Treatment of Obesity

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Disclosures

None

Learning Objectives

- Review treatment of Obesity

Disclaimer

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Obesity in Patients with HIV

- Incidence is rising
- Some antiretroviral therapy is weight-promoting
- Obesity can increase cardiometabolic risk and cancer
- **Patients with HIV are already at a much higher cardiometabolic risk**
  - Management of obesity in patients with HIV is critical to help reduce this risk!

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Weight Stigma

- **Health care settings are a significant source of weight stigma**
- Research shows that pts with obesity are less likely to undergo preventive cancer screening related to weight stigma ☹
- A study by Amy et al *(Int J Obesity 2006)* surveyed 498 patients with overweight and obesity
  - 83% reported their weight was a barrier to getting appropriate health care

Weight Stigma

- Causes physical and psychological harm
  - →Internalized weight bias: Self-blame and self-directed weight stigma

Adults and children who experience weight-based stigma are more likely to avoid exercise and engage in unhealthy eating behaviors like binge eating which leads to weight gain overtime

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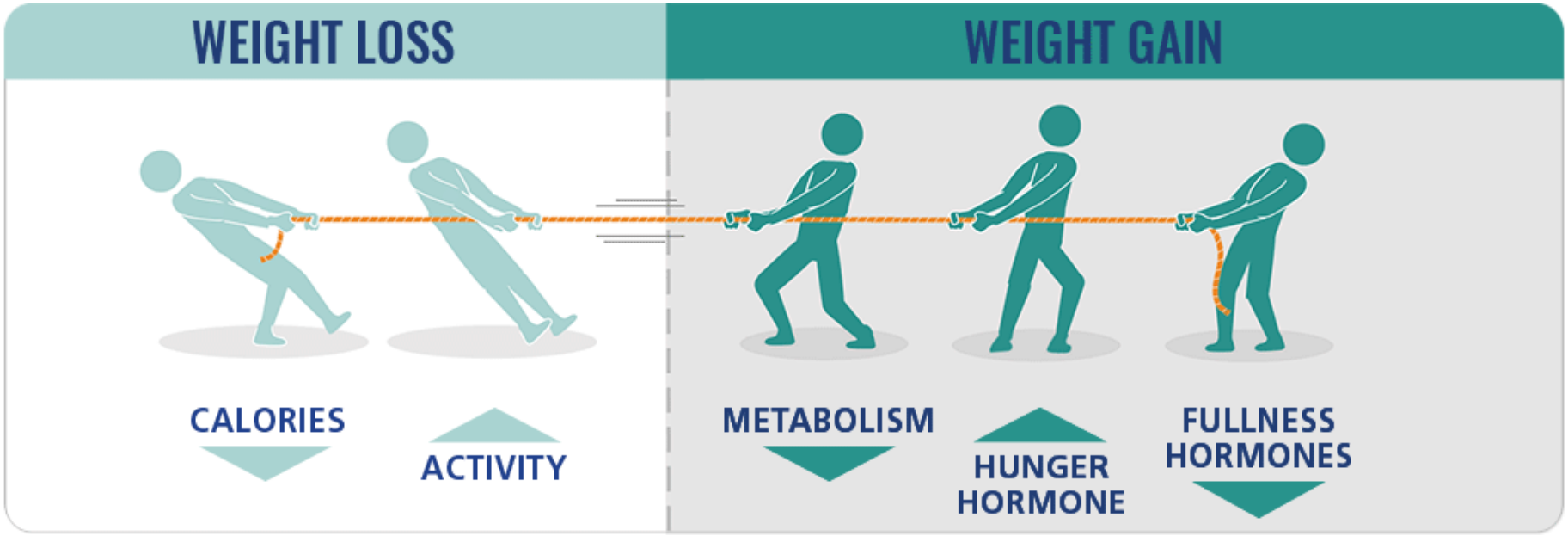
Let’s reduce the stigma!

- When we talk about obesity it is important that we:
  - Use patient-first language
  - Always ask our patients’ permission when we talk about weight
  - Do not use BMI and weight alone to evaluate a patient’s health

Our body defends an elevated fat-mass set point



https://www.rethinkobesity.com/metabolic-adaptation.html

Metabolic Adaptation

- The more weight lost the greater the metabolic slowing
- Once weight is reduced, metabolism does not return back to pre-weight loss levels and grehlin will remain elevated even years after weight loss!
- Treatment plan must be sustainable and long-term!

Fothergill E, Guo J, Howard L, Kerns JC, Knuth ND ,Brychta R, Chen KY, Skarulis MC, Walter M, Walter PJ, Hall KD. Persistent metabolic adaptation 6 years after "The Biggest Loser" competition. Obesity (Silver Spring). 2016 Aug;24(8):1612-9.

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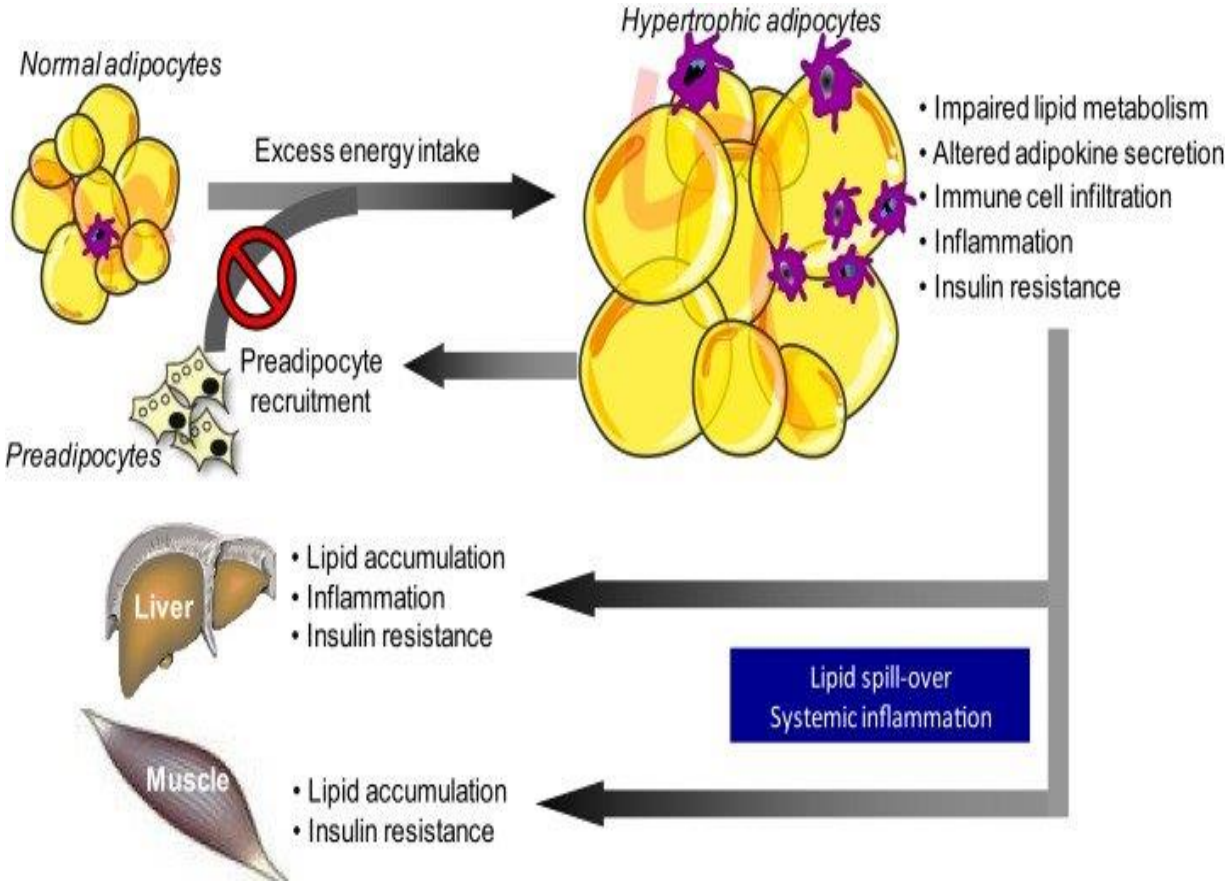
Adiposopathy: pathogenic adipose tissues



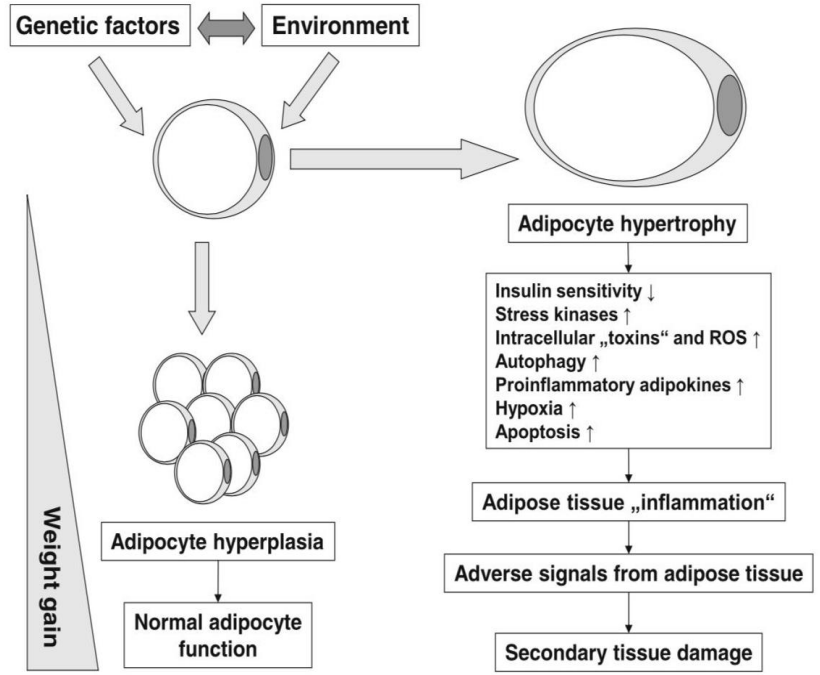


Fig 2 Consequences of adipocyte hypertrophy. With a continued positive energy balance body weight and fat accumulation increase. Most likely due to genetic and environmental factors and their interaction, some individuals may increase the size of adipose tissue depots by both increasing adipocyte size and number (hyperplasia of adipose tissue), which is typically associated with normal adipose tissue function. However, the majority of patients may respond to the positive energy balance by adipocyte hypertrophy, which is frequently associated with pathogenic factors causing impaired adipose tissue function. As a result, adipose tissue inflammation may develop and could contribute to secondary organ damage via adverse signals from adipose tissue

Goossens GH, Blaak EE. Adipose tissue dysfunction and impaired metabolic health in human obesity: a matter of oxygen? Front Endocrinol (Lausanne).2015 Apr 24;6:55.

Doc how much weight should I lose?

Overweight or Obesity	BMI ≥25 (≥23 in certain ethnicities)	Metabolic syndrome	10%	Prevention of T2DM
		Prediabetes	10%	Prevention of T2DM
		T2DM	5% to ≥15%	• Reduction in A1C • Reduction in number and/or doses of glucose lowering medications
		Dyslipidemia	5% to ≥15%	• Lower triglycerides • Higher HDL-c • Lower non-HDL-c
		Hypertension	5% to ≥15%	• Lower systolic and diastolic BP • Reductions in number and/or doses of antihypertensive medications
		Nonalcoholic fatty liver disease – Steatosis	5% or more	Reduction in intrahepatocellular lipid
		Nonalcoholic fatty liver disease – Steatohepatitis	10% to 40%	Reduction in inflammation and fibrosis
		Polycystic ovary syndrome	5% to 15% or more	• Ovulation • Regularization of menses • Reduced hirsuitism • Enhanced insulin sensitivity • Reduced serum androgen levels
		Female infertility	10% or more	• Ovulation • Pregnancy
		Male hypogonadism	5% to 10% or more	Increase in serum testosterone
		Obstructive sleep apnea	7% to 11% or more	• Improved symptomatology • Decreased apnea-hypopnea index
		Asthma/reactive airway disease	7% to 8% or more	• Improvement in forced expiratory volume at 1 second • Improved symptomatology
		Osteoarthritis	• ≥10% • 5% to 10% or more when coupled with exercise	• Improvement in symptomatology • Increased function
		Urinary stress incontinence	5% to 10% or more	Reduced frequency of incontinence episodes
		Gastroesophageal reflux disease	10% or more	Reduced symptom frequency and severity
		Depression	Uncertain	• Reduction in depression symptomatology • Improvement in depression scores

AACE guidelines on Obesity 2016

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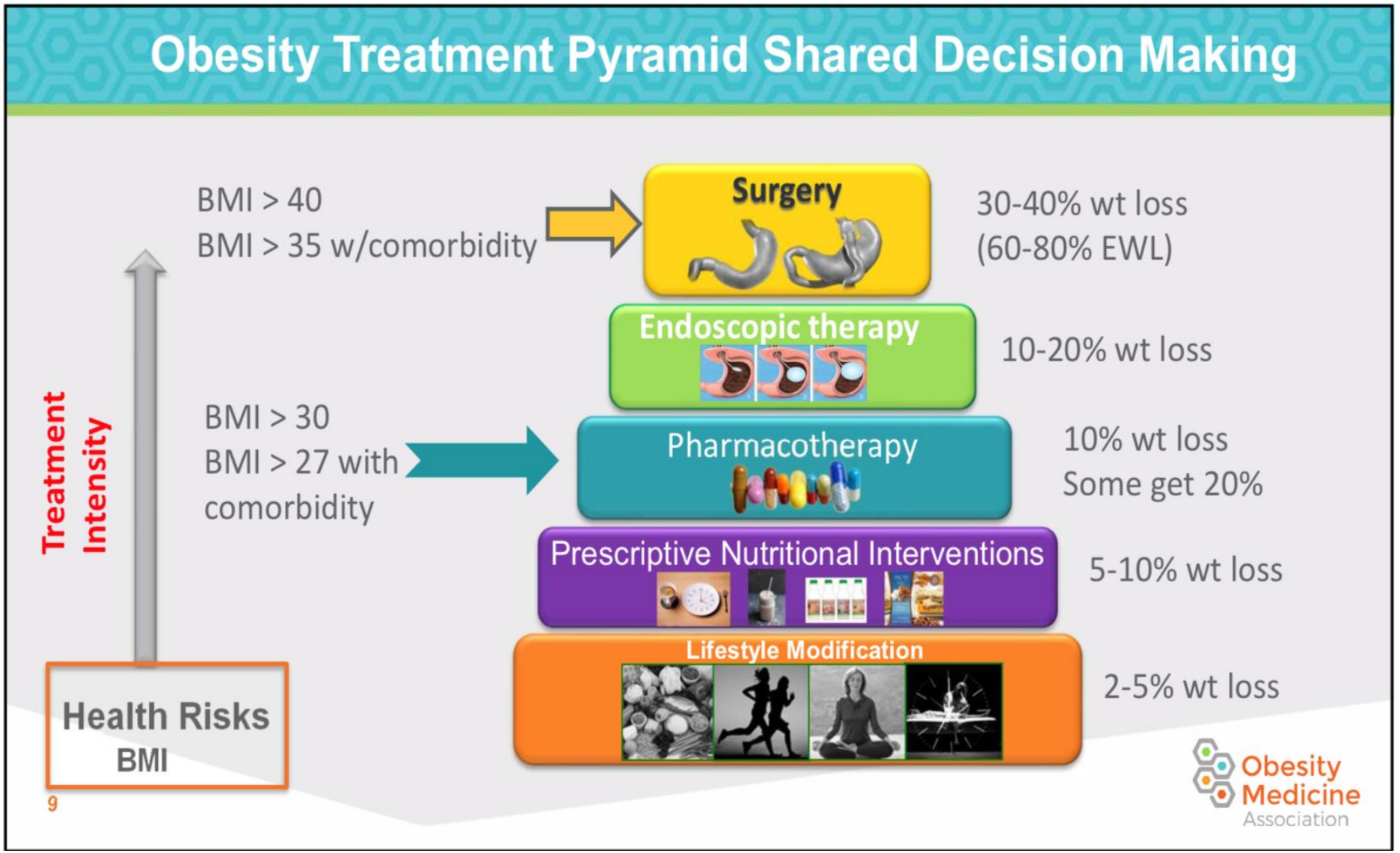
Important Considerations: Treatment Intensity



Surgical Treatment of Obesity

Comorbidity	% Improved	% Resolved
Osteoarthritis/Joint Pain	47	41
Hyperlipidemia	33	63
Gastroesophageal Reflux	24	72
Hypertension	18	70
Sleep Apnea	19	74
Depression	47	8
Peripheral Edema	55	41
Urinary Incontinence	39	44
Asthma	69	13
Diabetes	18	82
Coronary Artery Disease	75	25

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Schauer et al, Ann Surg 2002

- **Surgery is not just the last resort!**
- **Bariatric surgery is a very important metabolic surgery.**

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Who can be considered for anti-obesity treatment?

Medical:

- **BMI greater than and equal to 27 with obesity-related comorbidity**
- **BMI over 30 with or without co-morbidity**

Surgical:

- **BMI greater than and equal to 35 with severe co-morbidity (T2D, high risk for T2D, poorly controlled Htn, non-alcoholic fatty liver/ Steatohepatitis, OSA, DJD (knee/hip), urinary stress incontinence**
- **BMI over 40 without co-morbidity**
- **BMI for bariatric surgery should be adjusted for ethnicity: BMI greater or equal to 25 is obesity in Asian (grade D), greater or equal to 30 is class 2 obesity (new AACE)**
- **Surgery can possibly change set point??**

ACCE guidelines on Obesity 2016

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Medical Treatment of Obesity

From the ACCE guidelines on obesity (2016):

Based RCT of meds vs placebo

Pts in these RCTs were on tx for 1 year and had BMIs 35-39.9

% weight loss was:

- Bupropion ER/Naltrexone ER- 8.1%
- Liraglutide 3mg- 9.2%
- Orlistat (lipase inhibitor)- 8.78%
- Phentermine /Topiramate ER (7.5/46mg- 9.6%, 15/92mg- 12.4%)

The next generation of Obesity tx: Nutrient Stimulating Therapies

- **Entero-endocrine and endo-pancreatic hormone-based treatment**
- **Target tx based on the importance of gut hormone secretion in response to nutrient intake**
- **Decrease energy intake, regulate body-fat mass and energy homeostasis, and some increase energy expenditure**

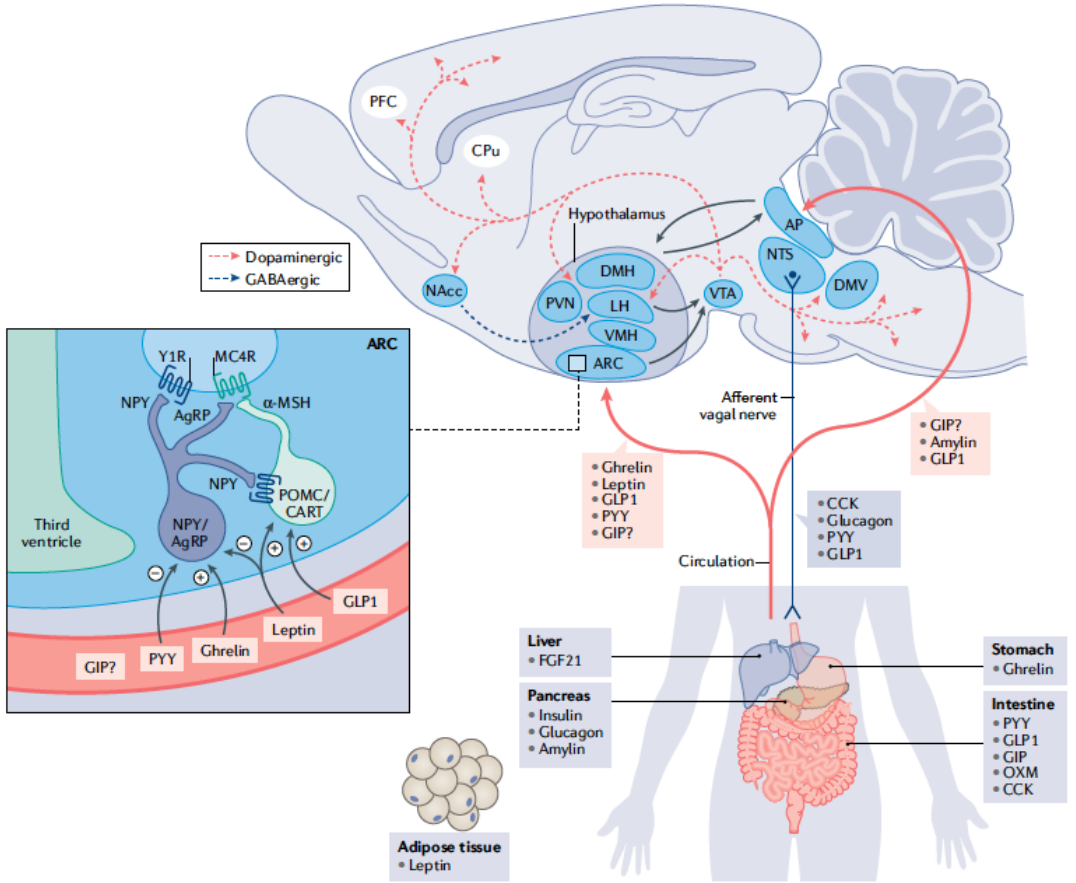

Fig. 2 | **Gut–brain regulation of food intake.** Peripheral hormones integrate in central control of homeostatic and hedonic eating behaviour. α-MSH, α-melanocyte-stimulating hormone; AgRP, agouti-related peptide; AP, area postrema; ARC, arcuate nucleus; CART, cocaine- and amphetamine-regulated transcript; CCK, cholescystokinin; CPu, caudate putamen; DMH, dorsomedial hypothalamus; DMV, dorsal motor nucleus of the vagus; FGF21, fibroblast growth factor 21; GIP, glucose-dependent insulinotropic polypeptide; GLP1, glucagon-like peptide 1; LH, lateral hypothalamus; MC4R, melanocortin 4 receptor; NAcc, nucleus accumbens; NPY, neuropeptide Y; NTS, nucleus tractus solitarius; OXM, oxyntomodulin; PFC, prefrontal cortex; POMC, pro-opiomelanocortin; PVN, paraventricular nucleus; PYY, peptide tyrosine tyrosine; VMH, ventromedial hypothalamus; VTA, ventral tegmental area; Y1R, neuropeptide Y receptor type 1.

GLP-1 RA

- Liraglutide
  - SCALE (Satiety and Clinical Adiposity- Liraglutide Evidence) trials
    - Mean wt loss vs placebo: 8% vs. 2.6&
    - Mean wt loss vs placebo with T2DM: 6% vs. 2%
- Semaglutide
  - STEP (Semaglutide Treatment Effect in People with Obesity) trials
    - Mean wt loss vs. placebo (at 68 weeks): 14.9% vs. 2.4% (withdrawal of drug at 68 weeks caused 11.6% weight regain by 120 weeks)
    - Mean wt loss vs. placebo with T2DM: 9.6% vs. 3.4%
  - SELECT (Semaglutide Effects on Heart Disease and Stroke in Patients with Overweight or Obesity)
    - 2.4mg once weekly was associated with 20% reduction in MACE among pts with established CVD and Obesity

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Use of semaglutide in patients with HIV

- Observational study using Centers for AIDS Research Network of Integrated Clinical Systems cohort
- 222 Adult patients with HIV who were started on semaglutide 2018-2022
- 75% male, mean age 53, average weight 108 kg, mean BMI 35.5, mean hab1c 7.7%, 77% had T2DM, 97% were on antiretroviral therapy (82% receiving integrase strand transfer inhibitors which cause most weight gain)
- 69.6% received low dose (0.25, 0.5, 1mg), 19.2% received high dose (1.7, 2, 2.4mg), 11.2% on oral dose (3, 7 or 14mg)
- At 1 year, average weight loss was 6.47kg, % bodyweight loss was 7.72%.
- There was no significant difference in weight loss for patients on integrase strand transfer inhibitors (-6.49 kg vs. -6.38kg)

Haidar etal. Weight loss associated with semaglutide treatment among people with HIV. AIDS. 2023 Nov 17.

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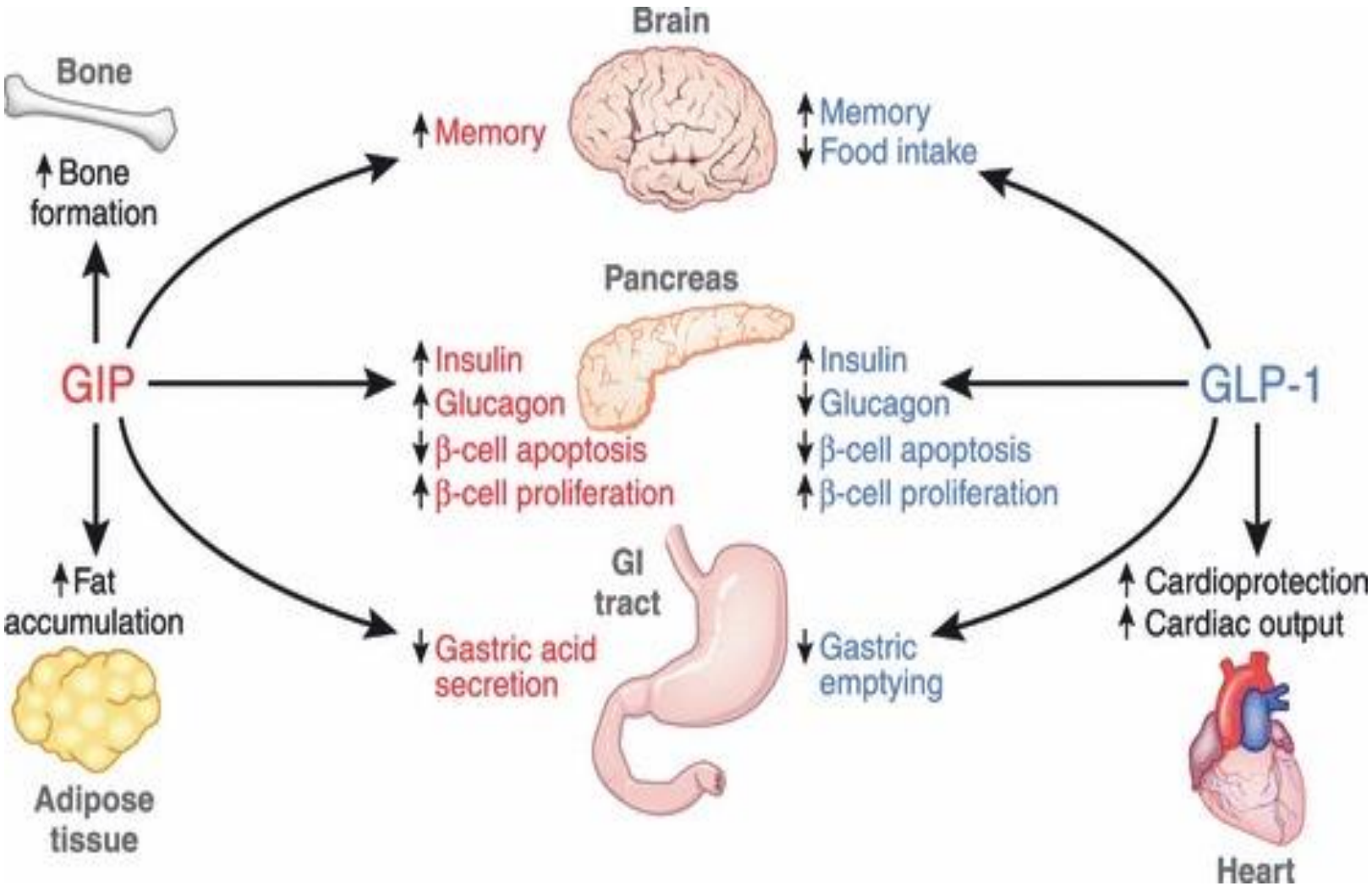
GLP1/GIP



Seino Y, Fukushima M, Yabe D. GIP and GLP-1, the two incretin hormones: Similarities and differences. J Diabetes Investig. 2010 Apr 22;1(1-2):8-23

GLP1/GIP RA/ Tirzepatide

- SURMOUNT 1: after 72 weeks of treatment, people taking tirzepatide at doses of 5, 10, or 15 mg lost an average of 15.0%, 19.5%, and 20.9%, respectively, compared with 3.1% in people taking placebo.
- SURMOUNT 2: Mean wt loss with T2DM: 15.7% at 15mg dose
- SURMOUNT 4 (Dec/23)- at 10 or 15mg average weight loss after 36 weeks 20.9%. Patients were randomized to placebo or continue tx and those who took placebo regained 14% weight lost and those who stayed on tx lost another 5.5%

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Some words of caution

- Preserving muscle mass is extremely important in weight management. Our muscles help determine metabolic rate. Try to eat protein with each meal/snack.
- On tx, Patients may need to set reminders to eat and drink. Patients can get very dehydrated on tx!
- Coverage for anti-obesity medications is limited. Patients who have T2DM can have coverage for GLP1RA. (metformin can be cheap alternative with up to 5% weight loss)
- Be very cautious using AOM with your patients who have disordered eating patterns since it can be harder for them to engage in behavioral therapy since much of this therapy will rely on the patient learning about their own hunger cues and intuitive eating
- Vitamin deficiencies are common in obesity and with obesity txs. (vitamin D, B12, Thiamine)

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Summary

- Obesity management should focus on health and lifestyle behaviors. Never rely solely on weight number or BMI.
- **Use of obesity medications must be combined with lifestyle and tx must be life-long**.
  - **None of the approved medications change metabolic rate (at least not yet) so it is important that patients continue to engage in lifestyle habits to support muscle and metabolism (diet, exercise, good sleep hygiene and stress management techniques)**
- Even low doses of semaglutide in patients on antiretroviral treatment can yield meaningful, therapeutic weight loss.
- Be aware of disordered eating patterns and weight stigma/internalized weight bias. These important issues need to be addressed prior to any discussion about weight management. Failure to recognize these issues could lead to ongoing weight cycling which is very harmful to mental and metabolic health.

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Teaching Evaluation - Laura Montour

Thank you!

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