		X
Are you currently taking prescribed medications for a chronic medical condition? Please list conditions and medications here: _____		X
Do you currently have (or have had within the past 12 months) a bone, joint, or soft tissue (muscle, ligament, or tendon) problem that could be made worse by becoming more physically active? Please answer NO if you had a problem in the past, but it **does not iimit your current ability** to be physically active. **Please list conditions here:** _____		X
Has your NP or physician ever said that you should only do medically supervised physical activity?		X

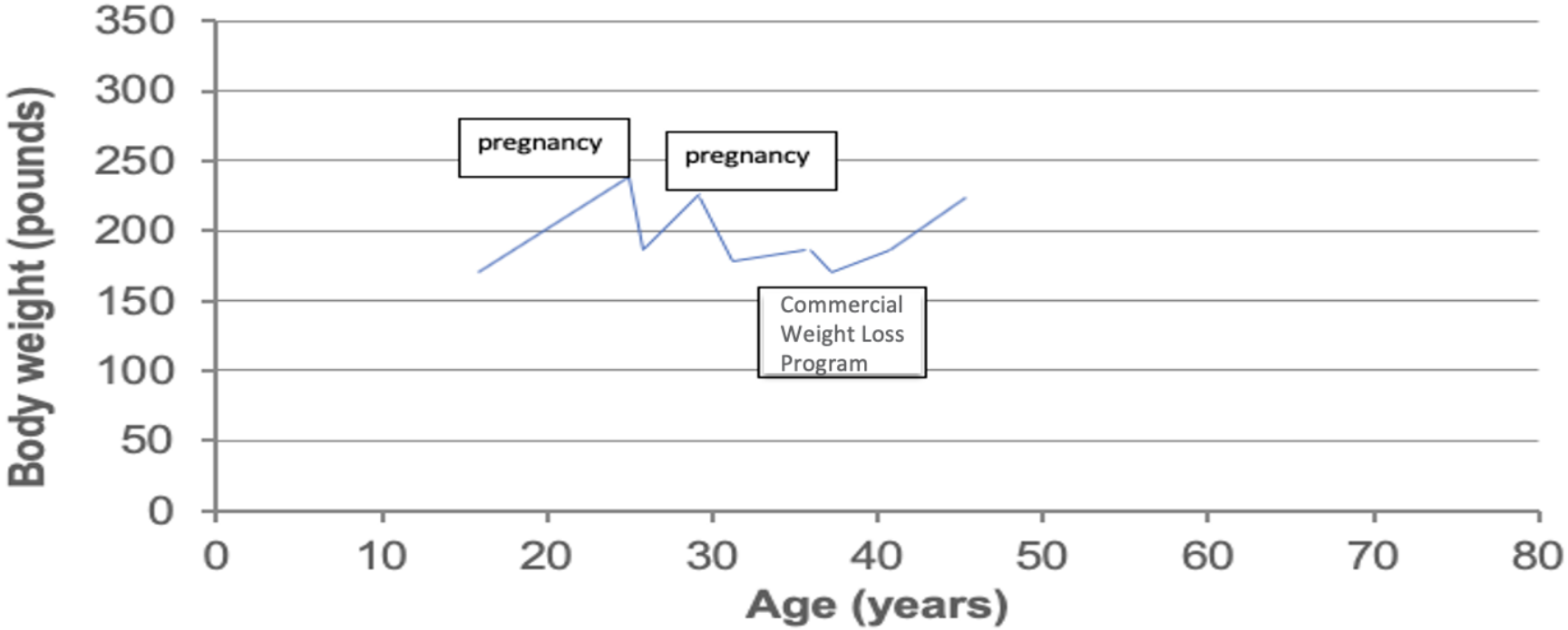
Adapted from PAR 7

First visit for obesity

- VS: 5'4" 212# 142/88 HR 78 RR 16 pOx 98
- BMI: 36.30 kg/m^2
- Waist circumference: 42"
- Neck circumference: 15"
- Screening tools: PHQ-9 (4), BED7 (neg), PAR-7, STOP-BANG negative

Body Weight Graph

Use this graph to chart life events, health conditions, times of stress, and other factors that influenced your weight



First visit for obesity

- Most recent labs: triglycerides 174, TC 236, LDL 134, HDL 48, AST 67, ALT 102, Vit D 34
- Fasting insulin 18, glucose 94 – HOMA IR is 4.17 – QUICKI 0.31
- Obesity Related Complications: elevated liver enzymes, dyslipidemia, HTN
- Obesity Co-morbidities: OSA, depression
- Obesogenic Medication: B Blocker
    - Staging of obesity
        - WHO Obesity Class II
        - EOSS – Stage 2
        - AACE/ACE – Stage 2

Image: © Obesity Action Coalition

Considerations for Selecting an AOM

Reimbursement/cost: Patient has good insurance, but will require prior authorization

e**X**cluded for contraindications or side effects (check allergies to medications) NKDA, No history of pancreatitis, seizures or FH of thyroid cancer

Additional reason to use an AOM: HTN and insulin resistance, HTN and depression are controlled. Has tried OTC orlistat and couldn't tolerate the SE. Craving of sweets in the evening

Off-label options – if not able to use on label medication

Medication selection with patient: Shared decision making

Your choice

Which medication would you recommend to the patient?

a. liraglutide
b. naltrexone/bupropion ER
c. orlistat
d. phentermine
e. phentermine/topiramate ER

Shared decision making

Liraglutide	No contraindications – benefit on insulin resistance. No personal history of pancreatitis, MTC, MEN2 or FH of MTC
Naltrexone/bupropion ER	No history of seizure. Craving of sweets in the evening
Orlistat	Patient tried this OTC and was unable to tolerate the GI side effects
Phentermine	No contraindications – but will need to consider dosing at lower for long term
Phentermine/topiramate ER	No contraindications, BP will need to consider dosing at lower for long term
Semaglutide	No contraindications – benefit on insulin resistance. No personal history of pancreatitis, MTC, MEN2 or FH of MTC
Tirzepatide	No contraindications – benefit on insulin resistance. No personal history of pancreatitis, MTC, MEN2 or FH of MTC

Measuring Success

Begin therapy with naloxone/bupropion	Initiate 8mg-90mg tablet one/day, moving up weekly until 4 tablets a day
Effective Response to Therapy	> 5% weight loss from baseline 12 weeks after maximum dose
Improvement in CV risk markers	Improvement in BP and insulin resistance

Continue to see the patient every 2-4 weeks

- IBT
  - Can be done by other providers as well: dieticians, PT/exercise physiologist, health coaches
- Monitoring: BP, weight

Visit at 16 weeks

- VS: 124/66 HR 82 RR 16 pOx 97% Weight 194#
- Since being at maximum dosing of medication (12 weeks) has lost only 3% of total body weight
- Continues to eat whole food plant based
  - Has been able to stop BP medication (has lost 8% since beginning of treatment, only 3% with medication)
- Activity is continuing with Jujitsu and walking
- Education at this meeting will be related to next medication

Ineffective Response to Therapy

If no clinical improvement (4-5% weight loss) after 12 weeks of maximum dose with one anti-obesity medication, consider:

Increasing anti-obesity medication dose, if applicable

O R

Alternative anti-obesity medication

Bray GA, et al. Lancet 2016;387:1947-56. Apovian CM, et al. *J Clin Endocrinol Metab* 2015;100:342-62.

Shared decision making

Liraglutide	No contraindications – benefit on insulin resistance. No personal history of pancreatitis, MTC, MEN2 or FH of MTC
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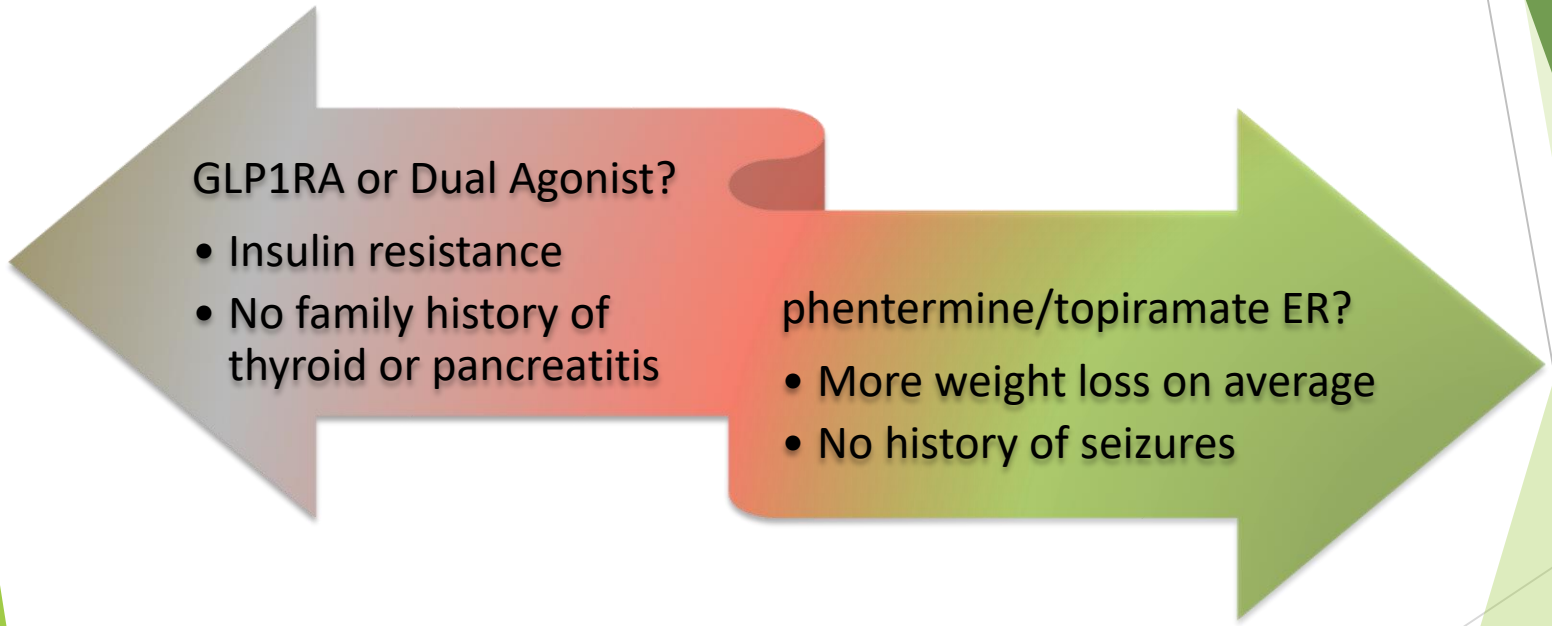
Considerations for Switching Ellen's Therapy



Off-Label Pharmacology

Reasons

- Cost
- Supply
- Evidence for use post bariatric surgery

Key Take Aways

- Obesity is a chronic and often progressive condition
- Obesity management is not about simply reducing numbers on the scale, but addressing complications
- Early intervention means addressing root causes and removing roadblocks
- Success is different for every individual
- **NO SHAME, NO BLAME**

Thank you

- Q and A

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