Cardiometabolic Treatments for Obesity

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Disclosure

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

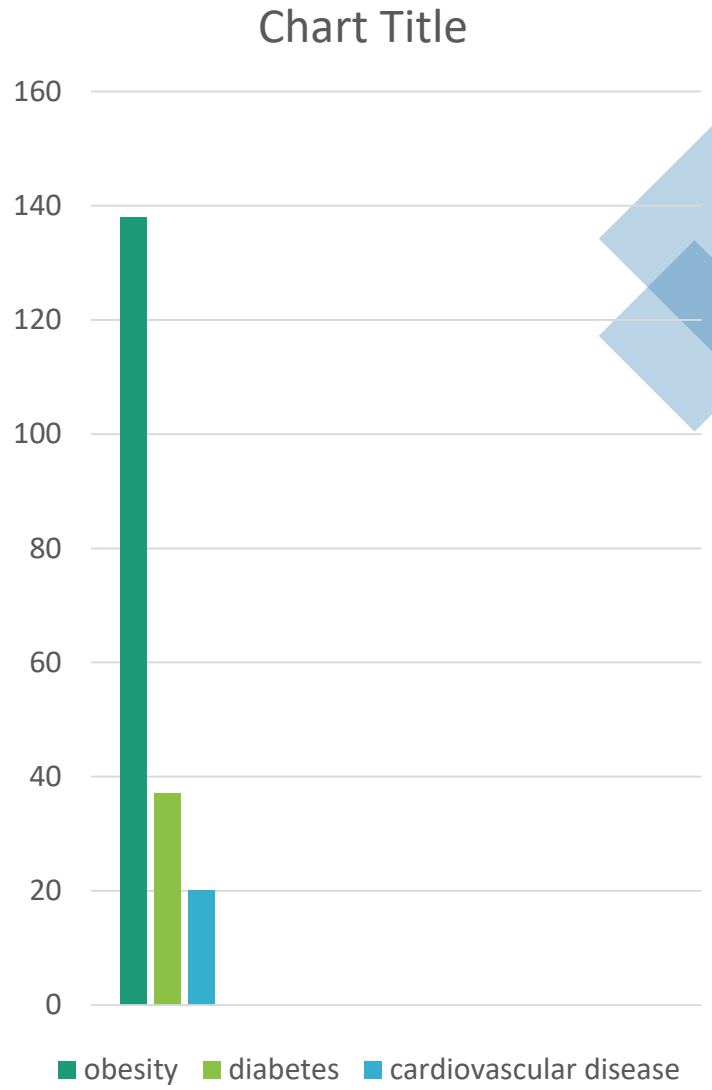
Describe	Describe the epidemiology, pathophysiology and history of cardiometabolic conditions with a focus on pre-obesity and obesity
Compare	Compare pharmacokinetics of novel and traditional obesity therapeutics which includes patients with Type 2 diabetes (SGLT2is, GLP1s and GIP/GLP-1 agonist)
Discuss	Discuss indications for novel anti-obesity therapies and their cardiac implications
Explain	Explain strategies to overcome barriers to medication access

Describe

Describe the epidemiology, pathophysiology and history of cardiometabolic conditions with a focus on overweight and obesity

Epidemiology

- Cardiovascular Heart **Disease**
  - 20.1 million adults have CAD
  - https://www.cdc.gov/heartdisease/facts.htm
- Diabetes (Type 2)
  - 37 million Americans have diabetes (about 1 in 10), and approximately 90-95% of them have type 2 diabetes
  - https://www.cdc.gov/diabetes/basics/type2.html
- Obesity
  - Obesity 41.9% of adults
    - 19.7% of children and adolescents
  - Obesity-related conditions include heart disease, stroke, type 2 diabetes and certain types of cancer. These are among the leading causes of preventable, premature death
  - https://www.cdc.gov/obesity/data/adult.html



DIFFERENCES IN HEALTHCARE

- Diabetes and CVD are not “carve outs” by insurances
- Obesity medications may be labeled ”vanity drugs”

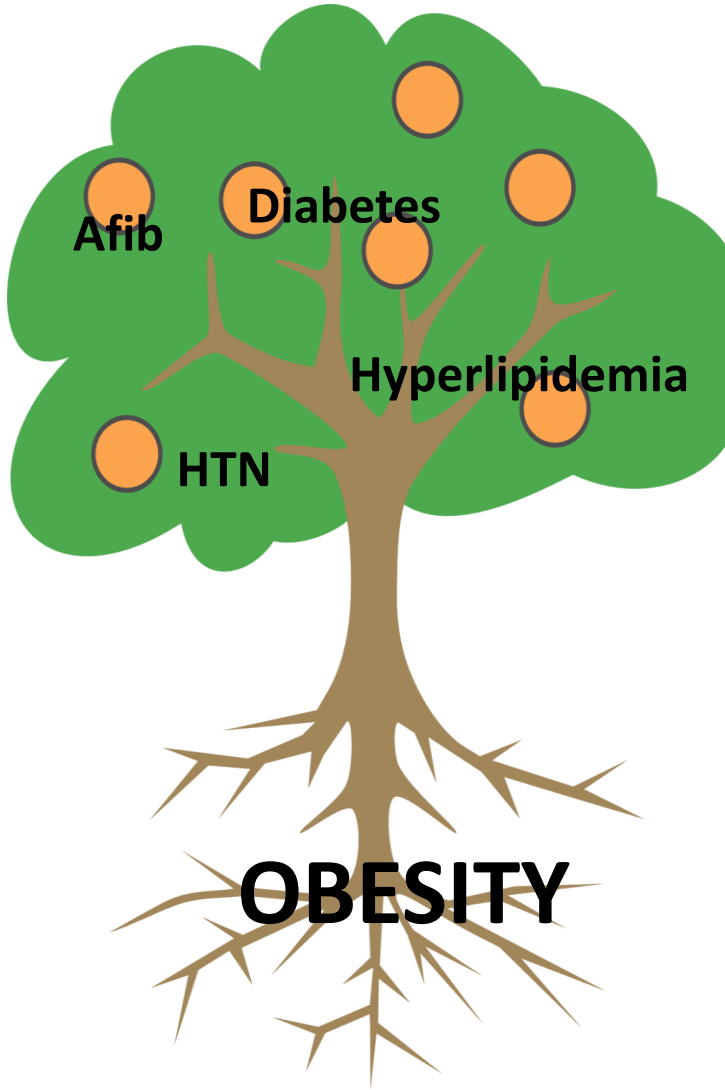
OBESITY

Diabetes

CVD

Treatment Difference

- Long standing medications targeting lipids, blood pressure, and glycemic control with clinical benefits through large randomized outcome trials
- Providers more likely to treat rather than to target the upstream cause >>>>> high-risk adiposity (Piche, 2020)
- Treat the roots not just the fruits (Dr. Lydia Alexander, 2022, OMA president elect)



Piché, M. E., Tchernof, A., & Després, J. P. (2020). Obesity Phenotypes, Diabetes, and Cardiovascular Diseases. *Circulation research*, *126*(11), 1477–1500. https://doi.org/10.1161/CIRCRESAH

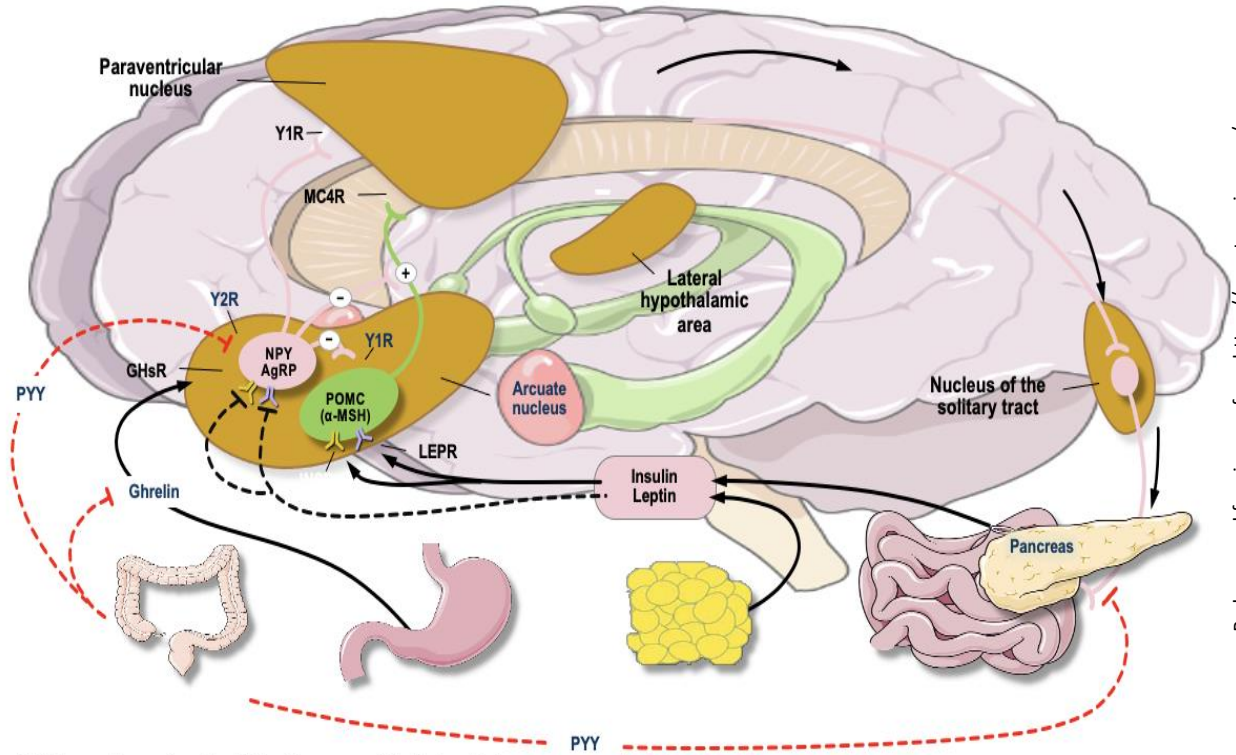
Obesity Pathophysiology

Disordered Energy Regulation System

Overeating does not cause obesity
Obesity causes overeating

1. Increase amount of adiposity
    - Intertwining of genetics, environment and biology
2. Biological defense of the increased adiposity
    - Evolution: conserve body fat
    - Physiologic defense of higher body weight

- **Question – how does excess body fat mass come to be biologically defended**
    - Hypothesis – inflammatory response in the hypothalamus, inducing injury of hypothalamic neurons involved in energy homeostasis



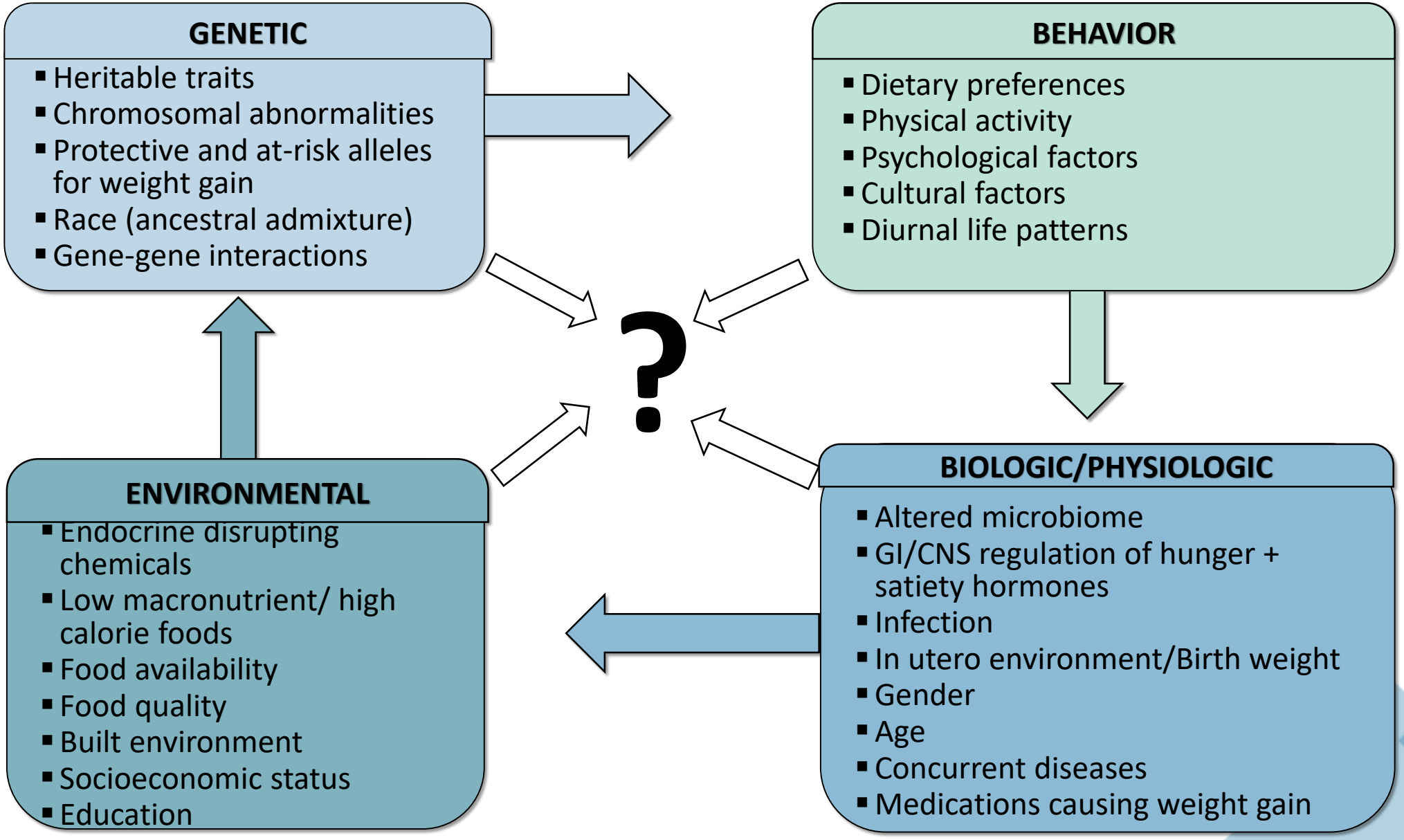
α-MSH, α-melanocyte-stimulating hormone; GHsR, growth hormone secretagogue receptor; INSR, insulin receptor; LEPR, leptin receptor; MC4, melanocortin-4 receptor; POMC, pro-opiomelanocortin; **Y1R, NPY Y1 receptor; Y2R, NPY Y2 receptor.**
Apovian CM, et al. *J Clin Endocrinol Metab.* 2015;100(2):342-362.

Redrawn and free images from https://smart.servier.com/

Neuroendocrine disease

Michael W Schwartz, Randy J Seeley, Lori M Zeltser, Adam Drewnowski, Eric Ravussin, Leanne M Redman, Rudolph L Leibel, Obesity Pathogenesis: An Endocrine Society Scientific Statement, *Endocrine Reviews*, Volume 38, Issue 4, 1 August 2017, Pages 267–296, https://doi.org/10.1210/er.2017-00111

Multifactorial Etiology

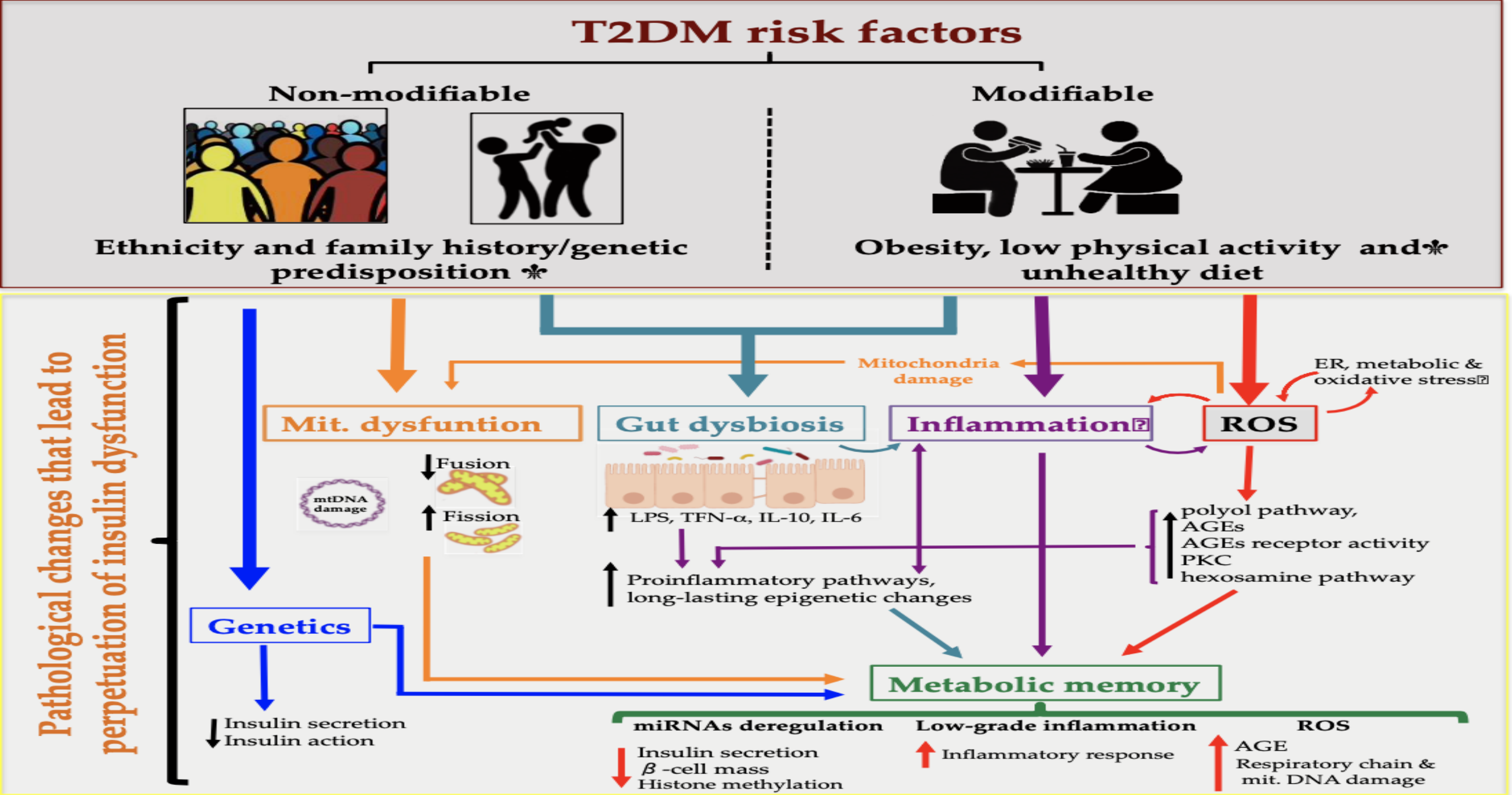


Golden A. Obesity. In A. Hollier (Ed.) 2016:281-285; Locke A. et al. *Nature*. 2015; 518(7538):197-206

Diabetes Pathophysiology

- Defective insulin secretion by pancreatic b-cells
  - Insulin secretion reduced
  - Body unable to maintain physiological glucose levels
- Inability of insulin – sensitive tissues to respond to insulin
  - IR increases glucose production in the liver and decreased uptake in the muscle, liver and adipose tissue
- Inadequate compensatory insulin secretory response

IR --> hyperglycemia ----> prediabetes ------> diabetes



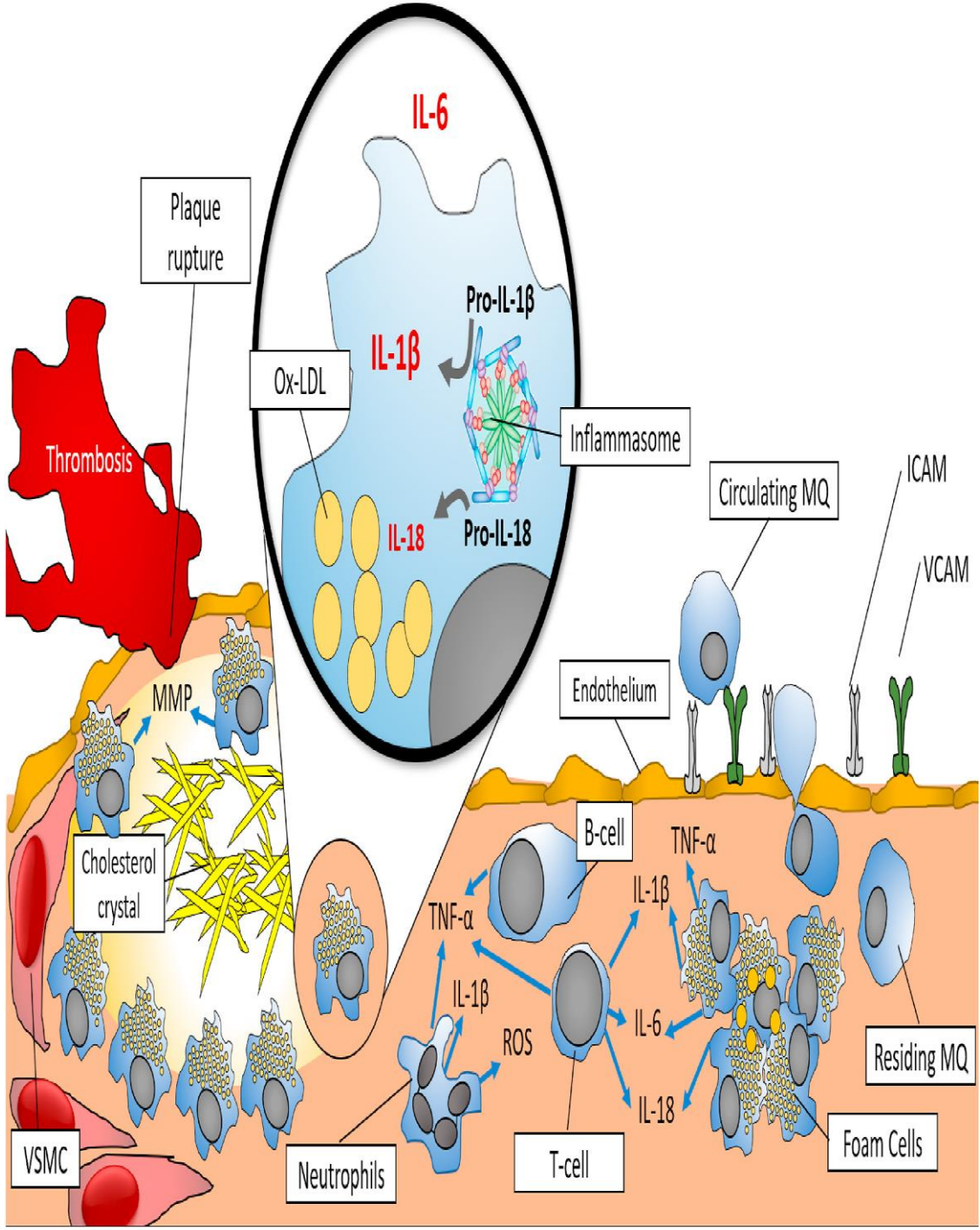
Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K. B., Ostolaza, H., & Martín, C. (2020). Pathophysiology of Type 2 Diabetes Mellitus. *International journal of molecular sciences*, *21*(17), 6275. https://doi.org/10.3390/ijms21176275. Figure 2

Cardiovascular Pathophysiology

Cardiovascular Disease

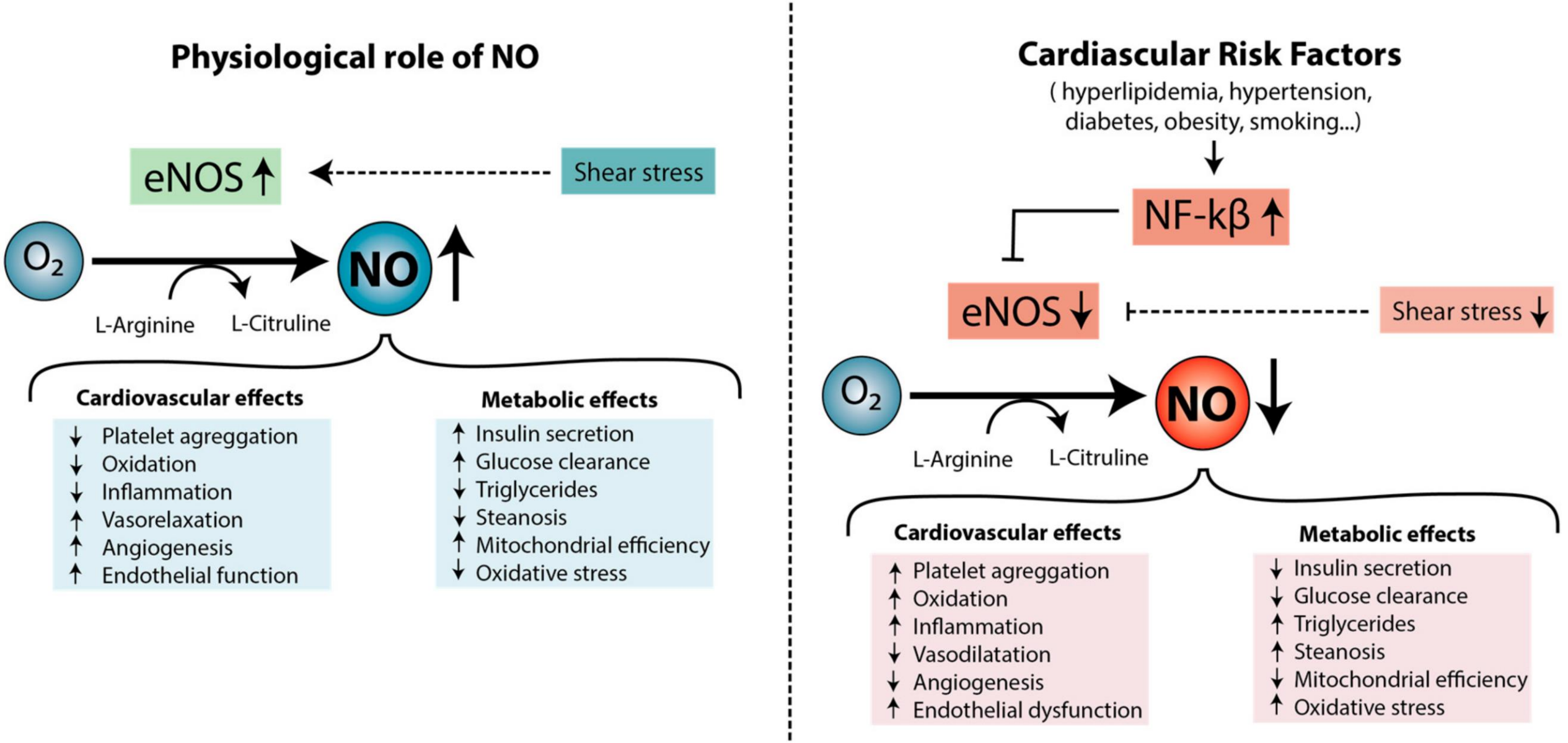
- Coronary artery disease (CAD) aka coronary heart disease (CHD)
- Cerebrovascular disease
- Peripheral artery disease (PAD)
- Aortic atherosclerosis

Common Denominator - Atherosclerosis



Alfaddagh, A., Martin, S. S., Leucker, T. M., Michos, E. D., Blaha, M. J., Lowenstein, C. J., Jones, S. R., & Toth, P. P. (2020). Inflammation and cardiovascular disease: From mechanisms to therapeutics. *American journal of preventive cardiology*, *4*, 100130. https://doi.org/10.1016/j.ajpc.2020.100130. (Figure 1)

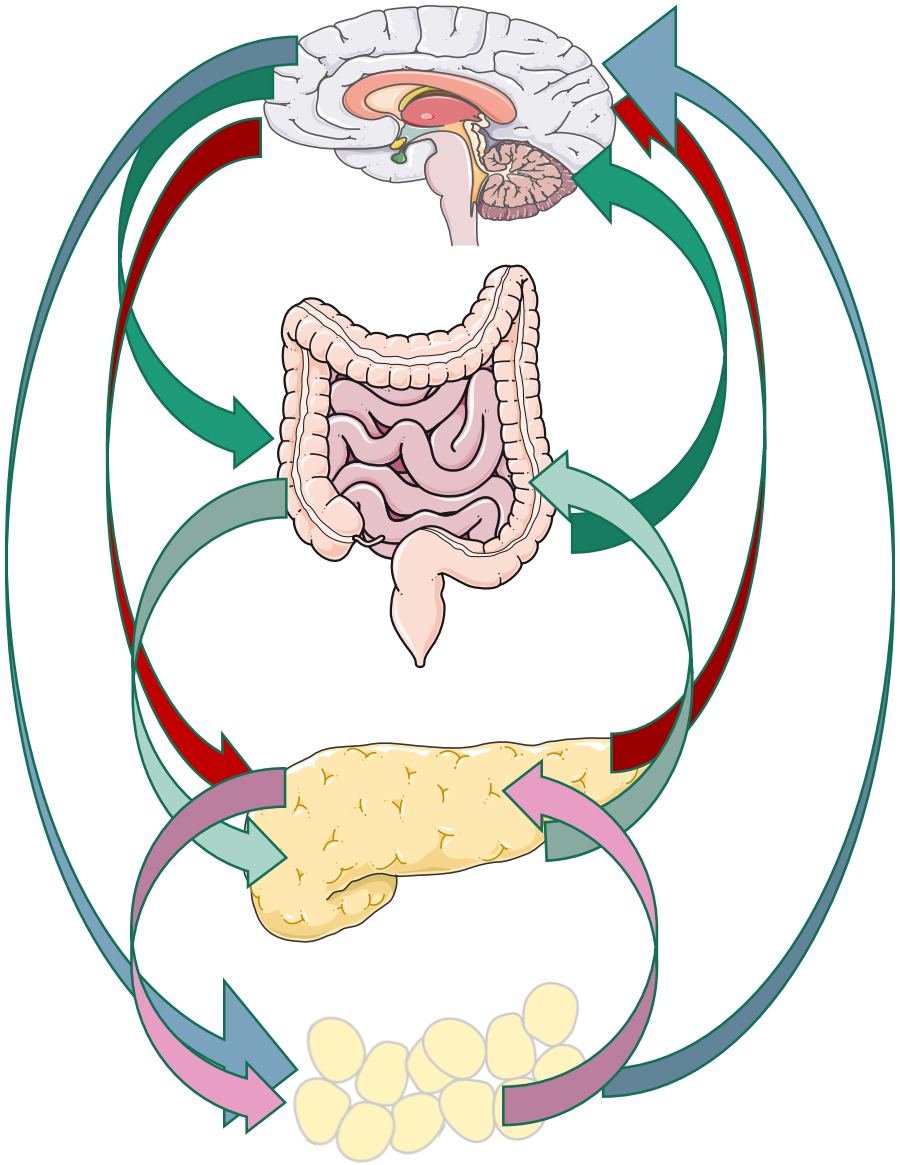
Powell-Wiley, et al. 2021). Obesity and Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation*, *143*(21), e984–e1010. https://doi.org/10.1161/CIR.0000000000000973



Jebari-Benslaiman, S., Galicia-García, U., Larrea-Sebal, A., Olaetxea, J. R., Alloza, I., Vandenbroeck, K., Benito-Vicente, A., et al. (2022). Pathophysiology of Atherosclerosis. *International Journal of Molecular Sciences*, *23*(6), 3346. MDPI AG. Retrieved from http://dx.doi.org/10.3390/ijms23063346. FIgure 2

Obesity, Diabetes and CVD

Pathophysiology of Obesity and T2DM



Chronic Inflammation

Ghrelin elevated
Leptin Resistance

Microbiota changes, Gut barrier dysfunction

Lipotoxicity

Insulin Resistance

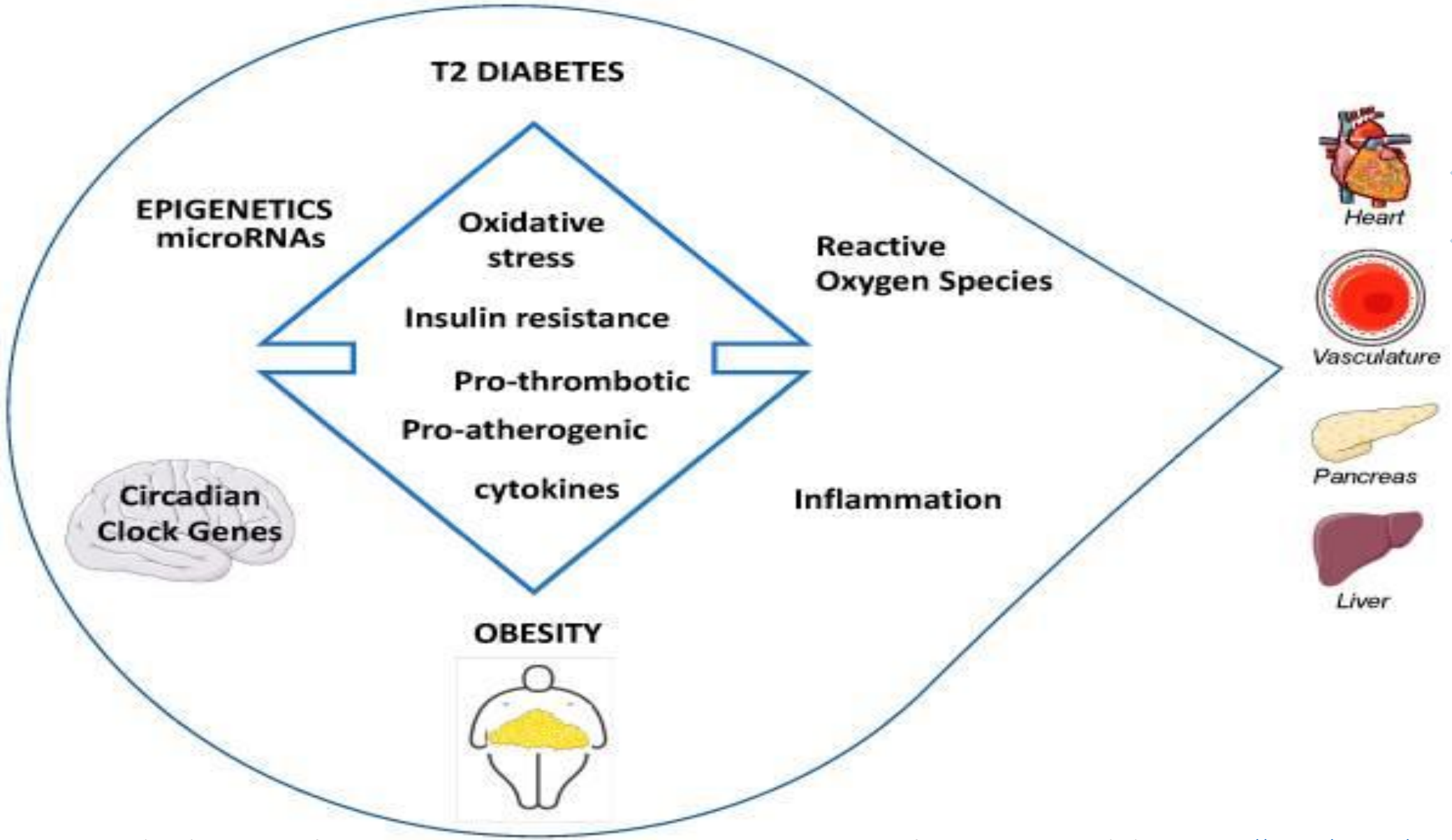
β-cell burden, dysfunction, or apoptosis

Pro-inflammatory cytokines, NEFA

Excess visceral fat - adiposopathy

Mitochondrial dysfunction

Pathophysiology of Obesity and T2DM Leading to CVD



La Sala, L., & Pontiroli, A. E. (2020). Prevention of Diabetes and Cardiovascular Disease in Obesity. *International journal of molecular sciences*, *21*(21), 8178. https://doi.org/10.3390/ijms21218178
Figure 1

Audience Engagement Question 1

- Which of the following is the underlying pathway for obesity, T2DM, and CVD
    a. Thrombosis
    b. Inflammation
    c. Oxidative stress
    d. Insulin resistance

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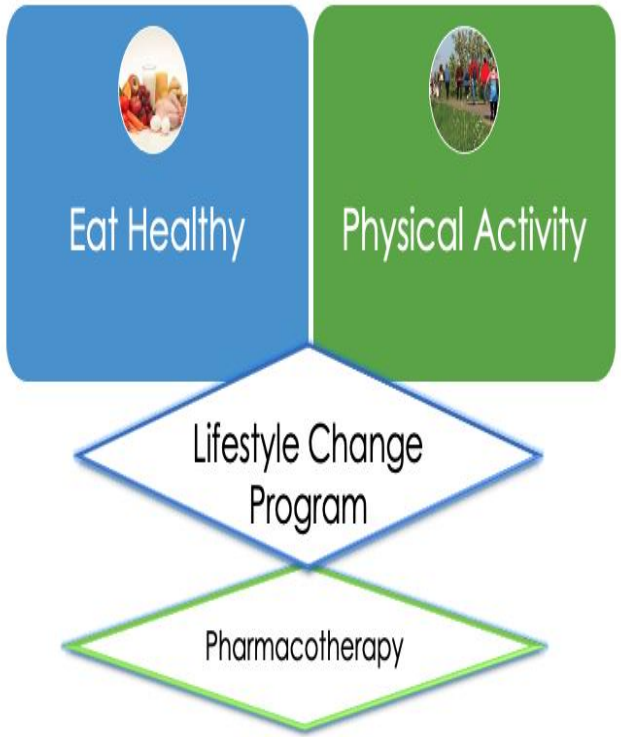
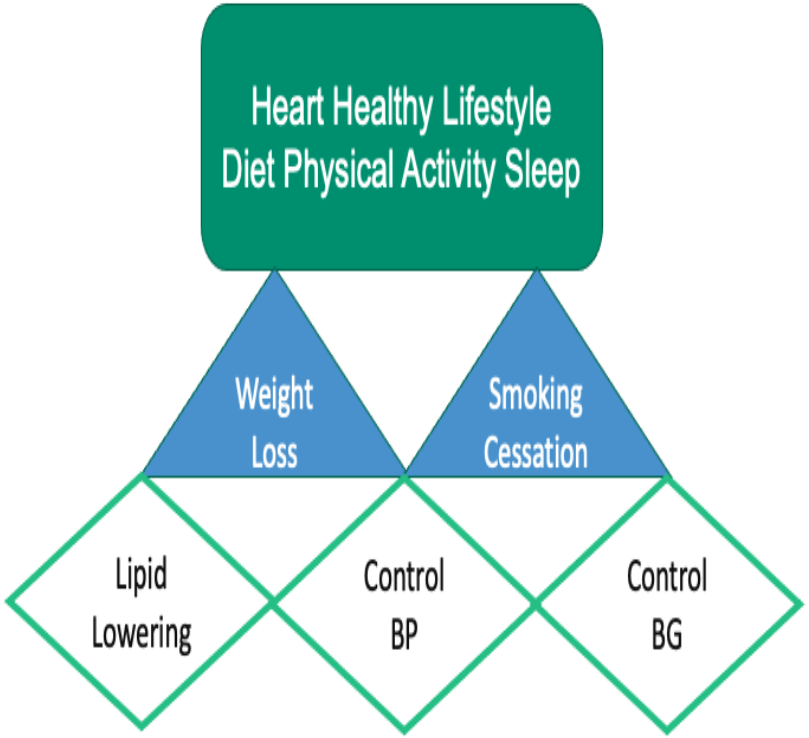
Treatment Overview

Obesity

Type 2 Diabetes

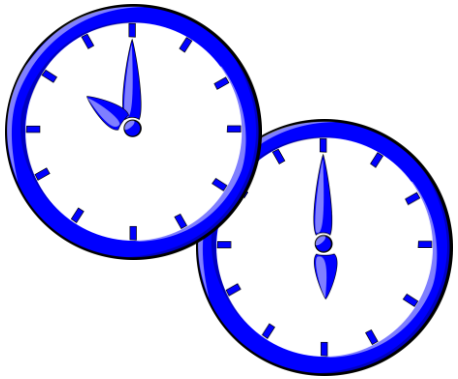


CVD



Eating plans with evidence for T2DM, CVD and Obesity

- Predimed study demonstrated improvement in T2DM when Mediterranean eating plan followed
- Low CHO with evidence of decreasing insulin



- Intermittent fasting showing some promise for reducing HgBA1C
- DASH

Ortega, M. A., Fraile-Martínez, O., Naya, I., García-Honduvilla, N., Álvarez-Mon, M., Buján, J., Asúnsolo, Á., & de la Torre, B. (2020). Type 2 Diabetes Mellitus Associated with Obesity (Diabesity). The Central Role of Gut Microbiota and Its Translational Applications. *Nutrients*, *12*(9), 2749. https://doi.org/10.3390/nu12092749

Lifestyle Overlap

	Weight Loss	HgBA1C Decrease	Systolic/Diastolic Decrease	
• Eating plans	~5.2%	- 0.15	-3/-10	DPP program
• Activity				
• IBT/DPP	~8.6%	- 0.3	- 5/3	Look Ahead Trial

https://www.cdc.gov/pcd/issues/2019/19_0053.htm. Putting the National Diabetes Prevention Program to Work: Predictors of Achieving Weight-Loss Goals in an Employee Population

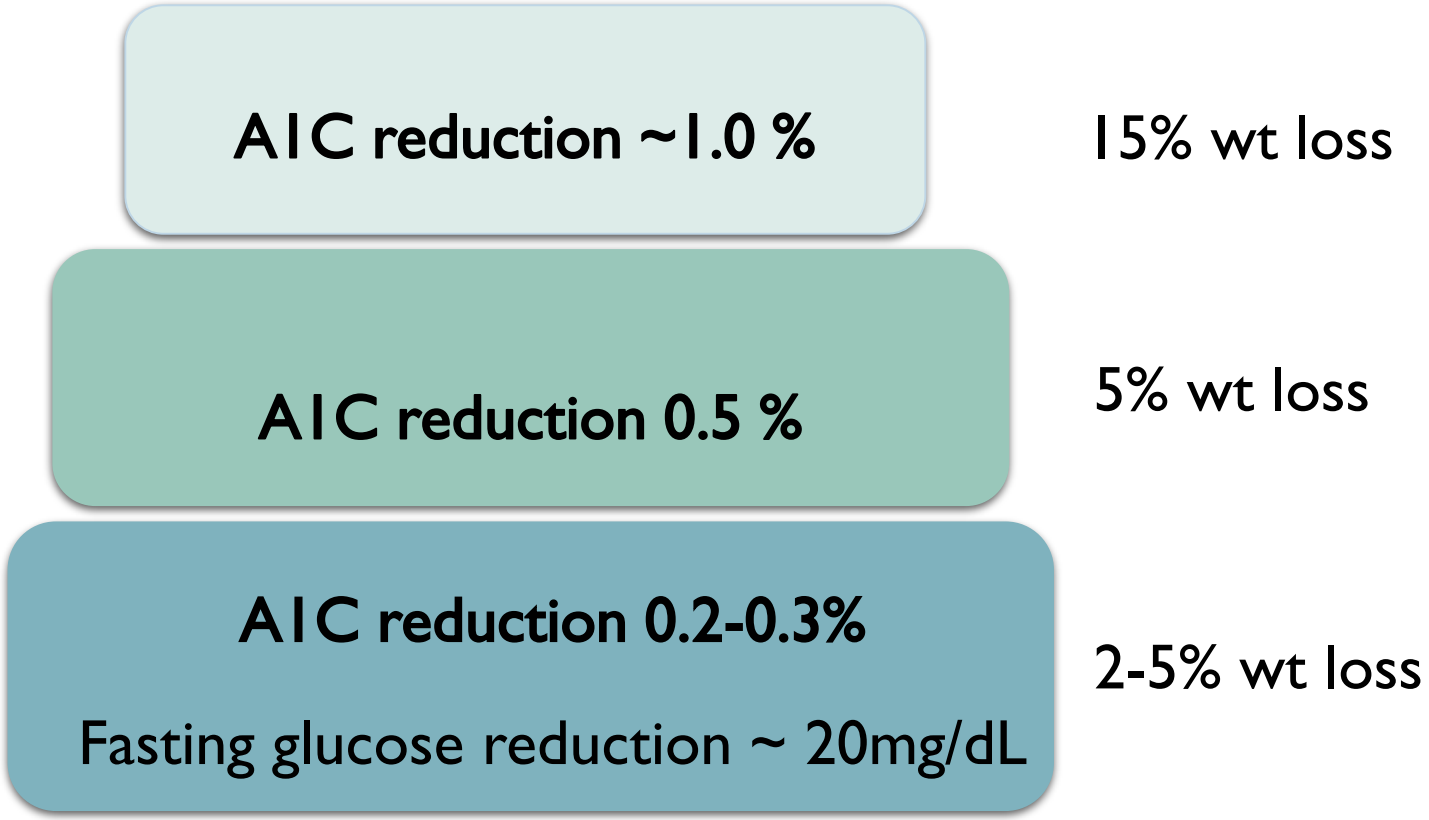
Wadden, T. A., West, D. S., Neiberg, R. H., Wing, R. R., Ryan, D. H., Johnson, K. C., Foreyt, J. P., Hill, J. O., Trence, D. L., Vitolins, M. Z., & Look AHEAD Research Group (2009). One-year weight losses in the Look AHEAD study: factors associated with success. *Obesity (Silver Spring, Md.)*, *17*(4), 713–722. https://doi.org/10.1038/oby.2008.637

Katula, J. A., Dressler, E. V., Kittel, C. A., Harvin, L. N., Almeida, F. A., Wilson, K. E., Michaud, T. L., Porter, G. C., Brito, F. A., Goessl, C. L., Jasik, C. B., Sweet, C. M. C., Schwab, R., & Estabrooks, P. A. (2022). Effects of a Digital Diabetes Prevention Program: An RCT. *American journal of preventive medicine*, *62*(4), 567–577. https://doi.org/10.1016/j.amepre.2021.10.023

A1C Reduction Pyramid

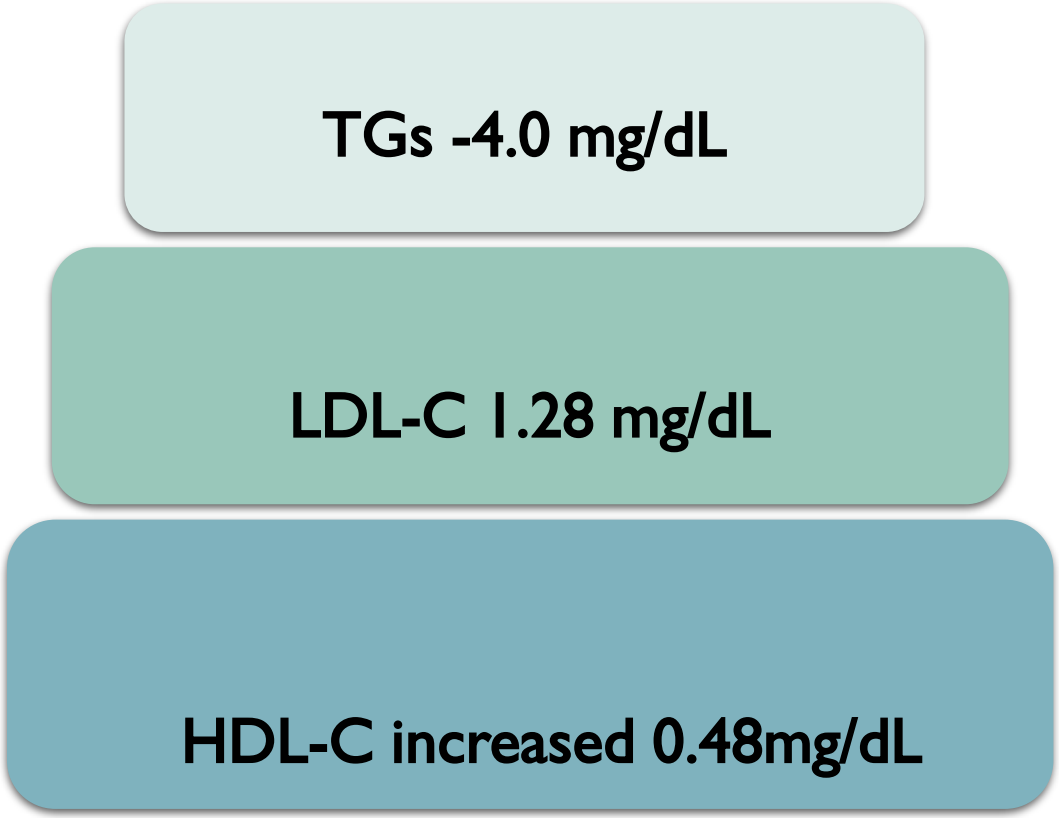
Other benefits

Decreased Diabetes Medications
Reduction in Blood Pressure
Improving LDL and HDL
Improving QOL



Kahan, S., & Fujioka, K. (2017). Obesity Pharmacotherapy in Patients With Type 2 Diabetes. *Diabetes spectrum : a publication of the American Diabetes Association*, *30*(4), 250–257. https://doi.org/10.2337/ds17-0044

Lipid Reduction per 1 KG weight loss



Hasan, B., Nayfeh, T., Alzuabi, M., Wang, Z., Kuchkuntla, A. R., Prokop, L. J., Newman, C. B., Murad, M. H., & Rajjo, T. I. (2020). Weight Loss and Serum Lipids in Overweight and Obese Adults: A Systematic Review and Meta-Analysis. *The Journal of clinical endocrinology and metabolism*, *105*(12), dgaa673. https://doi.org/10.1210/clinem/dgaa673

Pharmacology - Obesity

- First Generation
  - Sympathomimetic
    - Phentermine
    - Diethylpropion
    - Phendimetrazine
    - Benzphetamine
- Third Generation
  - GLP1-RAs
    - Liraglutide
    - Semaglutide
  - GLP1-RA/GIP
    - Tirzepatide
- Second Generation
  - Noradrenergic + GABA-receptor activator, kainite/AMPA glutamate receptor inhibitor causing appetite suppression
    - Phentermine/topiramate
  - Opioid receptor antagonist; dopamine and noradrenaline reuptake inhibitor
    - Naltrexone/bupropion
  - Pancreatic lipase inhibitor
    - Orlistat

Pharmacology - Diabetes

Biguanimide

- Metformin

Incretin Mimetics

GLP1sRAs

- exenatide
- Liraglutide
- Lixisenatide
- semaglutide
- dulaglutide

GIP/GLP1 receptors

- tirzepatide

SGLT2Is

- Canagliflozin
- Dapagliflozin
- Empagliflozin

DPP-4Is

- Alogliptin
- Linagliptin
- Saxagliptin
- Sitagliptin

Thiazolidinediones

- Rosiglitazone
- Pioglitazone

Sulfonylurea

- Glimepiride
- Glipizide
- Glyburide

A-Glucosidase inhibitors

- Acarbose
- Miglitol

Meglitinides

- Nateglinide
- Repaglinide

Bile acid sequestrant

- colesevelam

Dopamine-2 agonist

- bromocriptine

Amylin mimetic

- Pramlintide

Insulins

- Human
  - Rapid acting
  - Short acting
  - Intermediate acting
  - Long acting
  - Ultra long acting
  - Pre-Mixed
- Analogs

Pharmacology - CVD

Anticoagulants
- Apixaban
- Dabigatran
- Edoxaban
- Heparin
- Rivaroxaban
- Warfarin

Antiplatelets
- Aspirin
- Clopidogrel
- Dipyridamole
- Prasugrel
- Ticagrelor

Digitalis preparation
- Digoxin

ACE Inhibitors
- Benazepril
- Captopril
- Enalapril
- Fosinopril
- Lisinopril
- Moexipril
- Perindopril
- Quinapril
- Ramipril

ARB II blockers
- Azilsartan
- Candesartan
- Eprosartan
- Irbesartan
- Losartan
- Olmesartan
- Telmisartan
- Valsartan

ARNs
- Sacubitril/valsartan

Beta Blockers
- Acebutolol
- Atenolol
- Betaxolol
- Bisoprolol/hydrochlorothiazide
- Bisoprolol
- Metoprolol
- Nadolol
- Propranolol

Combined α and β Blockers
- Carvedilol
- Labetalol

Calcium Channel Blockers
- Amlodipine
- Diltiazem
- Felodipine
- Nifedipine
- Nimodipine
- Nisoldipine
- Verapamil

Cholesterol lowering Statins
- Atorvastatin
- Fluvastatin
- Lovastatin
- Pitavastatin
- Pravastatin
- Rosuvastatin
- Simvastatin

Nicotinic acids
- Niacin

Cholesterol absorption inhibitor

Ezetimibe

Combination

Ezetimibe/Simvastatin

PSCK9 Inhibitor
- Alirocumab
- Evolocumab

Diuretics
- Acetazolamide
- Amiloride
- Bumetanide
- Chlorothiazide
- Chlorthalidone
- Furosemide
- Hydrochlorothiazide
- Indapamide
- Metalozone
- Spironolactone
- Torsemide

Vasodilators
- Isosorbide dinitrate
- Isosorbide mononitrate
- Hydralazine
- Nitroglycerin
- Minoxidil

Common Medications for Weight Loss in Patients With Diabetes

FDA – Approved Medications for Obesity

- Liraglutide 3.0 mg
- Naltrexone-bupropion SR
- Phentermine*
- Phentermine-topiramate ER
- Orlistat
- Semaglutide 2.4mg
- Tirzepatide 15 mg

* Approved for 13 weeks only by FDA with three other sympathomimetics

Medications with weight loss but not approved by the FDA for that purpose

- Metformin
- Pramlinitide
- SGLT2 Inhibitors
- “other” GLP1RAs

Kahan, S., & Fujioka, K. (2017). Obesity Pharmacotherapy in Patients With Type 2 Diabetes. *Diabetes spectrum : a publication of the American Diabetes Association*, *30*(4), 250–257. https://doi.org/10.2337/ds17-0044

Common Medications for CVD in Patients with Diabetes and Obesity

- High Intensity statins
  - PwD aged 40-75 with one or more ASCVD risk factors
    - Target LDL goal < 70 mg/dL or by ≥ 50% of baseline
    - Consider PCSK9 Inhibitor or ezetimibe addition to maximum statin therapy
    - Continue statin in PwD > 75
  - PwD and existing ASCVD LDL goal <55mg/dL
  - GLP1-RA or SGLT2i (or both) for PwD and ASCVD risks

  - SGLT2i Proven HF benefit with T2DM

ElSayed, N. A., Aleppo, G., Aroda, V. R., Bannuru, R. R., Brown, F. M., Bruemmer, D., Collins, B. S., Cusi, K., Das, S. R., Gibbons, C. H., Giurini, J. M., Hilliard, M. E., Isaacs, D., Johnson, E. L., Kahan, S., Khunti, K., Kosiborod, M., Leon, J., Lyons, S. K., Murdock, L., … on behalf of the American Diabetes Association (2023). Summary of Revisions: Standards of Care in Diabetes-2023. *Diabetes care*, *46*(Suppl 1), S5–S9. https://doi.org/10.2337/dc23-Srev

Obesity Pharmacology

AOM responses

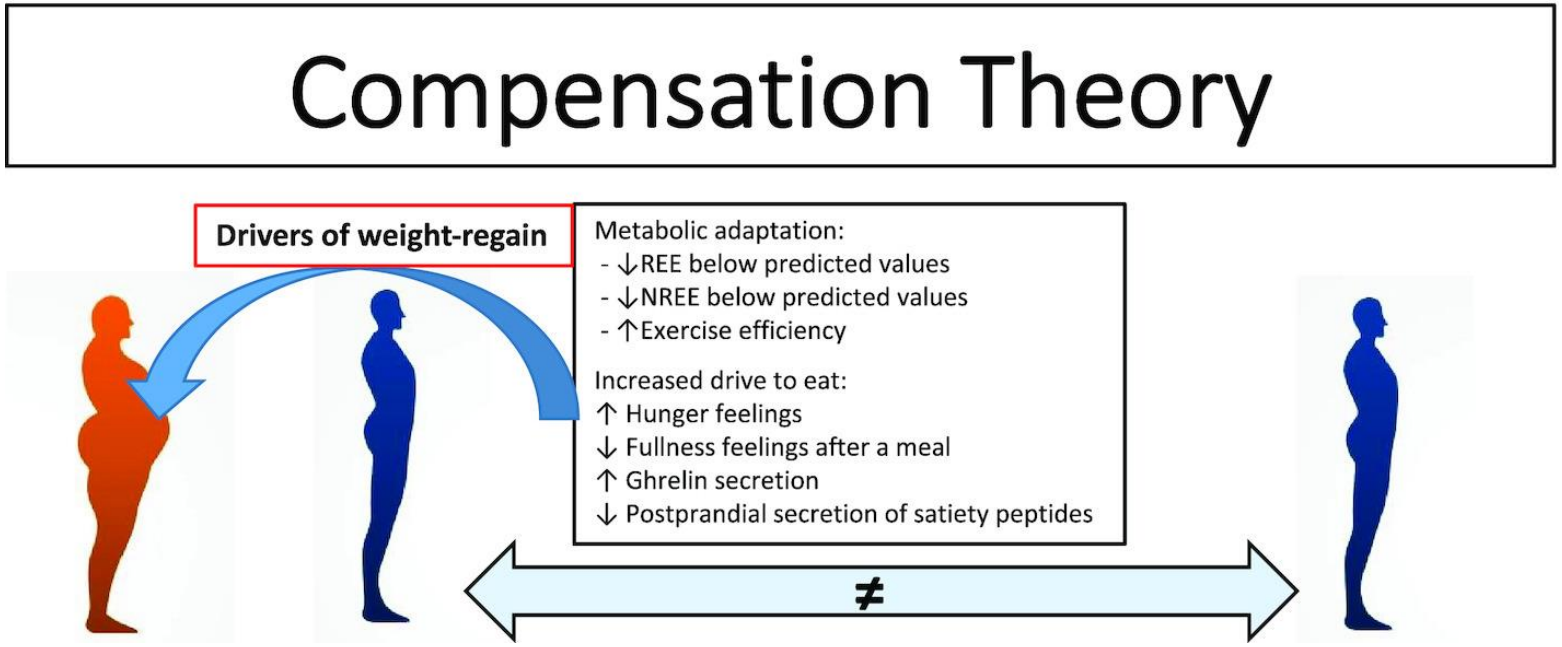
Medication	Early responder	Weight loss	HgBA1C response
Liraglutide	≥ 4% weight loss during the initial 16 weeks	8.5% at end of year one	0.9-2.2%
Naltrexone/bupropion SR	≥ 5% weight loss by week 16 continue the medication	5.9% at end of year one	0.6% reduction
Phentermine	> 3.4 % at 12 weeks	10.7% at 24 months	Not studied
Phentermine-Topiramate ER	≥ 3% weight loss by week 12 continue the medication	9% over 2 years	1.6%
Orlistat	No information	5.8 kg at end of 4 years	0.3-0.5%
Semaglutide	≥ 5% weight loss by week 20 continue the medication	9.6% at end of year one	1.6%
Tirzepatide	~10% weight loss by week 20, at least 5% to continue the medication	14.7%at end of year one in patients with diabetes	2.34%

Kahan, S., & Fujioka, K. (2017).. *Diabetes spectrum*, *30*(4), 250–257. https://doi.org/10.2337/ds17-004. Davies, M., et al, I. (2021). *Lancet (London, England)*, *397*(10278), 971–984. https://doi.org/10.1016/S0140-6736(21)00213-0Lewis, K. H.,et al. (2019). *Obesity 27*(4), 591–602. https://doi.org/10.1002/oby.22430

PATHOLOGY OF WEIGHT REGAIN – METABOLIC ADAPTATION

Adaptive responses to weigh loss promotes weight regain

- Fall in energy expenditure
- Increase in appetite
- Dysfunctional hormonal system



Martins, C., Dutton, G. R., Hunter, G. R., & Gower, B. A. (2020). Revisiting the Compensatory Theory as an explanatory model for relapse in obesity management. *The American journal of clinical nutrition*, *112*(5), 1170–1179. https://doi.org/10.1093/ajcn/nqaa243 Figure 1. open access CC 4.0

Metabolic adaptation – STEP 1 Extended

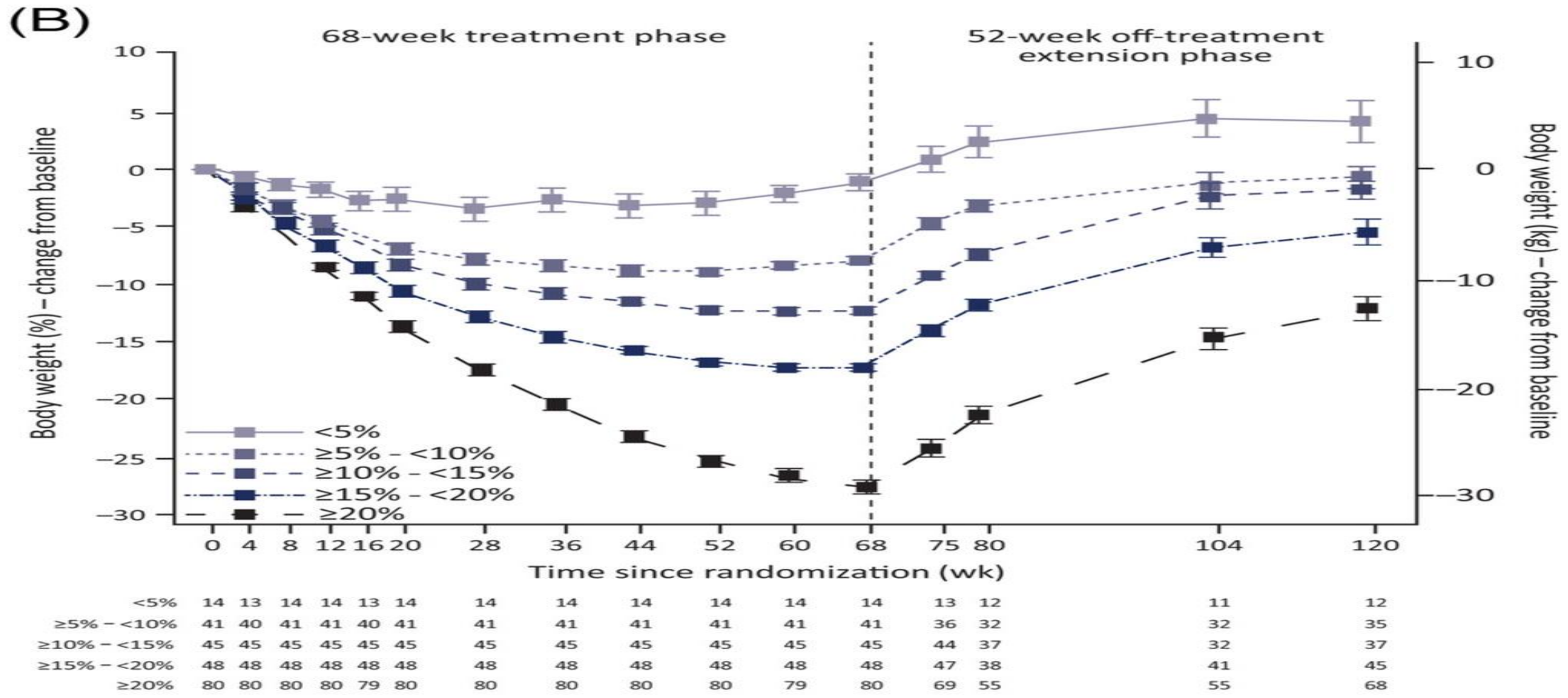


FIGURE 1

Wilding, J., Batterham, R. L., Davies, M., Van Gaal, L. F., Kandler, K., Konakli, K., Lingvay, I., McGowan, B. M., Oral, T. K., Rosenstock, J., Wadden, T. A., Wharton, S., Yokote, K., Kushner, R. F., & STEP 1 Study Group (2022). Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. *Diabetes, obesity & metabolism*, 10.1111/dom.14725. Advance online publication. https://doi.org/10.1111/dom.14725

Metabolic Adaptation – STEP 1 Extended

BP response

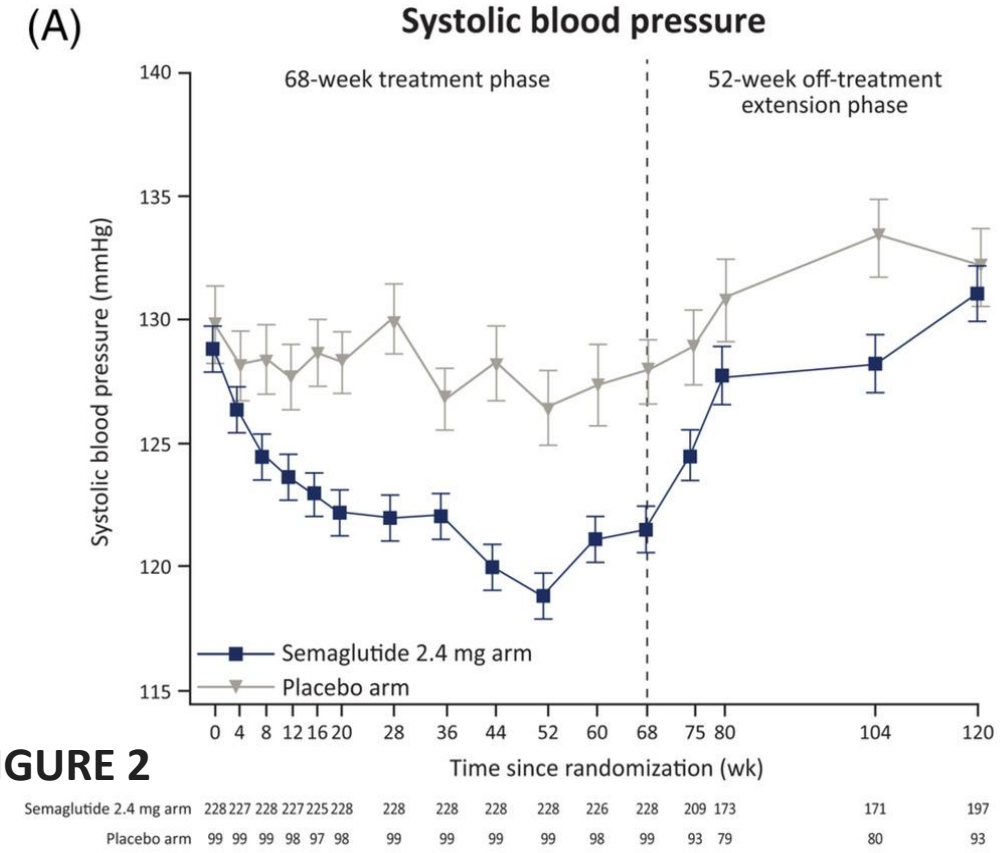
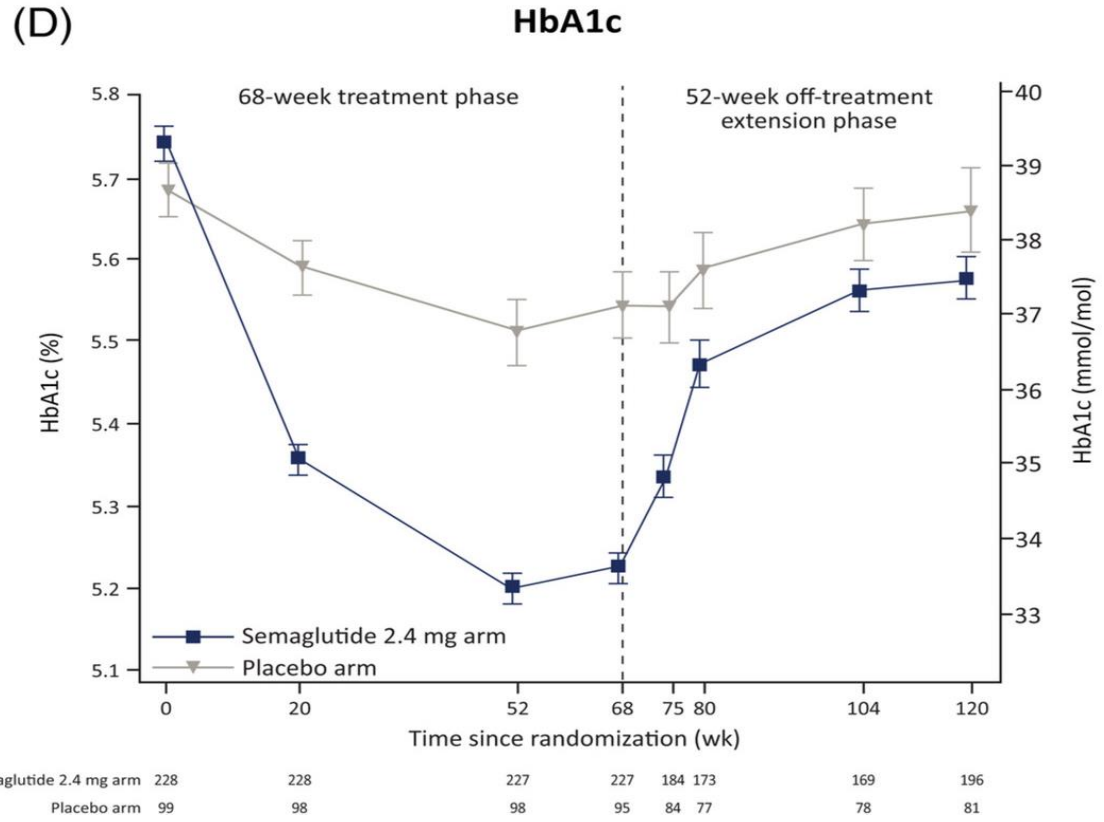


FIGURE 2

HgBA1C Response



Wilding, J., Batterham, R. L., Davies, M., Van Gaal, L. F., Kandler, K., Konakli, K., Lingvay, I., McGowan, B. M., Oral, T. K., Rosenstock, J., Wadden, T. A., Wharton, S., Yokote, K., Kushner, R. F., & STEP 1 Study Group (2022). Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. *Diabetes, obesity & metabolism*, 10.1111/dom.14725. Advance online publication. https://doi.org/10.1111/dom.14725

Diabetes and CVD Pharmacology Weight Impact

Diabetes Pharmacology

- Impact on obesity
  - Obesogenic medications
    - The percentage of patients attaining a goal A1C of < 7.0% is significantly higher in patients receiving diabetes medications that are weight neutral or have weight loss side effects
    - Those prescribed an obesogenic anti-diabetes medication were 53% less likely to lose weight and 29% less likely to be at HbA1c goal

McAdam-Marx, C., Mukherjee, J., Bellows, B. K., Unni, S., Ye, X., Iloeje, U., & Brixner, D. I. (2014). Evaluation of the relationship between weight change and glycemic control after initiation of antidiabetic therapy in patients with type 2 diabetes using electronic medical record data. *Diabetes research and clinical practice*, *103*(3), 402–411. https://doi.org/10.1016/j.diabres.2013.12.038

Potentially Obesogenic Medications

	Weight Gain
Sulfonylureas	2-3 kg
Insulins	1.5 – 5.75 kg
Thiazolidinediones	2 – 4.8 kg
Meglitinides	1-3 kg
Beta Blockers	1-3 kg

- Apovian, C. M., Okemah, J., & O'Neil, P. M. (2019). Body Weight Considerations in the Management of Type 2 Diabetes. *Advances in therapy, 36*(1), 44–58. https://doi.org/10.1007/s12325-018-0824-8
- Provilus, A., Abdallah, M., & McFarlane, S.I. (2011). Weight gain associated with antidiabetic medications. *Therapy, 8*, 113-120.

Weight Neutral Diabetes Medications

DDP-4 Inhibitors

a-Glucosidase inhibitors

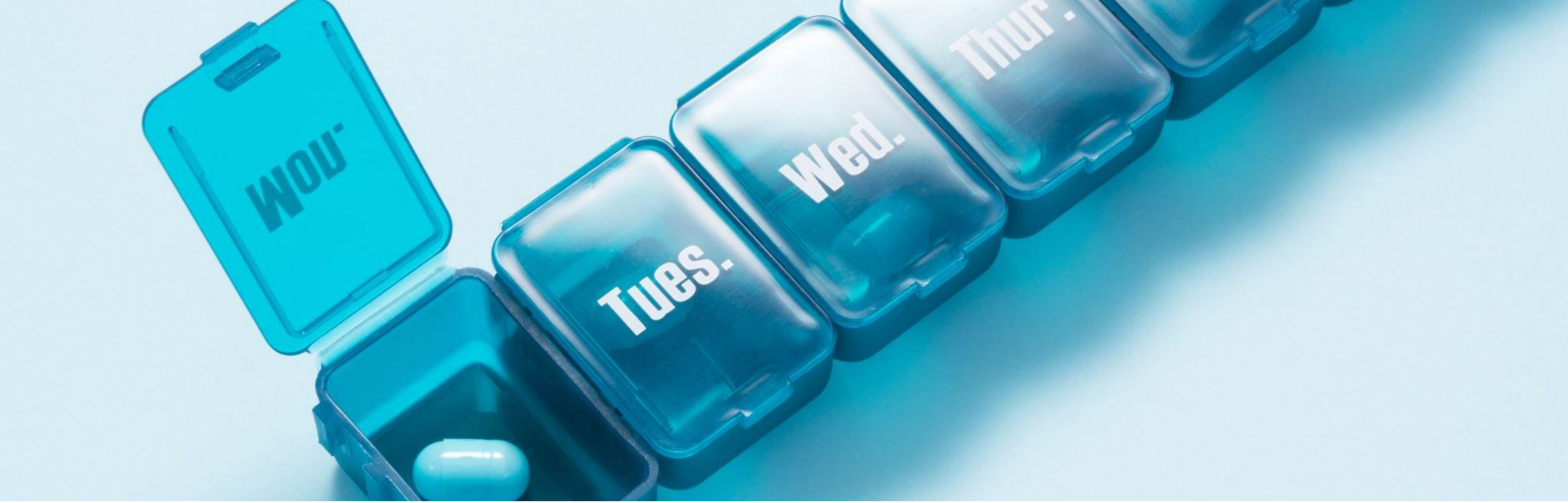
Bile Acid Sequestrants

Apovian, C. M., Okemah, J., & O'Neil, P. M. (2019). Body Weight Considerations in the Management of Type 2 Diabetes. *Advances in therapy*, *36*(1), 44–58. https://doi.org/10.1007/s12325-018-0824-8
Provilus, A., Abdallah, M., & McFarlane, S.I. (2011). Weight gain associated with antidiabetic medications. *Therapy, 8*, 113-120.

Other Medications Responses

Medication	Weight loss	HgBA1C response
Metformin	2-4kg	1-2%
Pramlintide	2.6 kg	0.3-0.4%
SGLT2 Inhibitors	1.5–2 kg	1.4%
GLP1 RA	1.5–6 kg	0.8-1.8%

Kahan, S., & Fujioka, K. (2017). Obesity Pharmacotherapy in Patients With Type 2 Diabetes. *Diabetes spectrum : a publication of the American Diabetes Association*, *30*(4), 250–257.
Pereira, M. J., & Eriksson, J. W. (2019). Emerging Role of SGLT-2 Inhibitors for the Treatment of Obesity. *Drugs*, *79*(3), 219–230. https://doi.org/10.1007/s40265-019-1057-0
https://doi.org/10.2337/ds17-0044
Nauck, M. A., Quast, D. R., Wefers, J., & Meier, J. J. (2021). GLP-1 receptor agonists in the treatment of type 2 diabetes - state-of-the-art. *Molecular metabolism*, *46*, 101102. https://doi.org/10.1016/j.molmet.2020.101102



Barriers for Medication

Challenge with Medication for Obesity

Pharmacotherapy

- Example of Bias related to obesity
- Cost
  - Example: semaglutide for diabetes ~$900, for obesity ~$1400
- Non Coverage - excluded

Solution with Medication for Obesity

Pharmacotherapy

- Continue prior authorizations with insurers
- Prescribe off label
  - Rule #1 Prescribe on label by EBP whenever possible
  - Use company prescribing sites/coupons for discounts
  - Beware! No literature to support off label prescribing, lots of presentations at obesity medicine conferences
- Non-Coverage – excluded
  - Ask for one time exclusion

Case Study

Image: © Obesity Action Coalition

Meet Victor

60-year-old presents for diabetes follow-up visit for Type 2 diabetes and medication refill.

He states, *“I’m sick and tired of feeling sick and tired” and “I hate taking so many medications*!”

VICTOR'S MEDICAL HISTORY

- PMH:
  - Obesity Class II, Stage 2
  - Type 2 diabetes: canagliflozin/metformin 50 mg IR/1000 mg ER and dulaglutide 1.5 mg subcutaneous/week
  - Hypertension: lisinopril 40 mg daily
  - Hyperlipidemia: lovastatin 80 mg daily
  - GERD: omeprazole 20 mg daily
  - Osteoarthritis of knees and hips: ibuprofen 400 mg up to three times a day as needed
  - Non-alcoholic fatty liver disease
  - Obstructive Sleep Apnea: on CPAP

Preventative Screening:

- UTD on colonoscopy, PSA (all WNL)

Surgical History:

- None

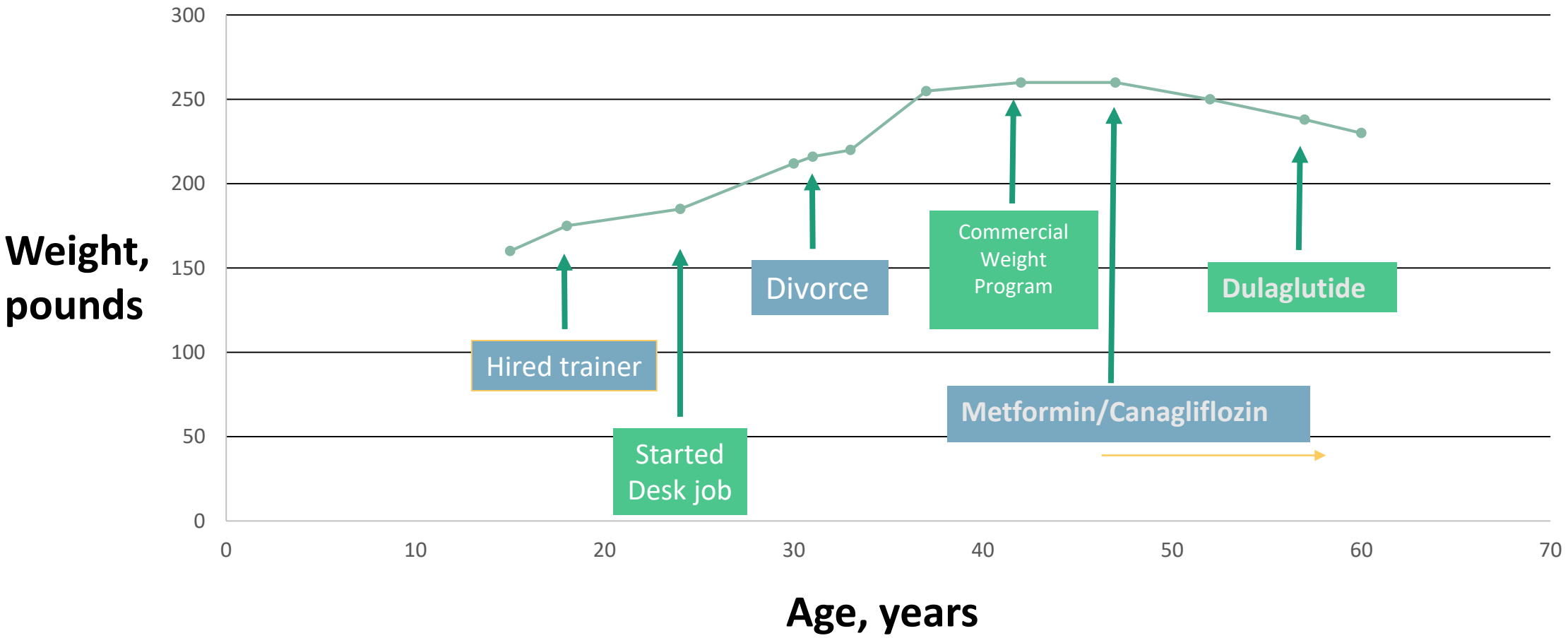
FH:

- Obesity, CVD and T2DM

SH:

- Lives with his brother
- IT support at insurance company
- No h/o tobacco, alcohol or drug use/abuse

Victor's Weight Graph (ASSESS)



Assessment

- Medications: No obesogenic meds
- Diet: Follows 3 meals a day with 1 snack. Mostly whole foods. Eats out 1 x per week. Beverages: water, black coffee Follows CHO restriction from CDCES < 100 grams/day
- Exercise: Gym 3 x 60 minutes (bike, weights), plus walks his dog daily x 20 minutes
- Sleep: 7-8 hours per night. Wears CPAP nightly
- Stress: 3-4/10: Mostly work related
    - Coping mechanisms: working out, walking his dog, talking with brother and son

ASSESS: Physical Exam, Labs

Pertinent Physical exam findings:

- Neck circumference: 21 inches
- Central adiposity
- Skin tags
- Acanthosis along neck and axilla

Point of Care testing

- UA nl
- HgBA1C 8.1

Height	Weight	BMI	BP
5’11”	269 lbs	37.5	146/88

Case study

Provider concern

- Obesity BMI 37.5, acanthosis
- Diabetes: HbGA1C despite canagliflozin/metformin 50 mg IR/1000 mg ER and dulaglutide 1.5 mg subcutaneous/week
- HTN marginal: lisinopril 40 mg daily

Patient concern

- Just on too many meds
- Tired of being “sick”

Audience Engagement Question 1

- What do you want to do?
  a) Refer patient for bariatric surgery
  b) Add or change antidiabetes medication
  c) Add another antihypertension medication
  d) Treat obesity including starting an anti-obesity medication

Case study

- What do you want to do?
  a) Refer patient for bariatric surgery
  b) Add or change antidiabetes medication
  c) Add another antihypertension medication
  d) Treat obesity including starting an anti-obesity medication

Case study

- Rationale for answers
  - Add or change antidiabetes medication
    - He is not at goal, so this is reasonable
      - However, patient does not want to have more medications
    - He is not on any medication that is causing weight gain
    - Already on the medications that cover his CV risk (SGLT2I and GLP1RA)
    - Could increase dulaglutide
    - Could consider adding insulin – but would likely be obesogenic
    - Addressing obesity can decrease HgBA1C
    - Consider CGM for time in range
  - Add another antihypertension medication
    - Consider home monitoring to get accurate readings
    - Consider thiazide diuretic or calcium channel blocker

Case study

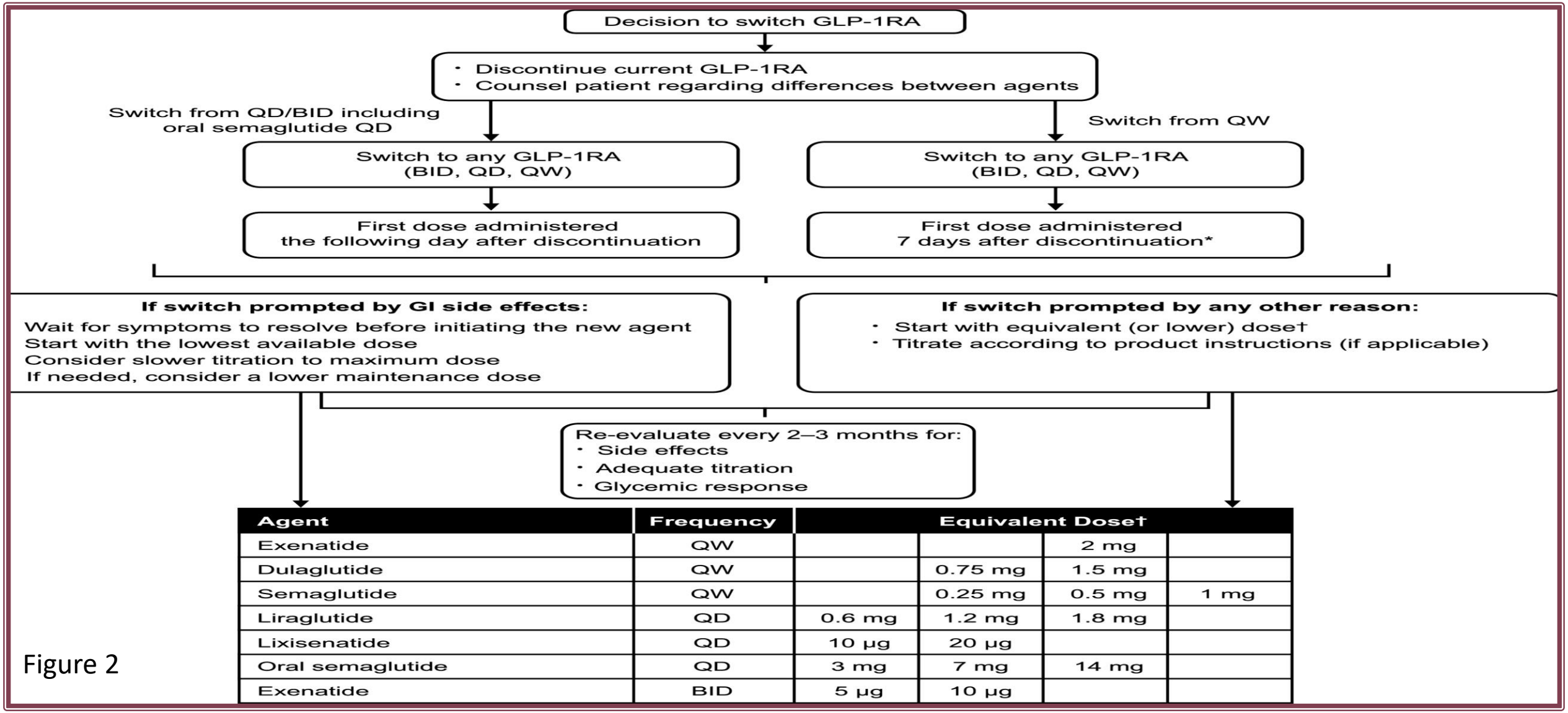
- What do you want to do?

  Treat obesity including starting an anti-obesity medication

  - Regardless of referral for surgery this could be appropriate
    - Patient is already eating well with follow-up with CDCES and activity is appropriate
    - Medication
      - Could change current GLP1 to higher dosing, different medication or obesity dosing
        - Dulaglutide 4.5 mg (top diabetes dose) average 5.0 kg weight loss
        - Semaglutide 2.4mg (obesity dose) average 9.6% weight loss (obesity with T2DM)
        - Tirzepatide 15 mg average 14.7% weight loss (obesity with T2DM)

Wise J. Diabetes drug results in substantial weight loss in people with obesity, study finds *BMJ* 2022; 377 :o1406 doi:10.1136/bmj.o1406
Bonora, E., Frias, J. P., Tinahones, F. J., Van, J., Malik, R. E., Yu, Z., Mody, R., Bethel, A., Kwan, A., & Cox, D. A. (2021). Effect of dulaglutide 3.0 and 4.5 mg on weight in patients with type 2 diabetes: Exploratory analyses of AWARD-11. *Diabetes, obesity & metabolism*, *23*(10), 2242–2250. https://doi.org/10.1111/dom.14465
Kushner RF, Calanna S, Davies M, Dicker D, Garvey WT, Goldman B, Lingvay I, Thomsen M, Wadden TA, Wharton S, Wilding JPH, Rubino D. Semaglutide 2.4 mg for the Treatment of Obesity: Key Elements of the STEP Trials 1 to 5. Obesity (Silver Spring). 2020 Jun;28(6):1050-1061. doi: 10.1002/oby.22794. PMID: 32441473; PMCID: PMC7318657.

SWITCHING GLP1S



Agent	Frequency	Equivalent Dose†			
Exenatide	QW			2 mg	
Dulaglutide	QW		0.75 mg	1.5 mg	
Semaglutide	QW		0.25 mg	0.5 mg	1 mg
Liraglutide	QD	0.6 mg	1.2 mg	1.8 mg	
Lixisenatide	QD	10 µg	20 µg		
Oral semaglutide	QD	3 mg	7 mg	14 mg	
Exenatide	BID	5 µg	10 µg		

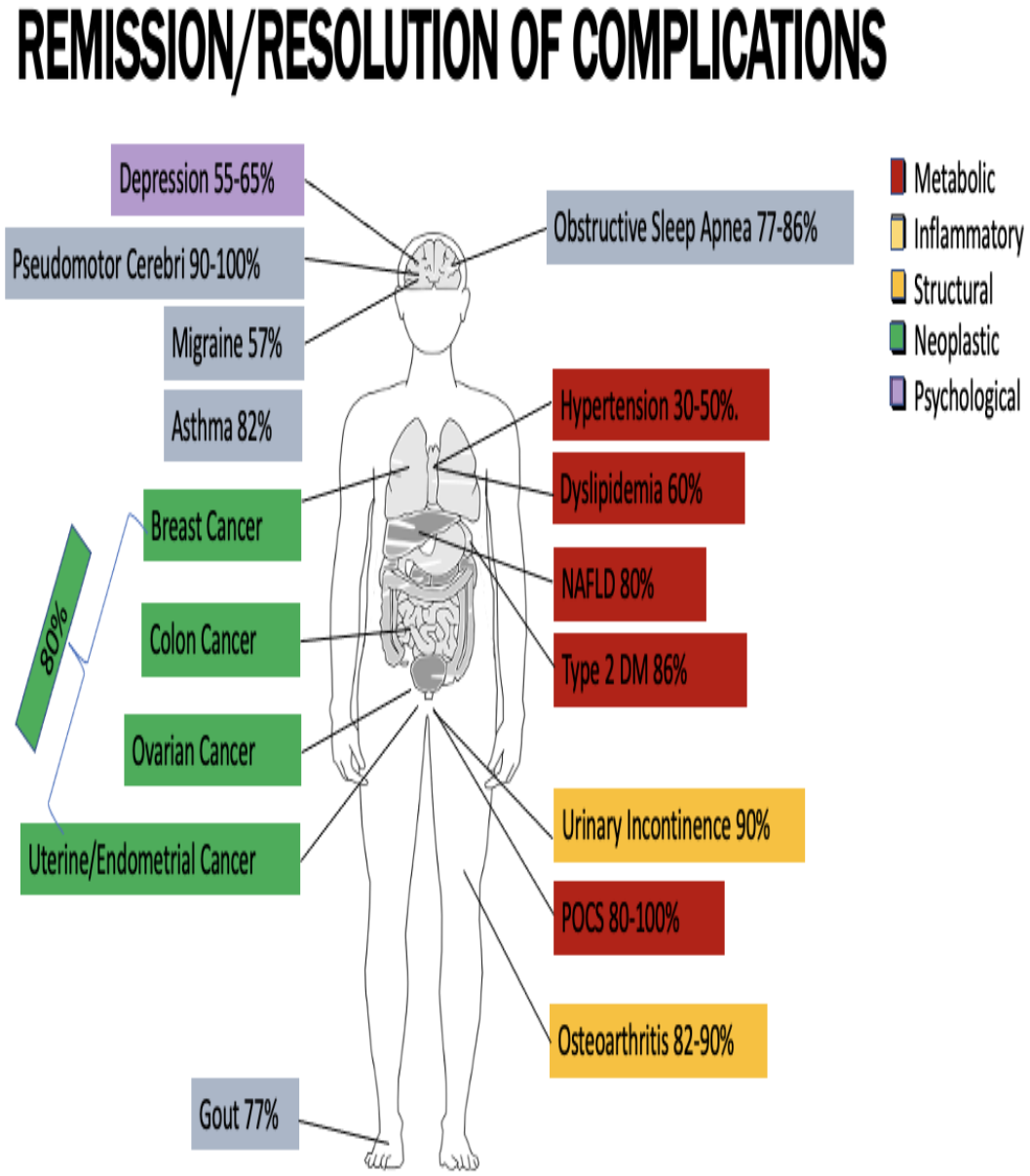
Figure 2

Almandoz, J. P., Lingvay, I., Morales, J., & Campos, C. (2020). Switching Between Glucagon-Like Peptide-1 Receptor Agonists: Rationale and Practical Guidance. *Clinical diabetes : a publication of the American Diabetes Association*, *38*(4), 390–402. https://doi.org/10.2337/cd19-0100

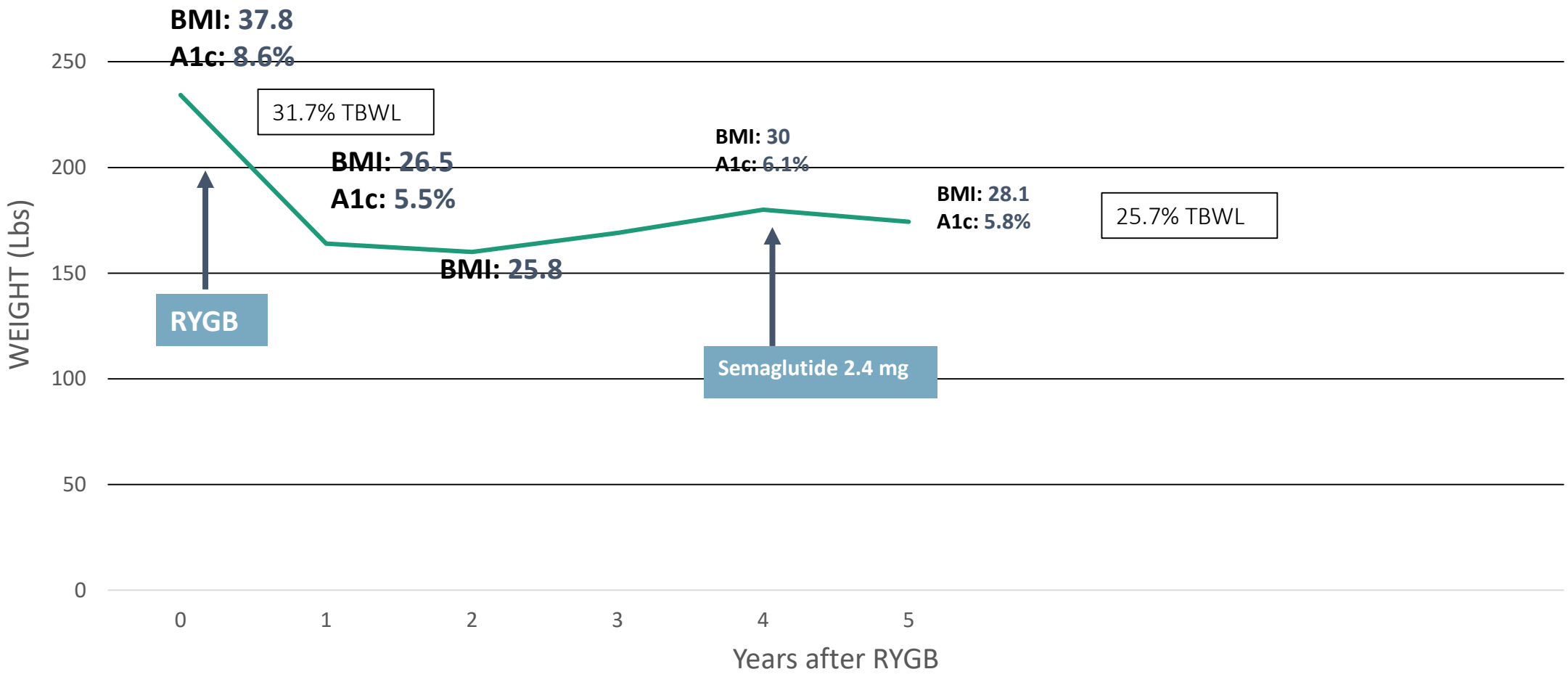
Case study

Refer patient for bariatric surgery

- Reasonable
- Greatest chance to reverse diabetes and improve hypertension



Victor's Weight History- After RYGB



Improved Medical Conditions

- Class II , Stage 2→ Improved, added back GLP-1 for more improvement
- Uncontrolled T2DM → Controlled, on metformin
- GERD → Resolved, off medications
- HTN → Resolved, off medications
- Hyperlipidemia/ Dyslipidemia → Resolved, off medication
- OA → Resolved, off medications
- NAFLD → Resolved, off medications
- OSA → Resolved, off CPAP

Thank you!

Resources

Image resources

- https://www.worldobesity.org/resources/image-bank
- https://www.obesityaction.org/get-educated/public-resources/oac-image-gallery/
- Canadian Obesity Network Image Bank: https://www.flickr.com/photos/144769815@N06/

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