A Review of Medications used in Weight Loss

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Objectives

1) Develop an appreciation for the mechanism of action for each of the medications used to treat obesity
2) Understand when one might prescribe a specific weight loss medication and when might avoid a specific medication
3) Learn the general guidelines of when GLP-1 RAs can be used as prevent secondary cardiac events and to treat obstructive sleep apnea and the need for frequent follow up

Obesity is

Pervasive

Resistant to treatment

Frequent recurrence

Multifactorial in cause (both individually an in public health)

End result of obesity is beyond CVD – infertility, cancers, orthopedic issues

Sugar Consumption

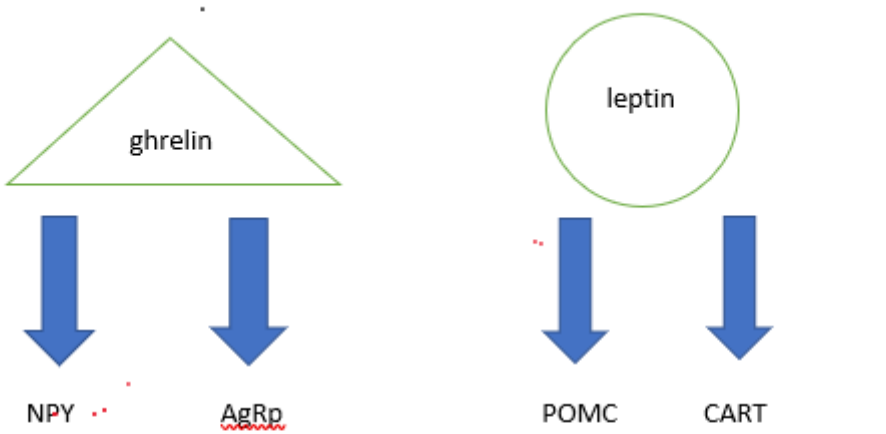
Average American eats 3 lbs of sugar a week (glucose hits DA)

1970 2 lbs a week

200 years ago – 2 lbs a year

https://www.dhhs.nh.gov/dphs/nhp/documents/sugar.pdf

Hunger



Hunger, cravings

Decreased energy expenditure

Decreased hunger

Increased energy expenditure

Medications

Review and mechanism

*All are disappointing without lifestyle changes

*Most do more than appetite suppression

*Weight loss way more complicated than just gross calories in versus predicted out (ie TEF cheestos vs protein)

General guidelines to treat obesity with medications is BMI 30 or 27 with co-morbidity

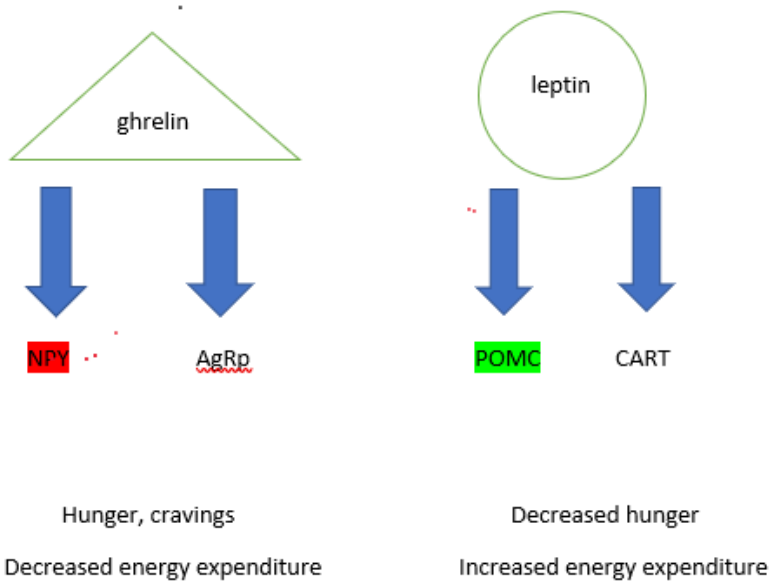
Topiramate

Not FDA approved (except when in combo with phentermine)

In Mice – Increased POMC and likely increased energy expenditure (Caricilli, et al, 2012)

In Mice – NPY (hunger for sweet/carbs) levels decreased in obese mice (Alkan, et al., 2019)

(Side note - protein also decreases NPY)



Topiramate

Who it is good for

- Soda pop habits
- Sweet tooth
- Evening eating
- Those using antipsychotics
- Migraines
- H/O seizures

Who it isn't good for

- Possibly pregnant
- Kidney stones
- Glaucoma
- Pre-existing dementia

Can cause kidney stones, brain fog. finger tingling, birth defects

Topiramate

How I use – 50 mg bid – have pt start with 1/2 pill bid x 7 days (if pt medication naïve or is older, I start at 25 qhs, then 25 bid).

If evening eating is issue, 2nd pill before dinner instead of qhs.

Topiramate

VA patients with obesity placed on topiramate for reasons other than weight loss

Overall, patients lost an average of 2.5 kg (98.2 kg pre-weight vs. 95.7 kg post-weight) and lowered their BMI from 32.3 to 31.4 kg/m^2 at an average follow-up of 7.8 months.

Grabarczyk, 2016

Metformin

Not FDA approved for weight loss

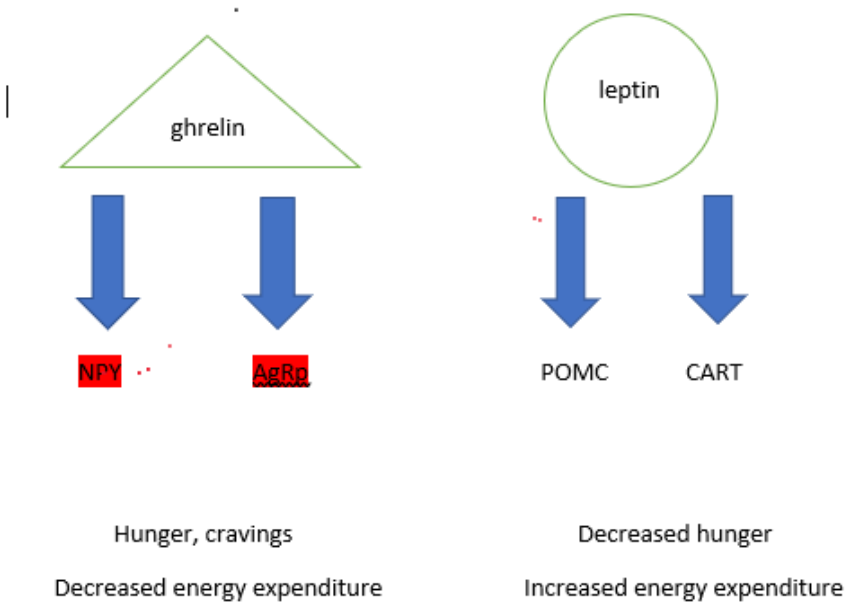
Metformin

Mice – decreases NPY and AgRP in the brain

Lv, et al., 2012

Humans – meta-analysis showed promotes weight loss, reduces proinflammatory markers like IL6 and TNF alpha

Dludia, et al., 2020



Metformin

Who it is good for

- females with PCOS
- episodes of hyperglycemia or who are prediabetic and not on it already
- patients on antipsychotics
- post-menopausal women

Who it isn't good for

- h/o lactic acidosis
- Liver or bad kidney disease
- CHF?? Or is it good for CHF??

Metformin in Weight Loss

Study with individuals BMI >27. Non diabetic. In 6 mo., those who got metformin had average loss 5.6-6.5%. Those who didn't gained .08 to 3.7%

HOMA scores improved in those treated.

Those with more insulin resistance lost a larger % of weight.

Seifarth et al, 2013

Metformin

500 bid – start is as mono therapy some, or as my 2nd med for many

Topiramate plus Metformin in women with PCOS

Dble blind, randomized study women with PCOS, BMI >30, on Metformin.

Metformin plus placebo vs Metformin plus Topiramate

Thirty-one participants were in the MTF+P group and 30 in the MTF+TPM group. The MTF+TPM group showed greater mean weight loss at 3 months (-3.4% vs. -1.6%, p=0.03) and 6 months (-4.5% vs. -1.4%, p=0.03).

Topiramate vs Metformin to combat antipsychotic med weight gain

Small study of inpatients with schizophrenia and obesity for 4 months

Metformin 1000 mg/day showed 3.8 kg loss vs Topiramate 100 mg/day at 2.7 kg

Peng, et al 2016

Phentermine

FDA approved to treat obesity

Lomaira 8 mg version

Phentermine – How it works

Increases NE and DA in brain

Has not been shown to increase BMR

Alexander et al, 2005

Hasn’t been shown to affect the ghrelin/leptin hormones

Phentermine

WHO IT IS GOOD FOR

As addition to other meds

Serving size issues

WHO IT ISN'T GOOD FOR

On stimulant

Addiction

Heart issues/stroke issues

Uncontrolled BP

Insomnia

Glaucoma

Phentermine

Pts treated at weight loss center before or after surgery

At 3 mo, non-surgical patients lost 7.65% and post surgery lost 7.62%

Nor Hanipah et al, 2017

Phentermine – how I dose

Start at ½ pill q am – if BP, pulse ok and they are tracking, I bump to 37.5 mg if needed

Lomaira – 8 mg form of Phentermine. 1 to 3 times daily. GOODRX – as cheap as generic phentermine

Topiramate/Phentermine

FDA approved as Qysmia

Doble blind randomized study with 232 participants.

12 weeks of diet/lifestyle education

At 56 weeks, the percentage change in body weight was -8.3% with PHEN/TPM CR and -2.3% with placebo (treatment difference -6.1%; $p < 0.001$)

Hong et al, 2024

Weight loss can occur without GLP-1

Bupropion/Naltrexone

FDA approved as Contrave

Bupropion/Naltrexone

WHO IT IS FOR

- Drinking etoh part of the weight gain
- Depression

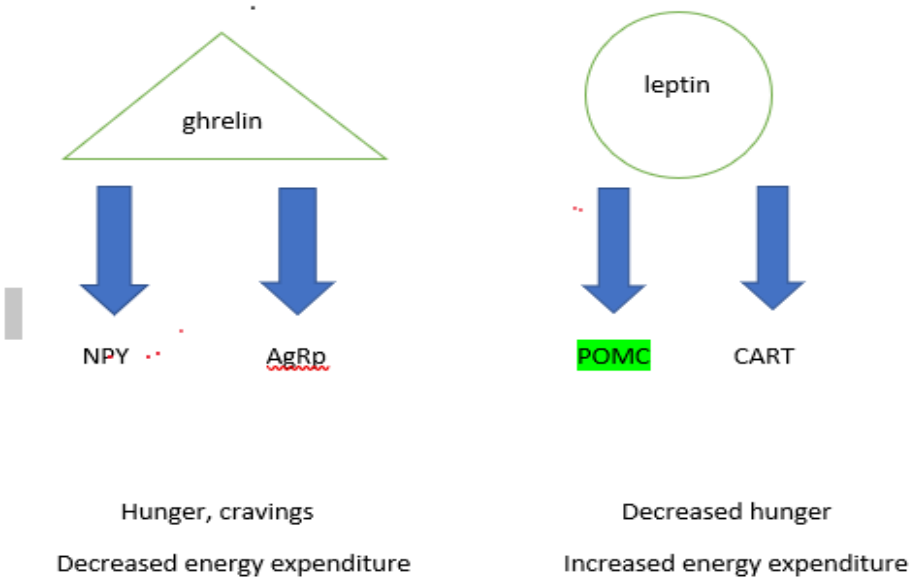
WHO IT ISN'T FOR

- H/O seizures
- On narcotics or have upcoming surgery
- Bulimia
- Htn
- Glaucoma

How it works

Bupropion increases DA and NE

Naltrexone blocks opioid receptor



Bupropion/Naltrexone

Canadian study, retrospective.

About 48% stayed on it for 6 mo

After 6 months, participants lost a mean of 4.23 kg (95% confidence interval or 4.05% of body weight, with 42.5% losing at least 5% of their body weight and 15.5% losing at least 10%.

Participants also experienced decreased appetite (14.7%), decreased cravings (13.9%), decreased hunger (9.4%) and felt full sooner (2.5%)

Wharton, et al 2024

Bupropion/Naltrexone – how I dose

Bupropion 150 mg XR for 7 days the add Naltrexone 50 mg ½ qam

Can later increase Bupropion to 300 mg XL

GLP-1 RA

T2DM	Obesity (FDA)	generic name
Victoza	Saxenda	liraglutide (now generic $300/mo)
Ozempic	Wegovy	semaglutide
Mounjaro	Zepbound	tirzepatide

These are GLP1RA + GIP

GLP-1 RA (liraglutide, semaglutide, tirzepatide)

Slows digestion

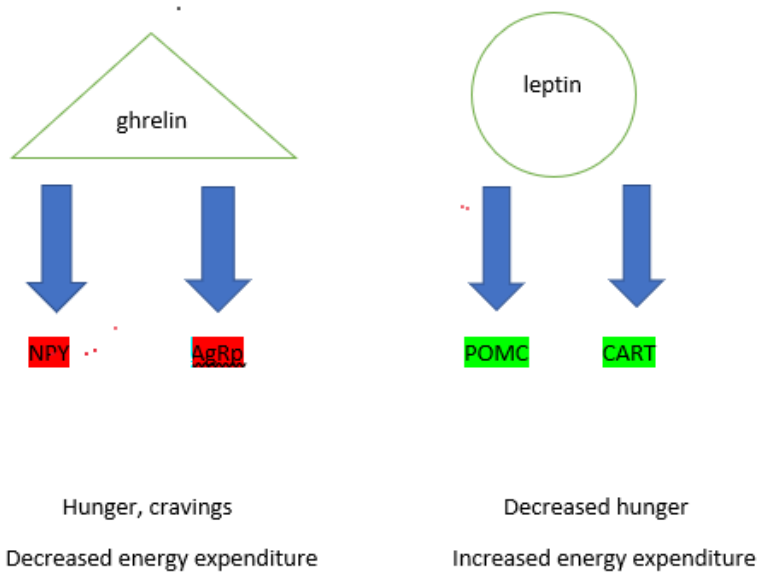
Decreases appetite

Slows gluconeogenesis

Increases insulin sensitivity

Increases leptin sensitivity

Normalizes insulin release



GLP-1

WHO IS IT FOR

- T2D (T1D will be coming)
- Insulin resistant
- People with obesity with good insurance or $$$
- Cardiac secondary prevention
- OSA treatment

WHO IT ISN'T FOR

- Pancreatitis history
- MEN2/Medullary Thyroid CA
- Gastroparesis
- People who can't/wont eat adequate protein

Liraglutide

Subjects with T2DM, obesity/overweight, on insulin; placebo vs liraglutide 3 mg (Saxenda dosing). Both groups got intensive behavioral therapy.

At 1 year, those on liraglutide lost 5.8% of weight vs 1.5%

Garvey et al, 2020

Semaglutide 2.4 mg weekly

Participants without T2D< with BMI > 30 or >27 with co morbidity

The mean change in body weight from baseline to week 68 was −14.9% in the semaglutide group as compared with −2.4% with placebo

Wilding et al, 2021

Wegovy FDA approved to prevent secondary CV events

Cardiovascular disease was defined as previous myocardial infarction, previous stroke, or symptomatic peripheral arterial disease.

Among 17,604 patients with a BMI of 27 or greater and preexisting cardiovascular disease but without diabetes, treatment with once-weekly subcutaneous semaglutide at a dose of 2.4 mg for a mean duration of 33 months reduced the risk of a composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke by 20% (hazard ratio, 0.80; 95% CI, 0.72 to 0.90)

Lincoff et al, 2023

Ozempic and CVD

Patients with type 2 diabetes and a glycated hemoglobin level of 7% or more were eligible if they had not been treated with an antihyperglycemic drug or had been treated with no more than two oral antihyperglycemic agents, with or without basal or premixed insulin. Key inclusion criteria were an age of 50 years or more with established cardiovascular disease (previous cardiovascular, cerebrovascular, or peripheral vascular disease), chronic heart failure (New York Heart Association class II or III), or chronic kidney disease of stage 3 or higher or an age of 60 years or more with at least one cardiovascular risk factor

Semaglutide-treated patients had a significant 26% lower risk of the primary composite outcome of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke than did those receiving placebo.

Marsco, et al 2016

Tirzepatide for Weight Loss

Participants BMI >30 or >27 with 1 cormorbidity. Not T2DM. Given lifestyle counseling

For 72 weeks. The mean percentage change in weight at week 72 was −15.0% with 5-mg weekly doses of tirzepatide, −19.5% with 10-mg doses, and −20.9% with 15-mg doses and −3.1% (95% CI, −4.3 to −1.9) with placebo (P<0.001 for all comparisons with placebo)

Jastreboff et al, 2022

Semaglutide vs Tirzepatide for weight loss

Among 41 222 adults meeting the study criteria (semaglutide, 32 029; tirzepatide, 9193), 18 386 remained after propensity score matching. On-treatment changes in weight were larger for patients receiving tirzepatide at 3 months (difference, -2.4%) 6 months (difference, -4.3%) and 12 months (difference, -6.9%). Rates of gastrointestinal AEs were similar between groups.

Rodriguez et al, 2024

Tirzepatide (Zepbound) for Sleep Apnea

Those with obesity and moderate to severe sleep apnea treated with either tirzepatide 10 or 15 mg

Phase 1 no CPAP – ASI decreases 25.3 events/hr vs placebo 5.3

Phase 2 used CPAP – ASI decreases 29.3 ASI vs placebo 5.5

Tirzepatide improved BMI, hypoxia, hsCRP and systolic BP

Malhota, et al 2024

If you are going to RX GLP1RA

PLEASE see them monthly until stable dosing

Make sure they are getting adequate protein (tracking) 80 g/day min

Consider body composition scale

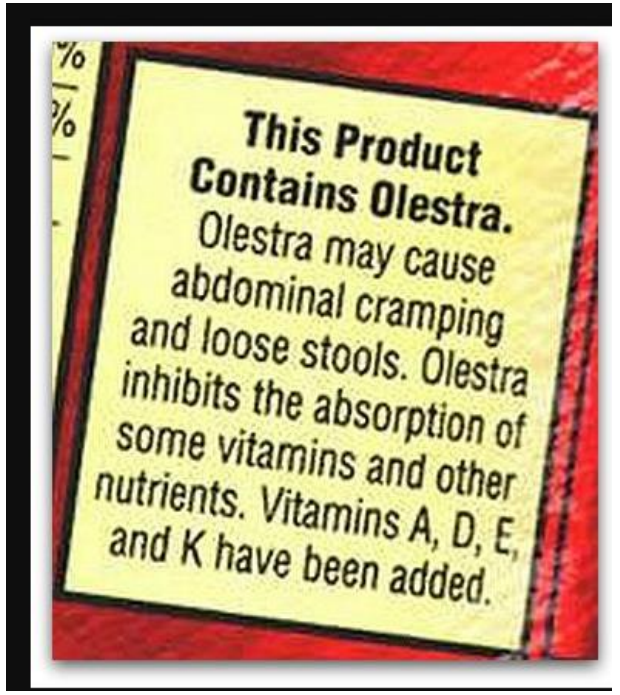
At least 1000 calories a day (real food best)

GI, gerd, LUQ pain, dehydration, constipation need managing

Know that for weight loss, many require 2nd PA at 4 mo

Not discussed

Orlistat – FDA approved



What is coming in medications??

More GLP-1 options and combos

Ghrelin Antagonists

Leptin Agonists

Cannabinoid-1 receptor blockers

Setmelanotide (activates MC4) – for POMC deficiency or Leptin Receptor Deficiency

Bariatric Surgery and life expectancy

For the general population, bariatric surgery is still considered the gold standard in treating obesity.

In a meta-analysis published in Lancet reviewing 1,470 articles and 174,722 participants, individuals who had obesity without diabetes who underwent bariatric surgery had an increase in life expectancy of 6.1 years over those who had usual care. For individuals with both obesity and diabetes, bariatric surgery was associated with a 9.3 years on increased expected life span.

Syn et al, 2021

New bariatric surgery guidelines ASMBS

Lower BMI to qualify for surgery:

30 plus comorbid

35 without comorbid

Asian descent:

27.5 plus comorbid

32.5 no comorbid

Some policies counting infertility, GERD, PCOS as comorbidities

3 things to remember

There are multiple meds to help with weight loss

Weight loss meds usually do more than appetite suppression

GLP1 RA have multiple uses but require frequent follow up

Mercy Weight Loss/Bariatric Center

How to refer

Clinic or patient calls MWL – 515-358-9400. Free appt to discuss options (dietician, meal replacement, medical weight loss, surgical weight loss)

Dr Stephen Hoeslcher – MWL

Dr Kara Thompson – Bariatric Center – medical support

Dr Mark Smolik – Bariatric surgeon (Sleeves, Roux, Conversions)

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