

# Anti-Obesity Medications



**Potential Targets**

**Mechanism of Action:**



**Contraindications\***

\*Not a complete list

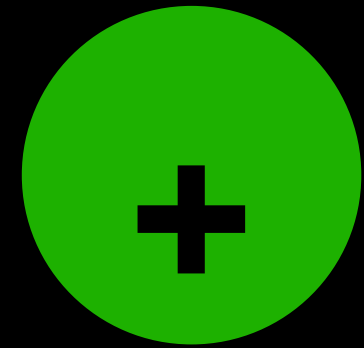
**Dosing:**



**Common Adverse Effects**

**Advice/Precautions:**

# Orlistat



**Hypercholesterolemia**  
**Low risk medication**



**Cholestasis**  
**Chronic malabsorption syndrome**



**Flatulence, diarrhea, bloating, cramping, abd pain**  
**Increase urinary oxalate**  
**Fat soluble vitamin deficiency**

## **Mechanism of Action:**

- Pancreatic lipase inhibitor—Blocks ~30% of fat intake

## **Dosing:**

- Start 120mg daily
- Range: 120mg/d—120mg TID
- Alli is an OTC available in 60mg

## **Advice/Precautions:**

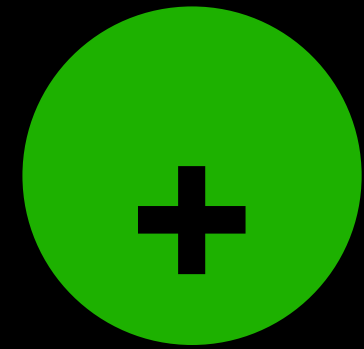
- Advise daily multivitamin
- Monitor fat-soluble vitamins (A,D,E,K)
- Decrease levels of cyclosporin if co-administered
- No causal relationship with liver failure

Please  
Excuse Me  
From Being  
Late.  
I HAVE  
Explosive  
Diarrhea.  
-K



allii™

# Phentermine



Increased hunger  
Low metabolic rate



Active CV disease  
Poorly controlled HTN  
Cardiac arrhythmias  
Hyperthyroidism  
Glaucoma



Dry mouth  
Constipation  
Insomnia  
Palpitations, HA, Irritability

## Mechanism of Action:

- Inhibits Na-dependent NE transporter to reduce NE uptake
- Inhibits serotonin and dopamine reuptake

## Dosing:

- 15-30mg capsule, 37.5mg tablet QD-BID
- 8mg TID
- 1/2 of 37.5mg tablet

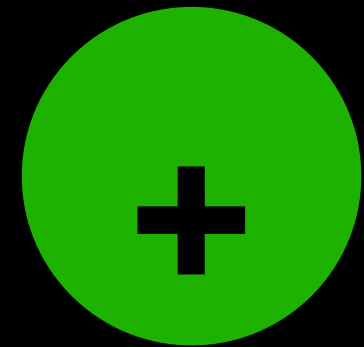
## Advice/Precautions:

- *Schedule IV controlled substance*
- Monitor BP, awareness of caffeine intake
- **NO** evidence of addiction, withdrawal
- **NO** established relationship related to cardiac valvulopathy or pulmonary hypertension

# Why you shouldn't be afraid of phentermine

- Phentermine is the most widely used anti-obesity drug in the U.S.
- Warnings of adverse CV and psychiatric effects are included in FDA labeling. However, the few clinical reports of such adverse effects are anecdotal.
- When phentermine was approved (1959) the expectations were that it would prove to be addictive. Due to the structural similarities between phentermine and amphetamine and on evidence in rats that phentermine stimulated spontaneous activity. No evidence suggesting the drug had human addiction potential appeared in clinical trials conducted prior to approval.
- After 60 years, there is no evidence in peer-reviewed medical literature to support the hypothesis that phentermine has significant human addiction potential.
- One retrospective study investigated symptoms occurring when patients treated with long-term phentermine ceased taking it. The study found that patients on long-term phentermine who ceased phentermine abruptly by their choice did not have an amphetamine-like withdrawal symptom complex. Significantly, **there was no evidence of phentermine cravings.**

# Topiramate (Topamax ®)



Migraines, seizures, binge eating, excessive cravings (carbs), on mood stabilizers (sub/alt), on phentermine



Severe depression  
Pregnancy  
Kidney Stones



**WARNING:** Acute angle glaucoma, SI, pregnancy

Parasthesias, somnolence, kidney stones, cognitive impairment, taste aversion

## Mechanism of Action: *Unclear*

- AMPA, Glutamate receptor
- Carbonic anhydrase
- GABA-A (isozymes II, IV)
- Voltage-dependent sodium channels

## Dosing:

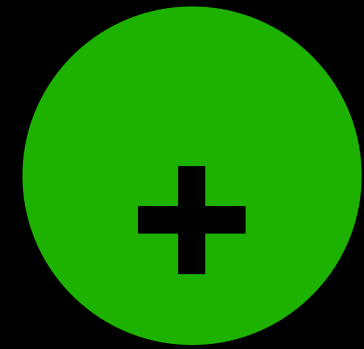
- Start 25mg daily
- Range: 25-200mg/day

## Advice/Precautions:

- Take at night if trouble with drowsiness
- Interaction with OCPs
- Use BIRTH CONTROL d/t increased risk of cleft lip and palate
- Hyperchloremic NAGMA

Try zonisamide if cognitive impairment or dyspepsia is intolerable

# Phentermine/Topiramate CR (Qysmia®)



**Non-child bearing pt**  
**Excessive hunger**  
**Mild SE with phentermine**



**Active CV Disease**  
**Uncontrolled HTN**  
**Hyperthyroidism**  
**Glaucoma**  
**Kidney Stones**  
**During or within one day of**  
**MAOI**



**Dry mouth, restlessness,**  
**insomnia, palpitations, HA,**  
**constipation**  
**Parasthesias, dysgeusia,**  
**somnolence, cognitive**  
**impairment**

## **Mechanism of Action:**

- Sympathomimetic (NE) release in hypothalamus decreases hunger
- AMPA, GABA receptor—decreases cravings

## **Dosing:**

- Start 3.75/23mg x14d then 7.5/46mg
- Range 3.75/23mg—15/92mg/day

## **Advice/Precautions:**

- Schedule IV controlled substance
- counsel on use of BIRTH CONTROL due to increased risk of cleft lip and palate
- Pregnancy test prior to start then MONTHLY
- Increase hydration
- 1/4 cup lemon/lime juice for paresthesias

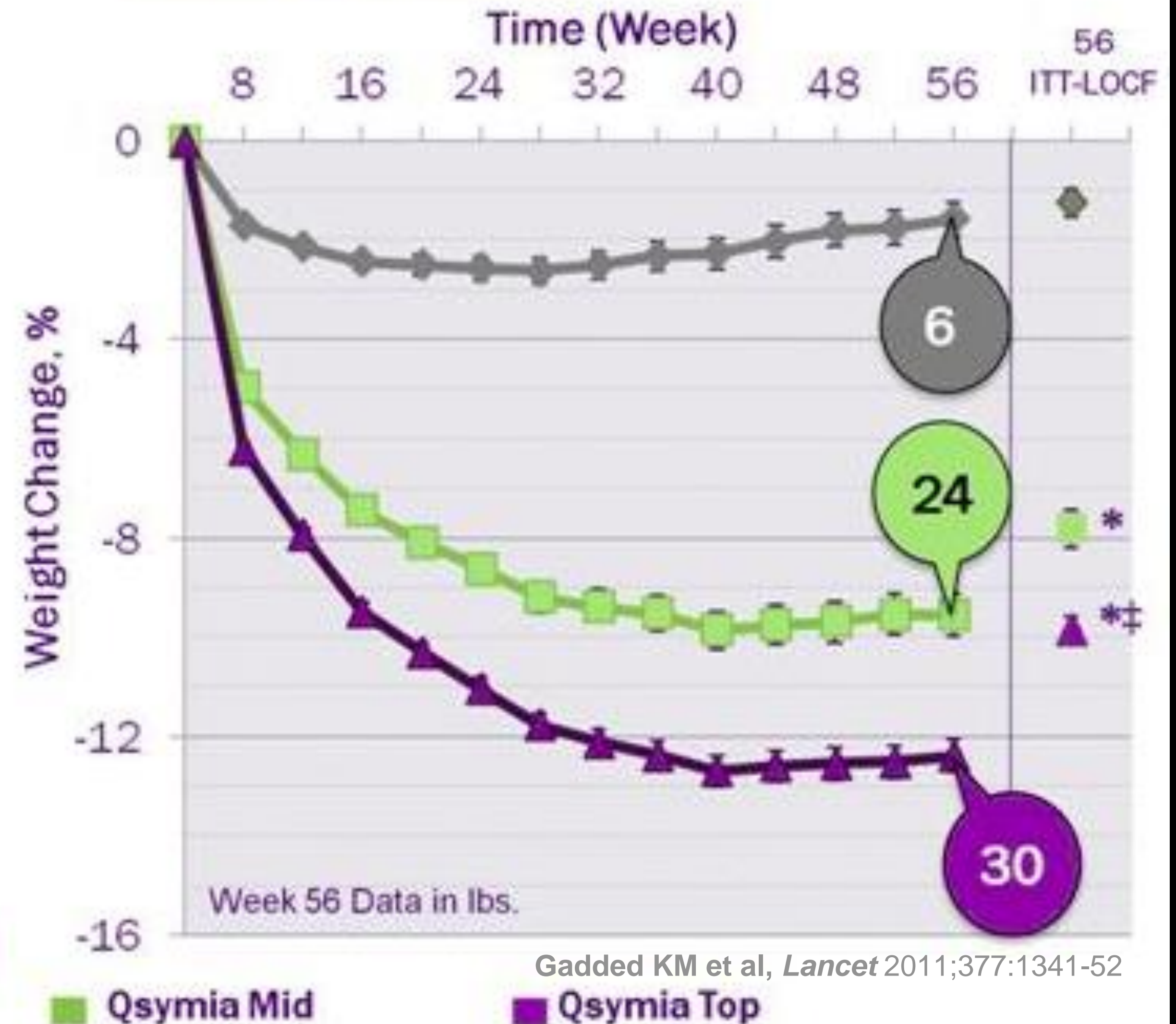
# Responders to Phentermine/Topiramate (Qsymia)

## Study 1 (EQUIP)



3.75/23mg/d

## Study 2 (CONQUER)

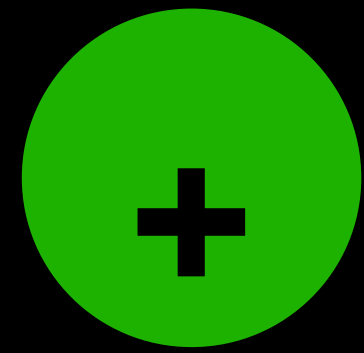


7.5/46mg/d

15/92mg/d



# Lorcaserin (Belviq ®)



Unable to tolerate phentermine  
Older pt on multiple meds  
Diabetes  
Night eating



Pregnancy



Headache, nausea  
dizziness, dry mouth, fatigue,  
nasopharyngitis  
priapism

## Mechanism of Action:

- Selective serotonin 5HT<sub>2c</sub> receptor agonist
- Increases satiety via alpha-MSH and POMC neuron activation

## Dosing:

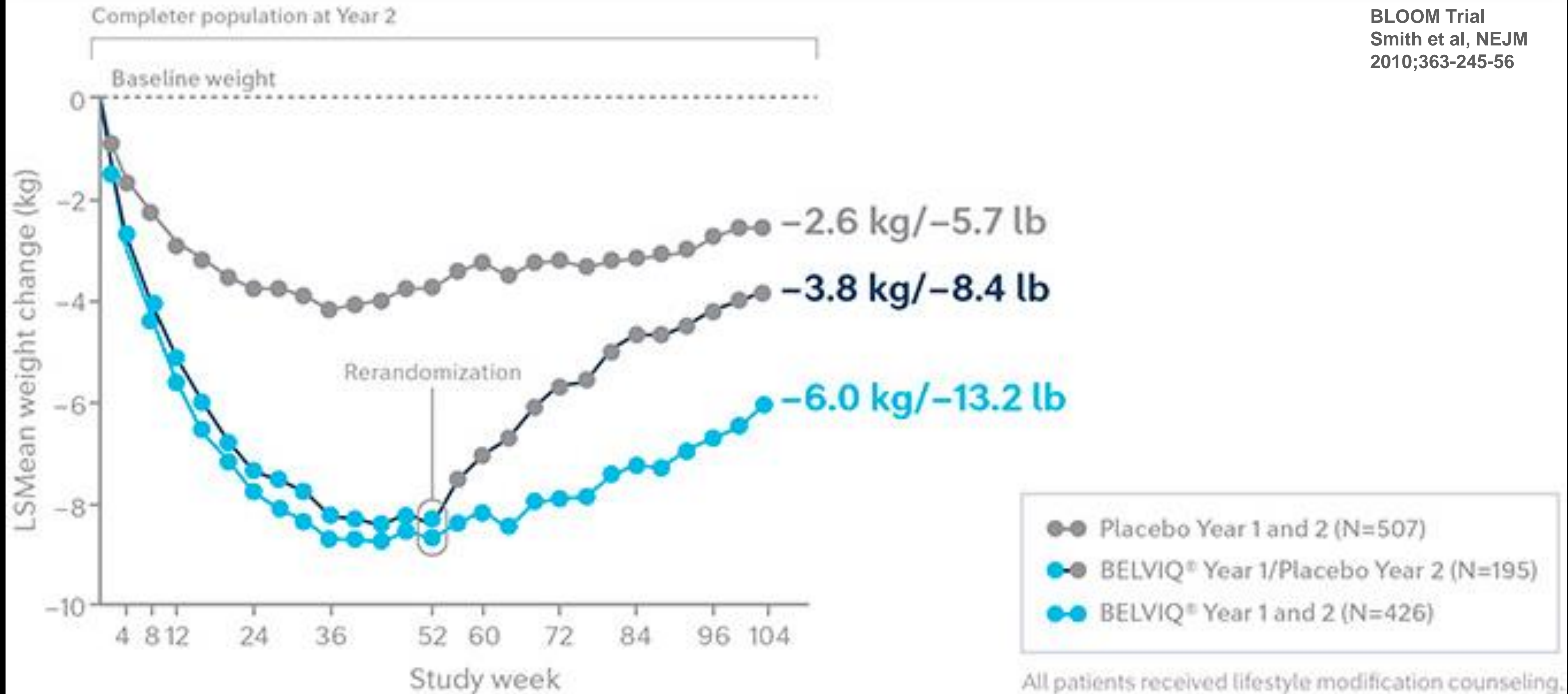
- 10mg BID or 20mg XR daily
- Can use QD daily in evening as combination

## Advice/Precautions:

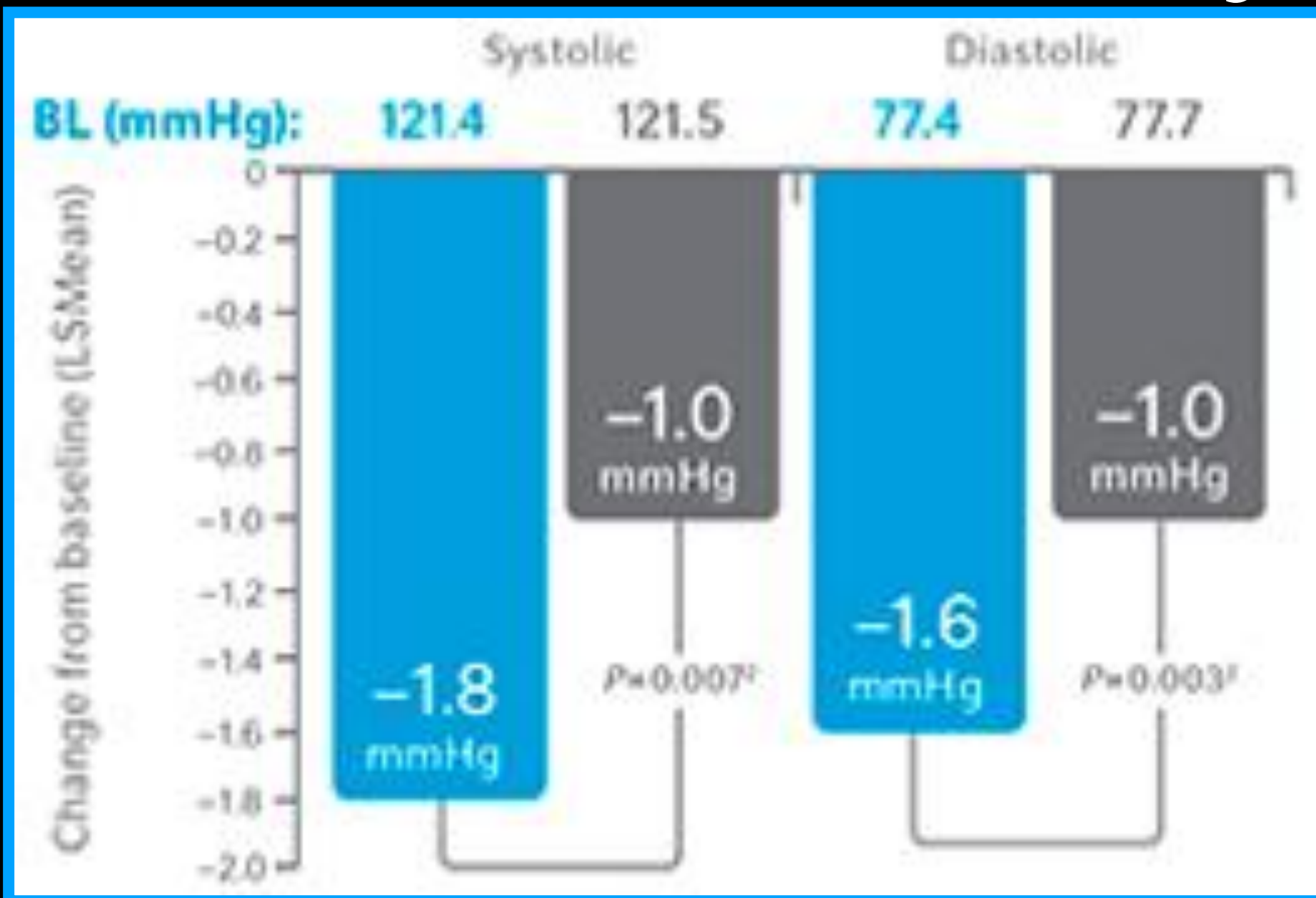
- Schedule IV controlled substance
- Watch co-administration with SSRIs, bupropion or concern about serotonin syndrome
- Caution with congestive heart failure
- No concern about combo with phentermine

# Weight Loss Over 2 Years

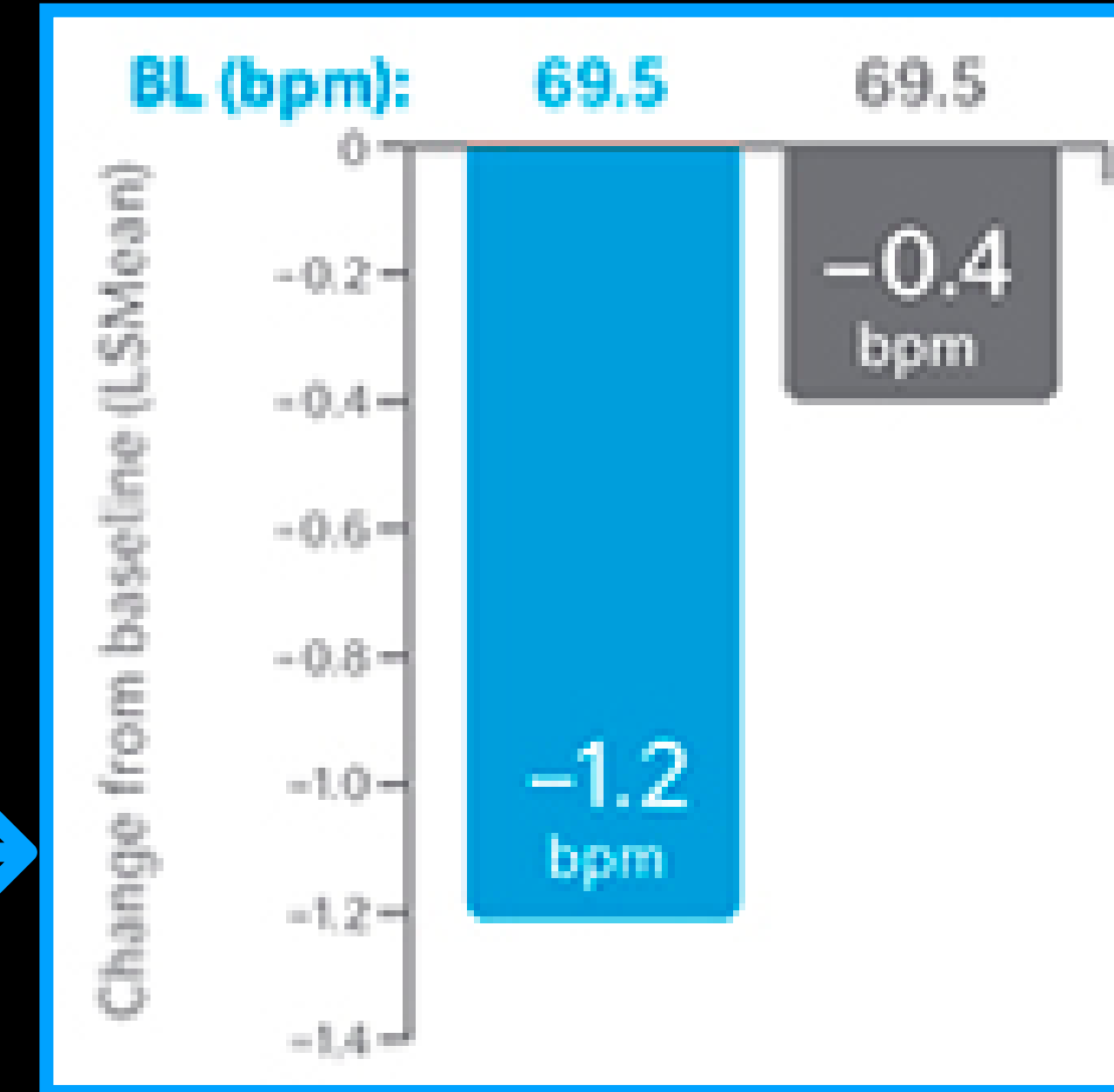
BLOOM Trial  
Smith et al, NEJM  
2010;363-245-56



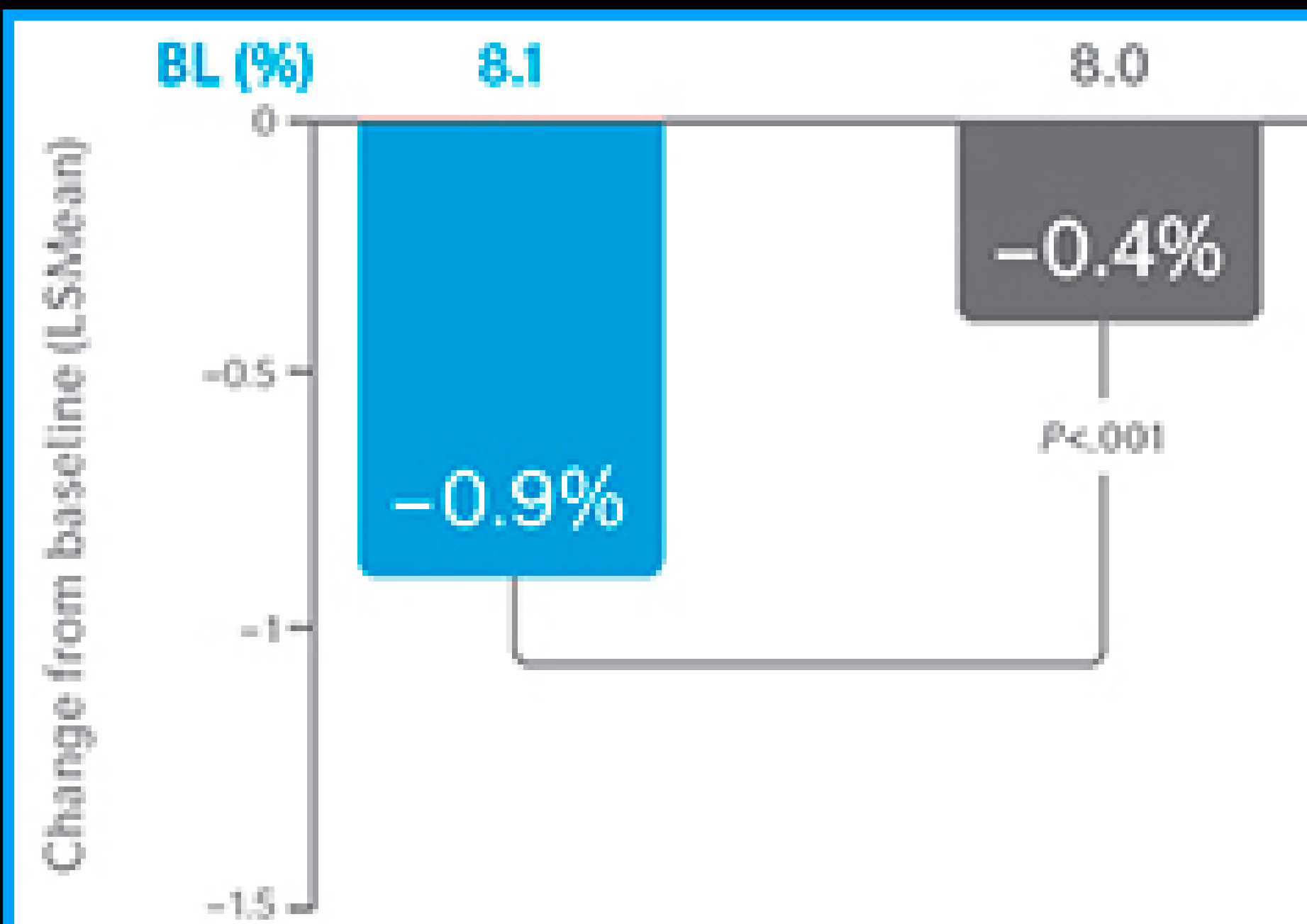
# Secondary End-Points of Lorcaserin



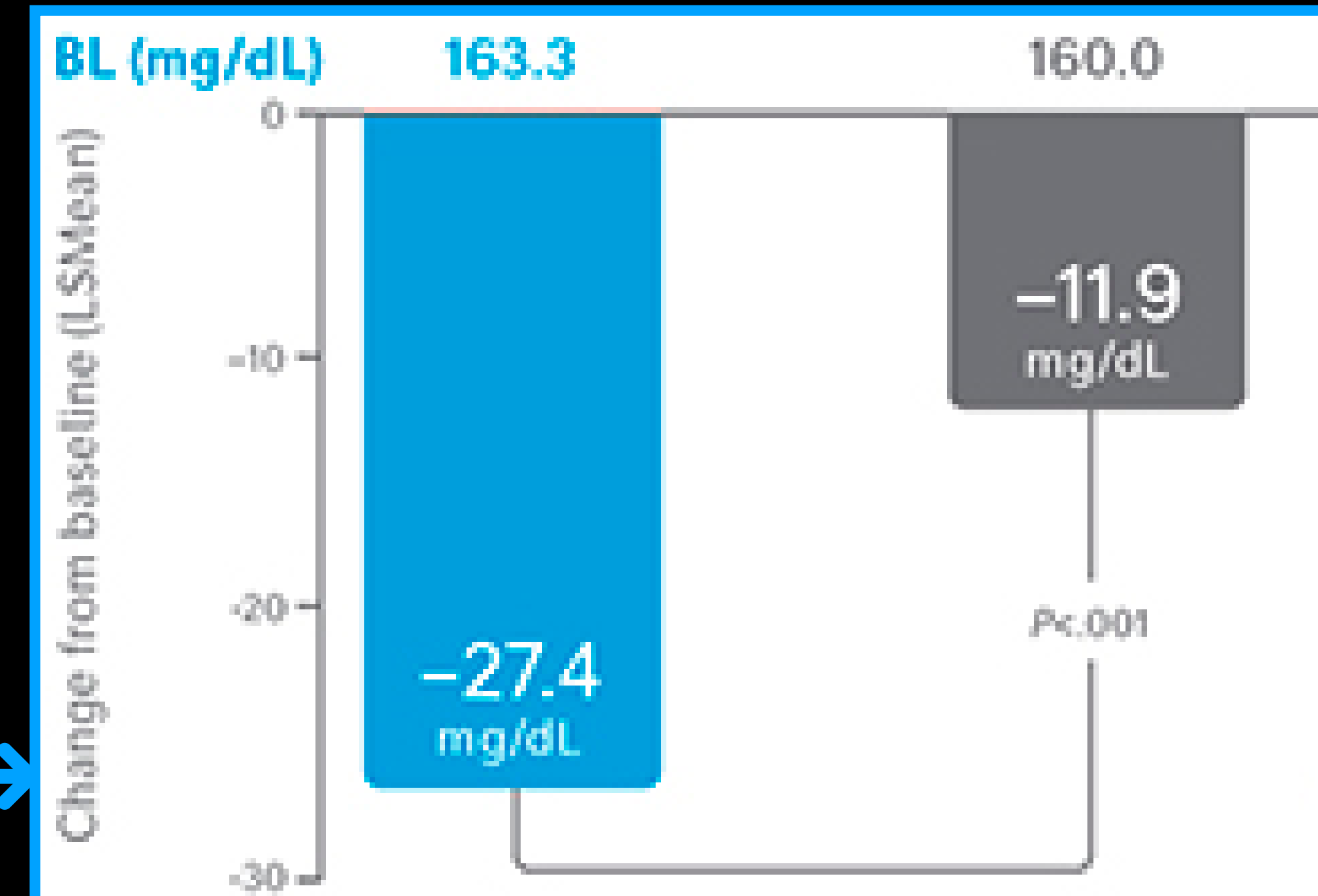
← Blood Pressure



Resting Heart Rate →

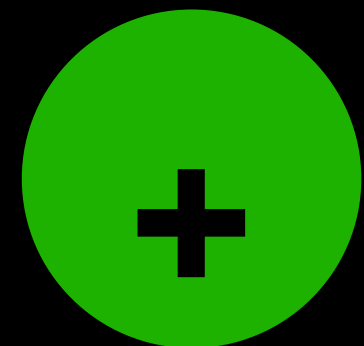


← HbA1c%



Fasting Glucose →

# Naltrexone/Bupropion (Contrave ®)



**Excessive hunger and cravings**  
**Patients who smoke**  
**On bupropion already**













**Seizures, uncontrolled HTN**  
**Bulimia**  
**Chronic Opioid Use**  
**Upcoming surgery**



**WARNING: Neuropsychiatric rxns, SI, behavior changes**  
**nausea, headache, insomnia,**  
**dizziness, dry mouth**

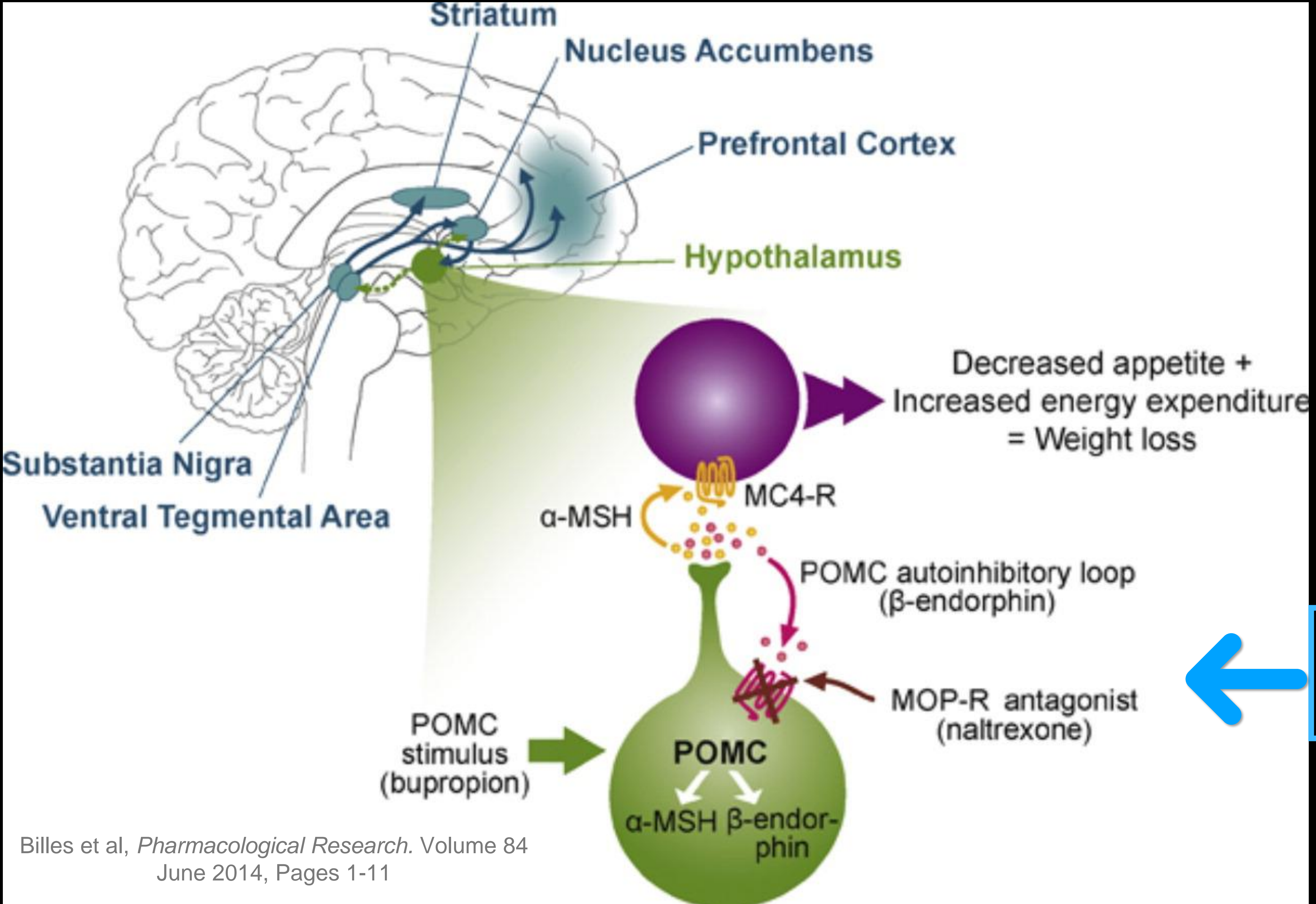
## Mechanism of Action:

- Reuptake inhibitor DA and NE activity increases POMC activity
- Naltrexone blocks B-endorphin, POMC auto inhibitor

	 Morning dose	 Evening dose
Starting: Week 1		
Week 2		
Week 3		
Week 4-onward		

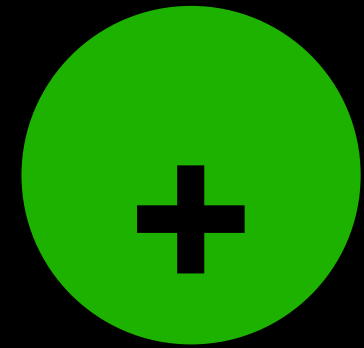
## Advice/Precautions:

- **Avoid opioid use, ask about surgery!**
- **Results of LIGHT trial (2016) do NOT show reduction in CV events**
- **Avoid high fat diet (increases bioavailability)**



**Reduces the probability  
 that compensatory  
 pathways mitigate drug  
 benefits over time!**

# Liraglutide (Saxenda ®)



**Diabetes or Prediabetes**  
(Not indicated for diabetes tx)  
**Pts with insurance coverage**



**Medullary thyroid CA**  
(including FHx)  
**MEN type II**  
**Hx of pancreatitis**



**Nausea, HA, Angioedema**  
**Gastroparesis**  
**Cannot be combined with DPP4i**

## Mechanism of Action:

- GLP-1 receptor agonist
- Increase satiety, decreases gastric emptying
- 97% homologous to human GLP-1
- Central acting by inhibition of NPY/AgRP

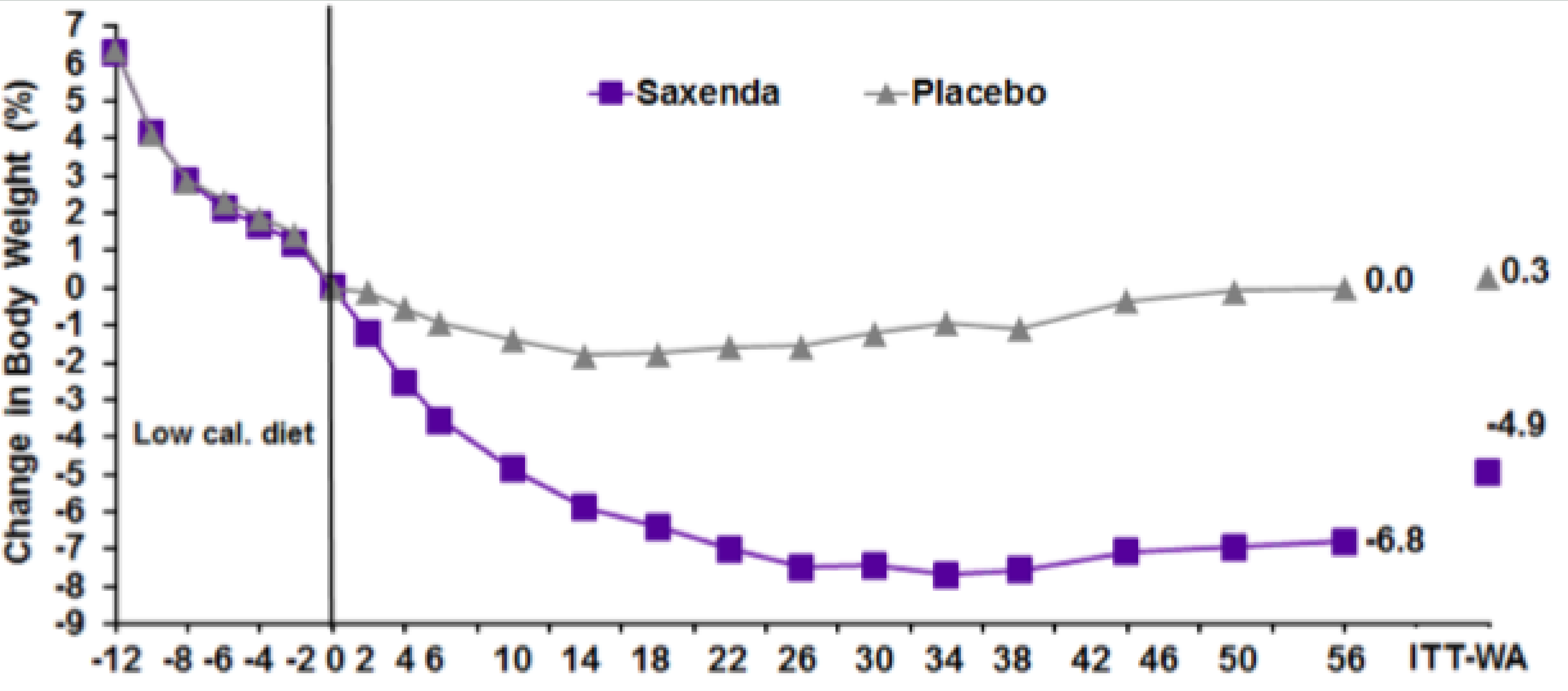
## Dosing: Daily SC injections



## Advice/Precautions:

- Nausea may improve with time
- No data to support reports on increased risk of pancreatic ductal neoplasia and pancreatic cancer

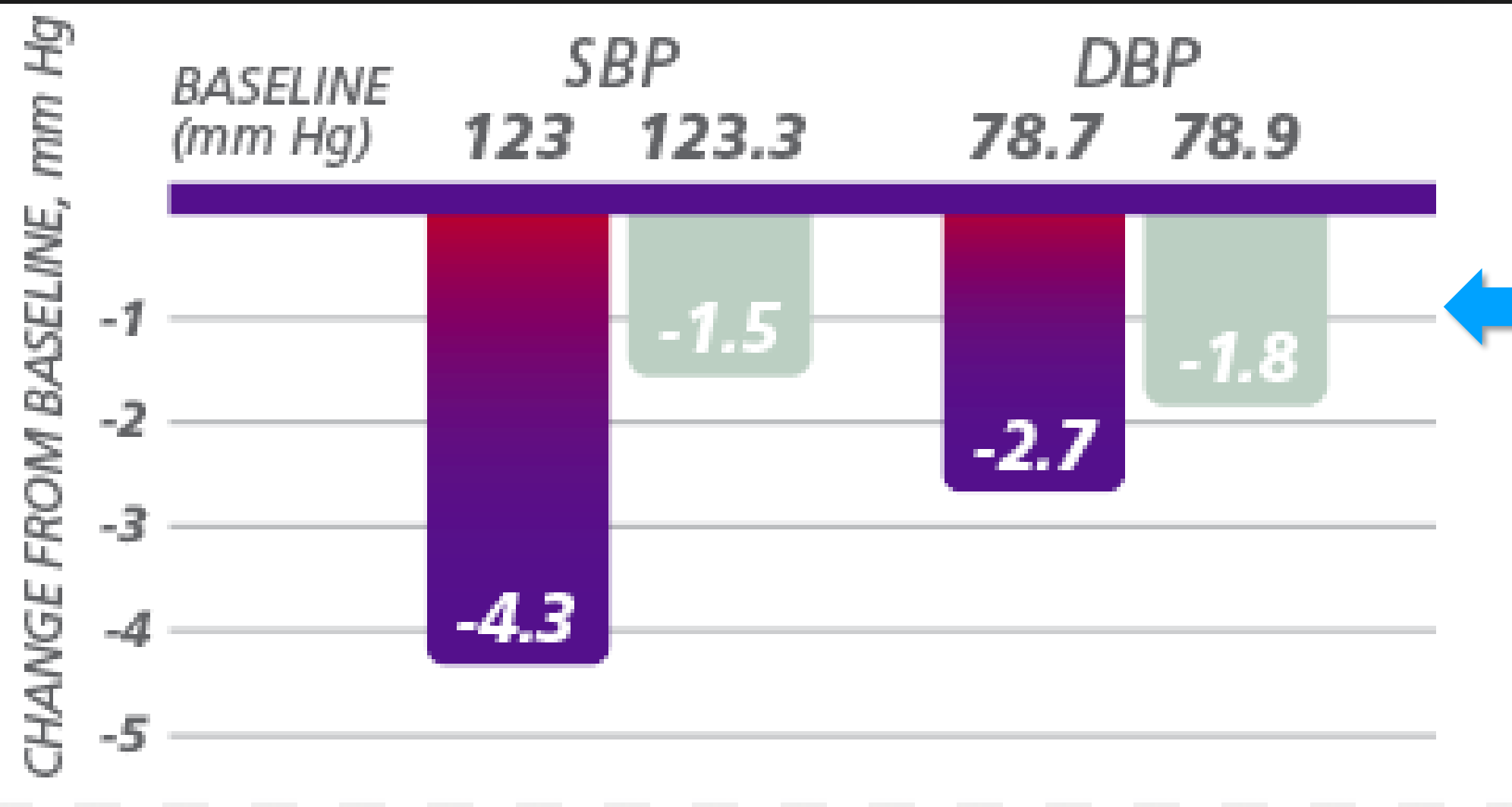
# Average Weight Loss With Liraglutide 3mg



Astrup A, et al. Int J Obes (Lond) 2012; 36: 843–854.

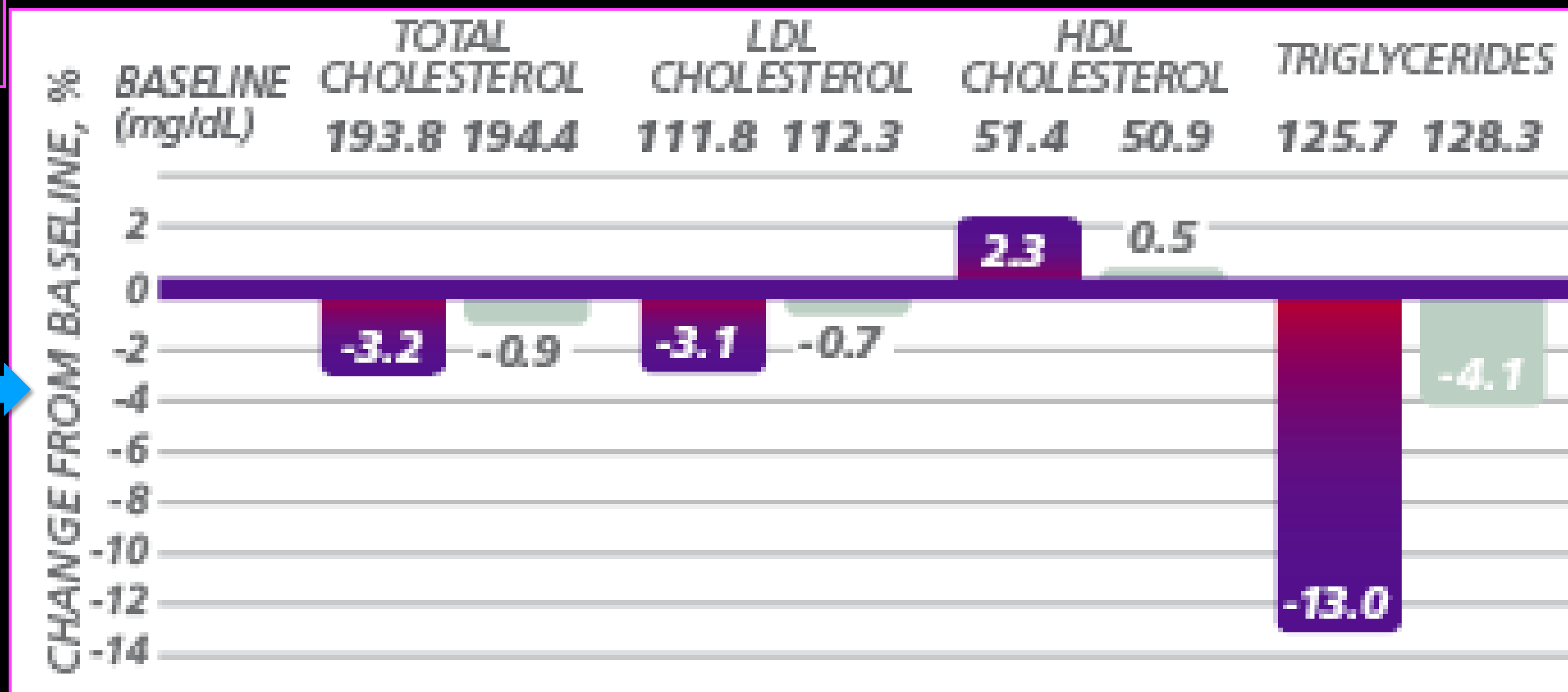
Wadden TA, et al. the SCALE study. Int J Obes (Lond) 2013; 37: 1443–1451.

# Improvements in Secondary End-Points with Liraglutide 3mg



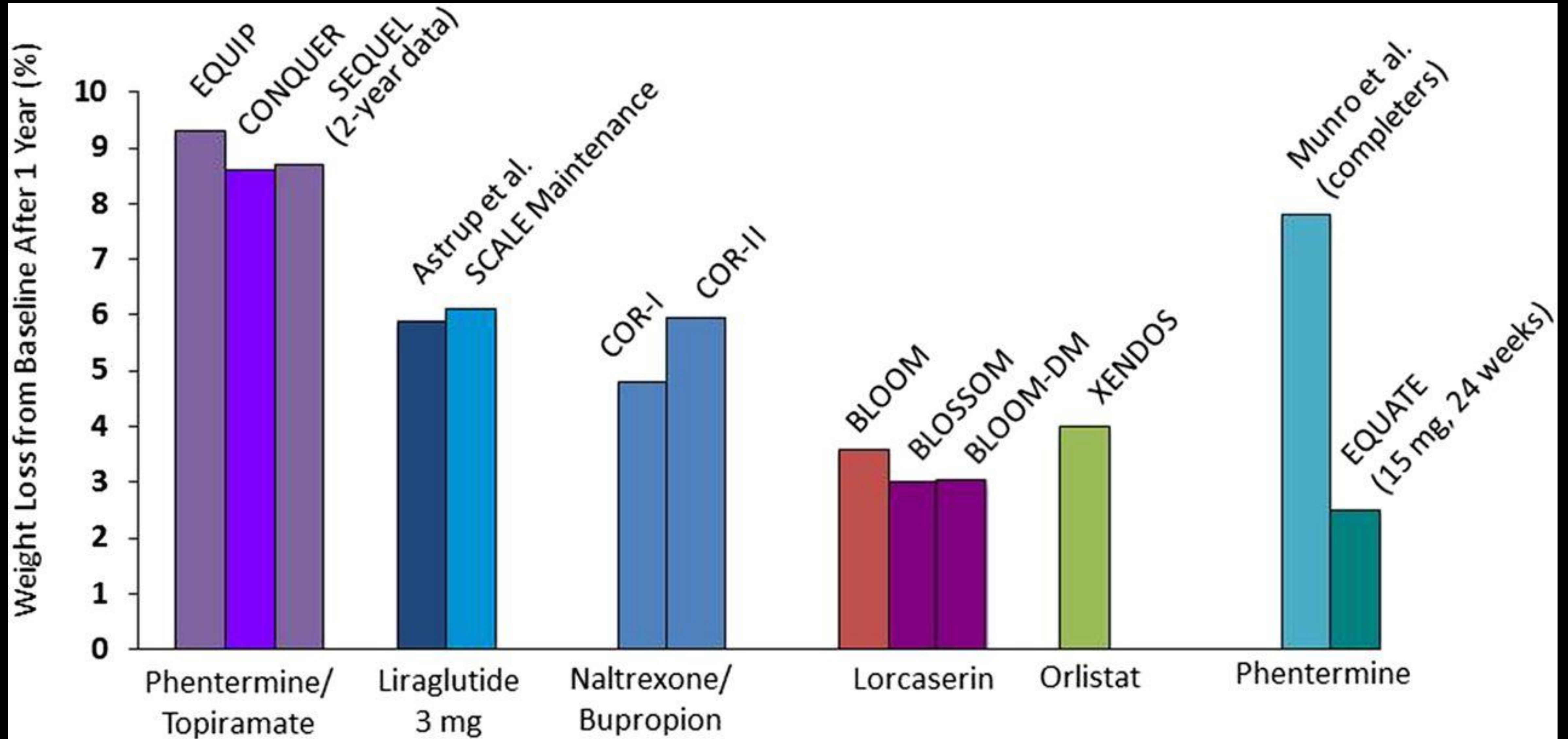
Blood Pressure

Lipids





# Comparison of Anti-Obesity Medications



# Before Adding A Med...

Determine if a med is the cause!



# Weight Gain Promoting Medications

# Alternate Agents

## Diabetes Treatments:

Insulin  
Sulfonylureas  
Thiazolidinediones

Amylin analog—pramlintide  
GLP-1 agonists  
metformin  
SGLT-2 inhibitors  
DPP4 inhibitors

## Glucocorticoids

Prednisone, Methyl-prednisolone, etc

Immunosuppressive agents  
DMARDs

## Contraceptives

Depo-provera

Non-hormonal contraception  
OCPs

## Beta-Blockers

Propranolol, Metoprolol, Atenolol

Other anti-hypertensives such as ACEi  
Third generation BBs have less weight gain (carvediolol, nebivolol)

## Anti-Histamines

Diphenhydramine, Hydroxyzine, Cetirizine, Fexofenadine

Loratadine

# Weight Gain Promoting Medications

# Alternate Agents

## Atypical Antipsychotics:

clozapine, olanzapine, quetiapine, risperidone, aripiprazole

ziprasidone

## Anti-Depressants:

Tricyclics: nortriptyline, amitriptyline

SSRIs: paroxetine, citalopram, escitalopram

Others: trazodone, mirtazipine, venlafaxine

bupropion

sertraline

CBT

memantine or ketamine

L-methylfolate (Deplin ®)

## Anti-Epileptics

gabapentin, valproic acid

topiramate

zonisamide

lamotrigine

## Mood Stabilizers

lithium

topiramate

zonisamide

lamotrigine

cariprazine (Vraylar ®)



Questions?

# Referrals



**Oklahoma State University  
Internal Medicine Clinic**

**Phone: 918-382-5064**

**Fax: 918-382-3589**

**Attn: Weight Loss Evaluation**

Learn about available clinical obesity treatment tools at our Fundamentals of Obesity Treatment Course!

[View Course Dates and Cities](#)



Feb. 2 | Portland, OR

Feb. 16 | Dallas, TX

March 2 | Chicago, IL

May 4 | Cleveland, OH

Oct. 19 | San Francisco, CA