

# Pharmacological Approaches to Weight Loss

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- A 47 year old woman comes to see you for obesity and type 2 diabetes.
- She has had DM x 4 years initially treated with metformin. Glyburide was added 18 months ago. A1C=8.2%
- Over the last year she has gained 19 lbs and now weighs 190 lbs giving her a BMI=32.6 kg/m<sup>2</sup>
- She is frustrated with her weight, says diets don't work for her and asks you for a weight loss medication.

# Which of the following do you advocate for her?

- a) Tell her to work on her diet and exercise
- b) Add canagliflozin
- c) Add lorcasarin
- d) Stop the glyburide and start liraglutide
- e) Stop the glyburide and start phentermine/topiramate
- f) Refer her for bariatric surgery

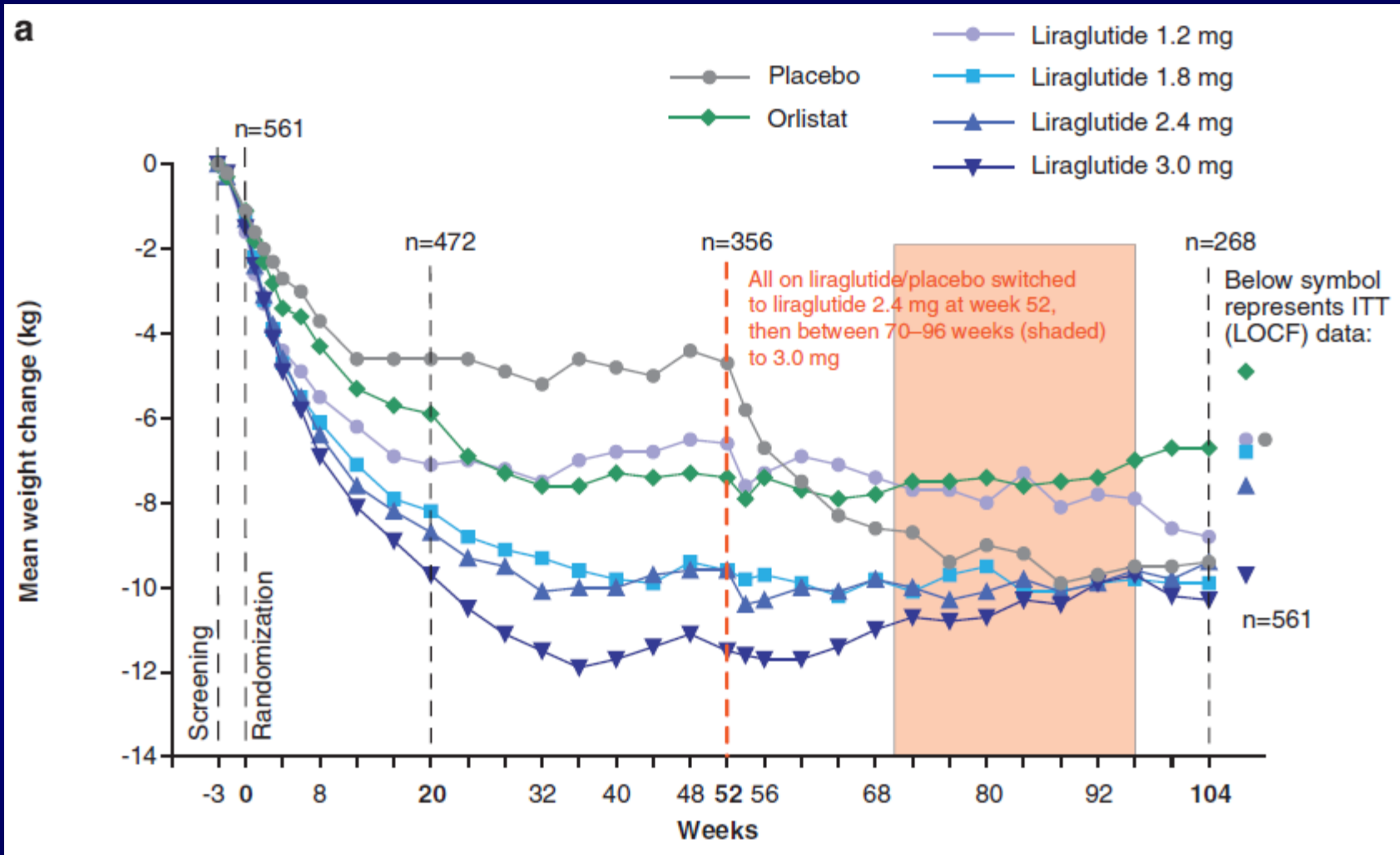
# Medications that may promote weight gain:

- Anti-diabetic medications
  - Sulfonylureas
  - Insulin
  - TZDs
- Mood Stabilizers, antipsychotics
- Birth Control Pills: Depo Provera
- Glucocorticoids: Prednisone

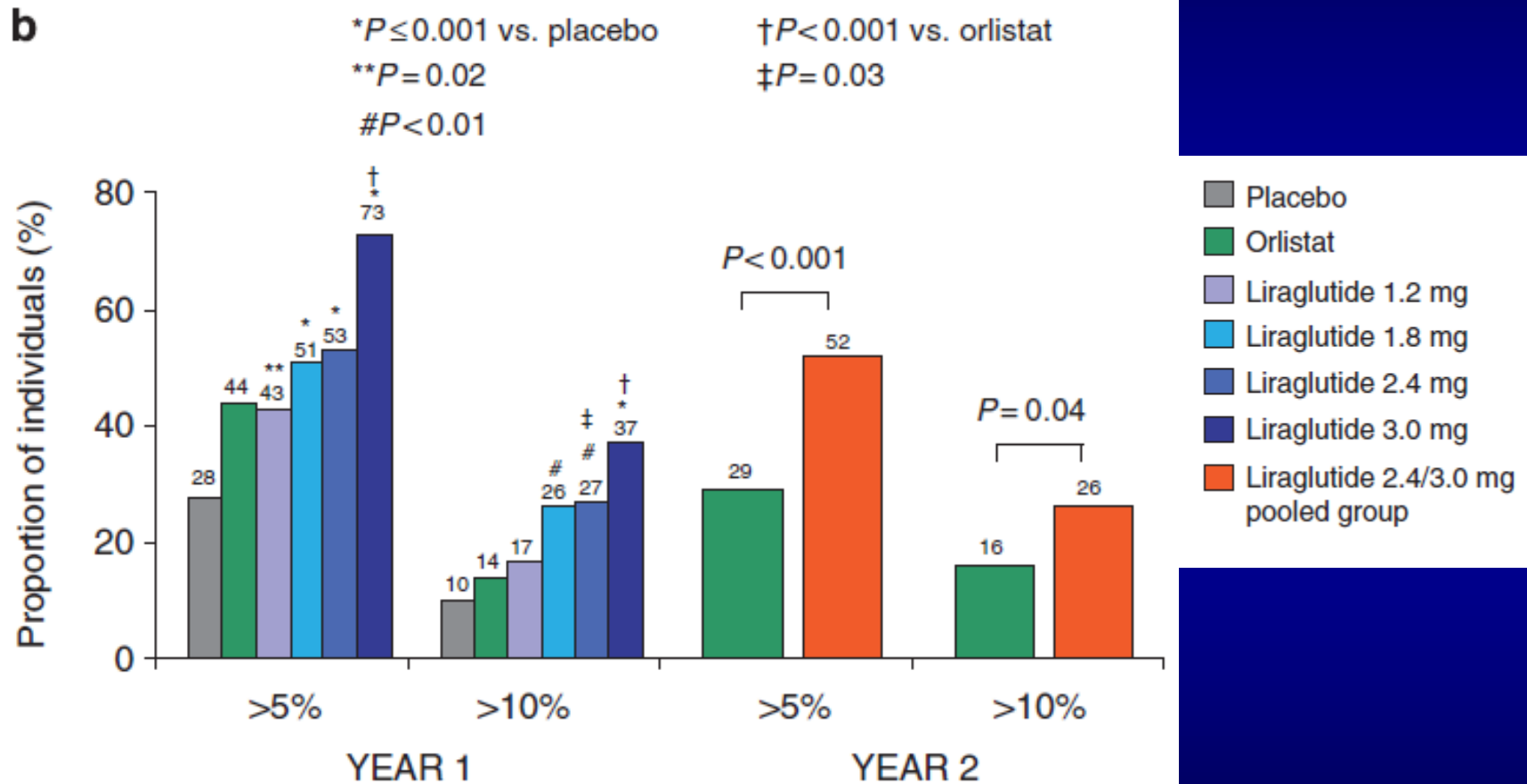
# What to do About These Medications

- Monitor weight and encourage lifestyle changes
- Choose a different medication that does not cause weight gain
- Choose a lower dose
- Weigh risks and benefits of the medication

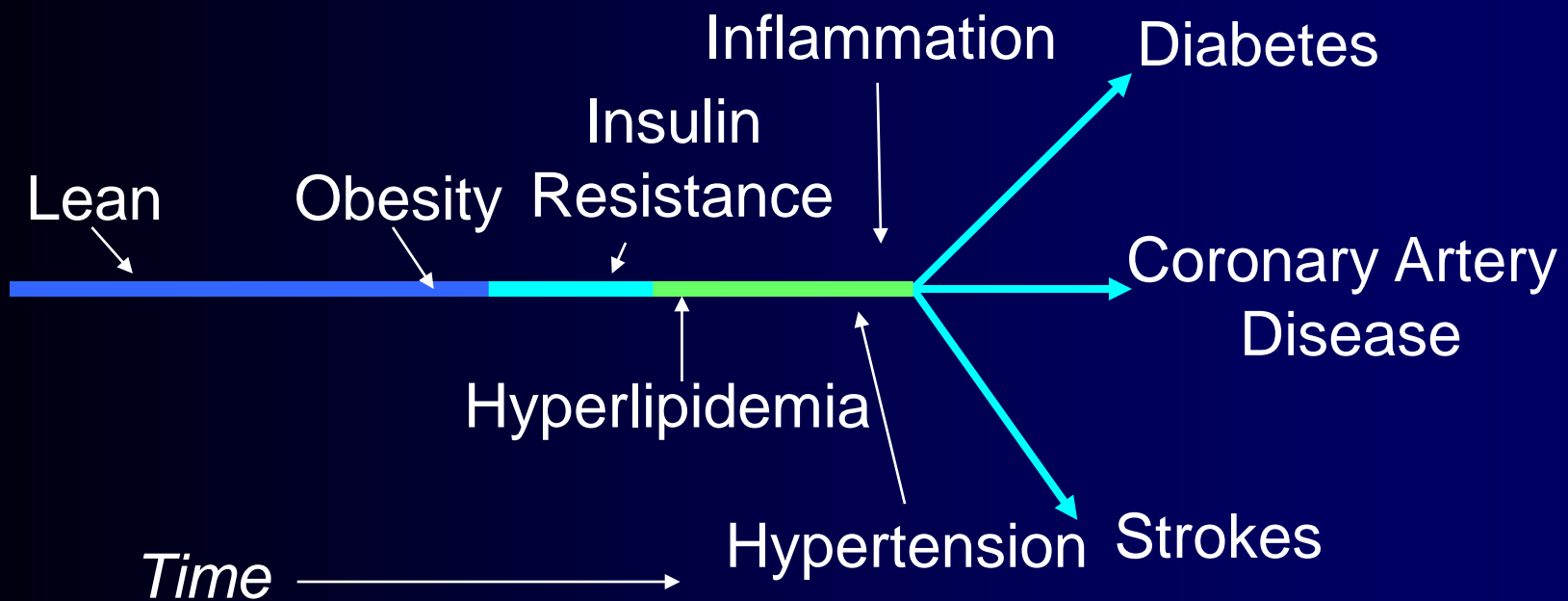
# Liraglutide for Weight Loss



# Liraglutide for Weight loss



# Is obesity a root cause of disease?





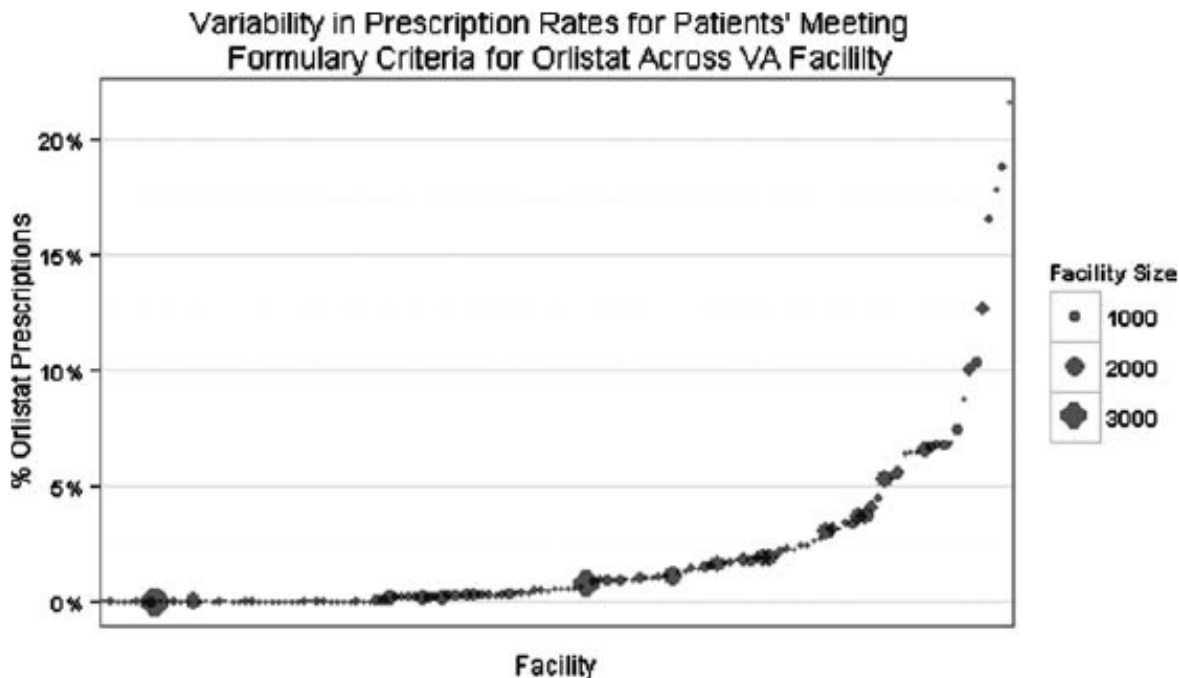
# Weight loss Drugs: Pharmacotherapy of Obesity is Mainstream

- NHLBI guidelines 2000
- ACP 2005
- AACE 2013
- Endocrine Society 2014
- ADA: not such strong advice

# Weight loss medications help people lose weight...

- NHANES 4021 obese adults, 63% tried losing weight 40% lost >5%, 20% lost >10%
- Odds ratio for losing >10%
  - Eating diet products 0.48
  - Skipped meals 1.27
  - Ate less fat 1.37
  - Commercial weight loss programs 1.72
  - Prescription weight loss medications 2.05

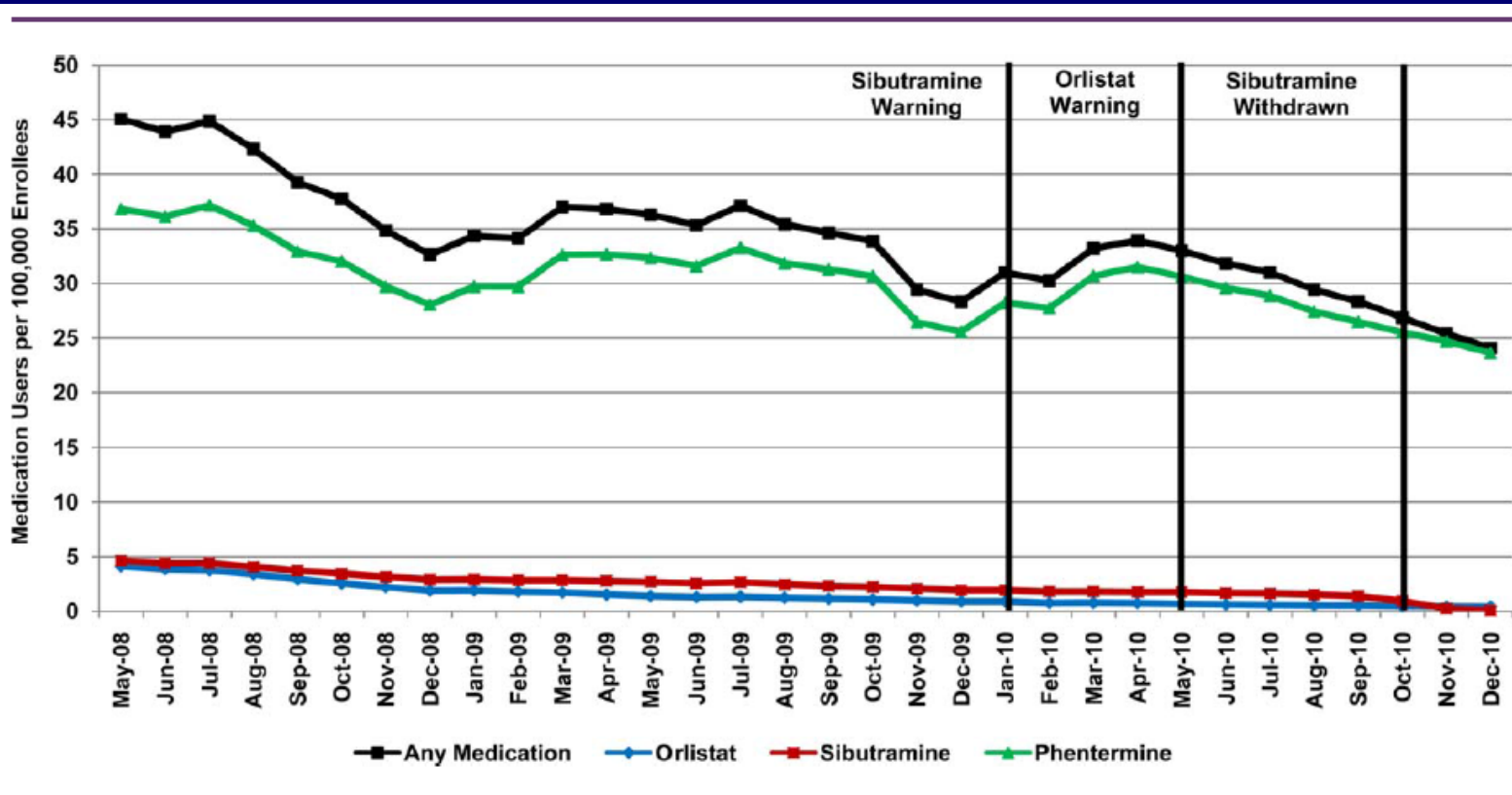
# Prescribing Weight Loss Agents is Uncommon and Variable



**Figure 1** Displayed is the facility level variability in percentage of patients prescribed orlistat in Cohort 2 (those meeting criteria for orlistat eligibility). The 140 VA facilities are ordered from smallest to largest percentage and the size of each point represents the number of overweight/obese patients within each respective facility.

Of >2 million Veterans who were eligible for weight loss medications, only 0.2% got a prescription

# Prescriptions for weight loss medications fell from 2008-10



**FIGURE 1** Weight loss medication users per 100,000 CVS caremark enrollees, May 2008 to December 2010. From May 2008 through December 2010, 10,398 enrollees received prescriptions for sibutramine, 4,593 for orlistat, and 59,583 for phentermine. Over this period, the number of users of these weight loss medications declined from 45 per 100,000 to 24 per 100,000. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

# 1<sup>o</sup> Drug Treatment of Obesity

- Current medications 5-12% wt loss
- Likely will need to use long term.
- Typically not paid for by insurance so cost is a big issue for patients.
- Issues of FDA approval, long term safety, and efficacy.
- Older medications: Phentermine and Orlistat
- Newer medications: phen/top, lorcaserin
- On deck: Liraglutide, Naltrexone/Bupropion

# Orlistat (120 mg or 60 mg)

- Thousands of patients studied up to 4 years of exposure.
- Approved for long term use
- 2-5% weight loss on average
- Cost: \$140/mo
- Side effects: Oily stools, diarrhea, urgency, theoretically fat soluble vitamin deficiency
- May be useful in those with poorly controlled hypertension or psych problems

# Phentermine/Topiramate (Qsymia, Vivus)

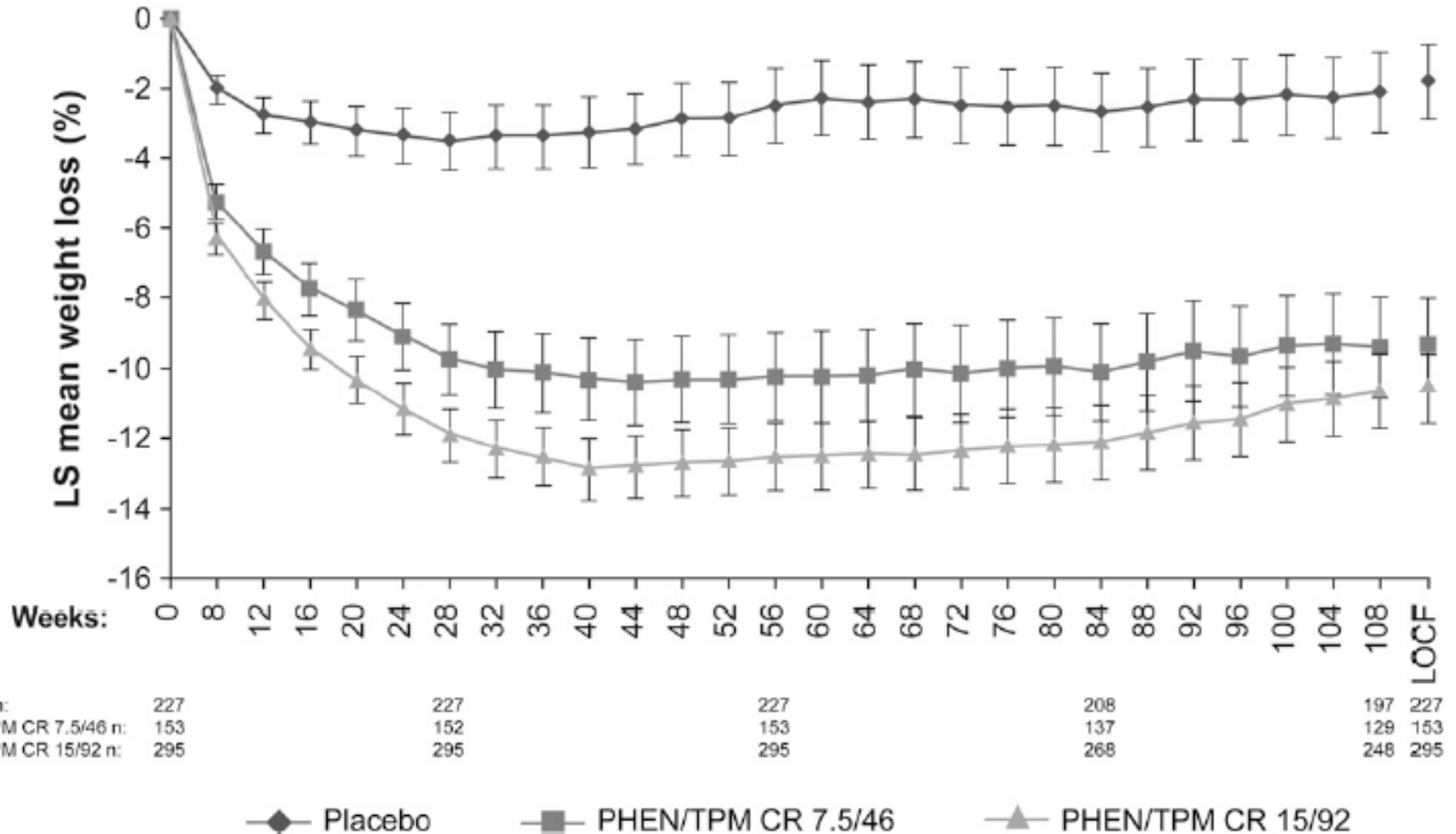
- Combination gives greater efficacy with fewer side effects
- Doses 7.5/46 mg and 15/92 mg phentermine/topiramate
- Cost: \$150.00/mo
- Side effects: dry mouth, paraesthesias, insomnia, dizziness, anxiety, irritability and disturbance in attention, tachycardia

# Phentermine/Topiramate

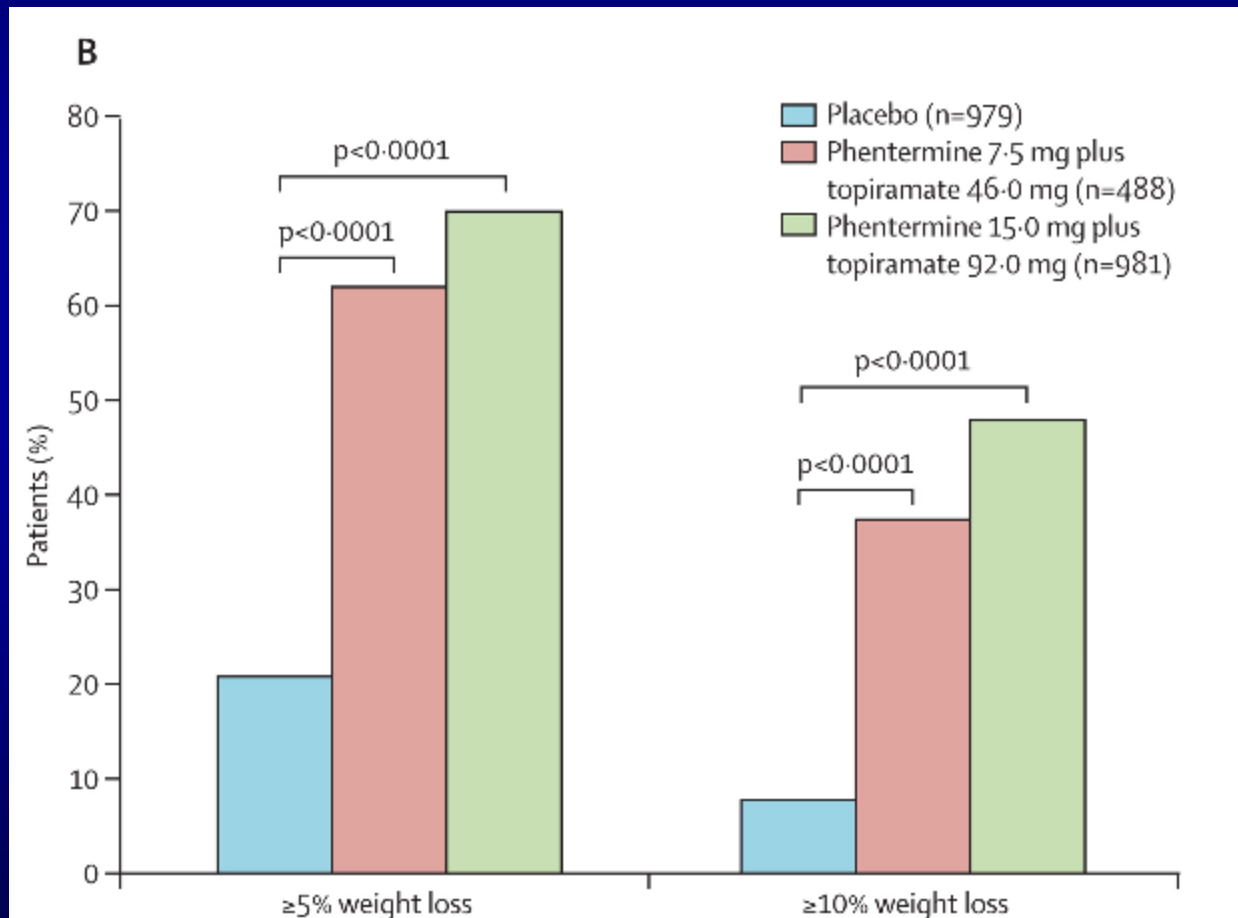
- Topiramate teratogenic risk: pregnancy test on starting and monthly while using.
- Most effective medication available 10-12% weight loss.
- Reduces blood pressure, glucose, insulin, triglycerides and raises HDL



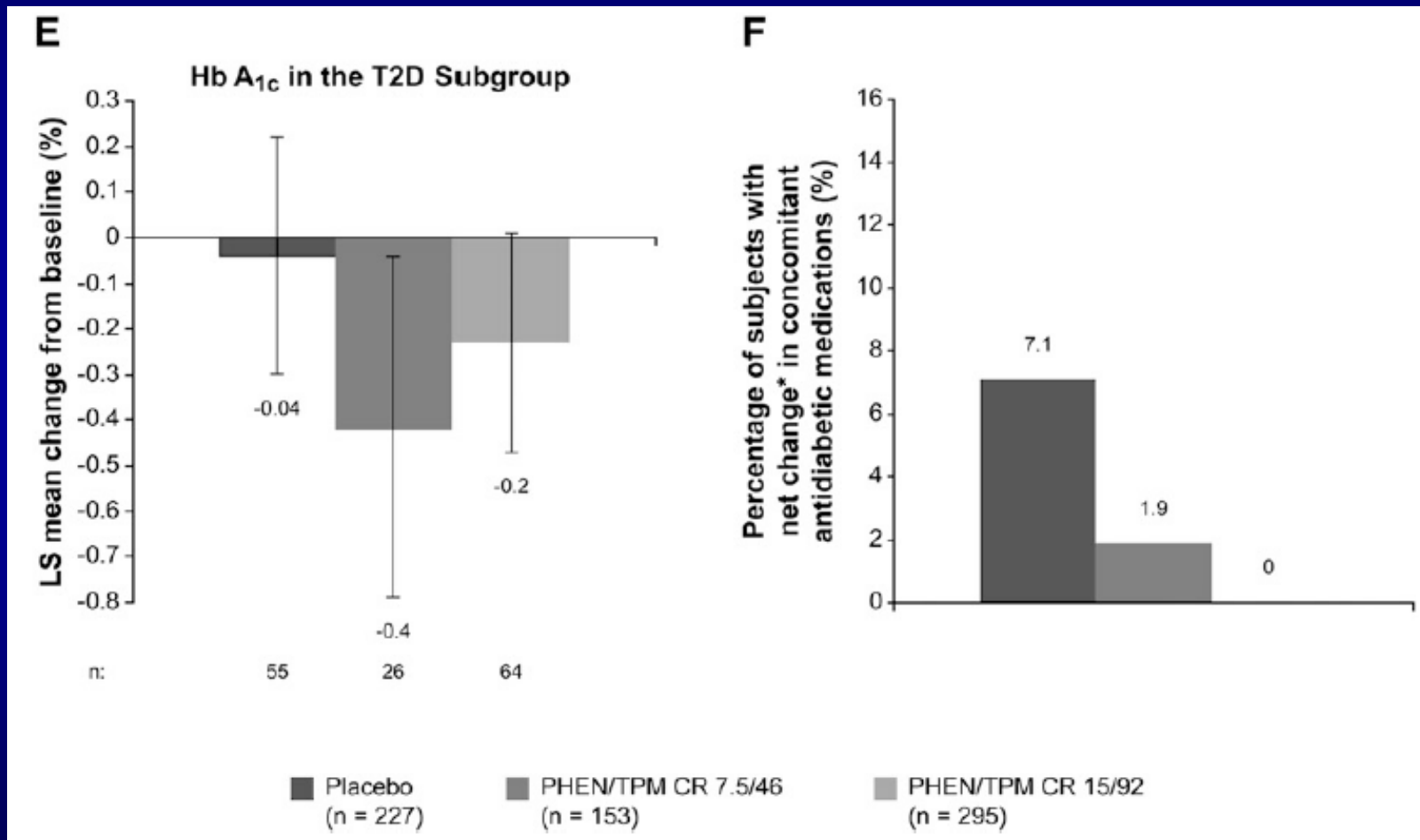
# Phen/Top (Qsymia) 2 year data on Weight: SEQUEL Trial



# Topiramate/Phentermine (Qsymia) Effects on Weight: CONQUER Trial



# Phen/Top (Qsymia): Effects on HbA1C in those with DM



Am J Clin Nutr 2012;95:297–308. 2 year data

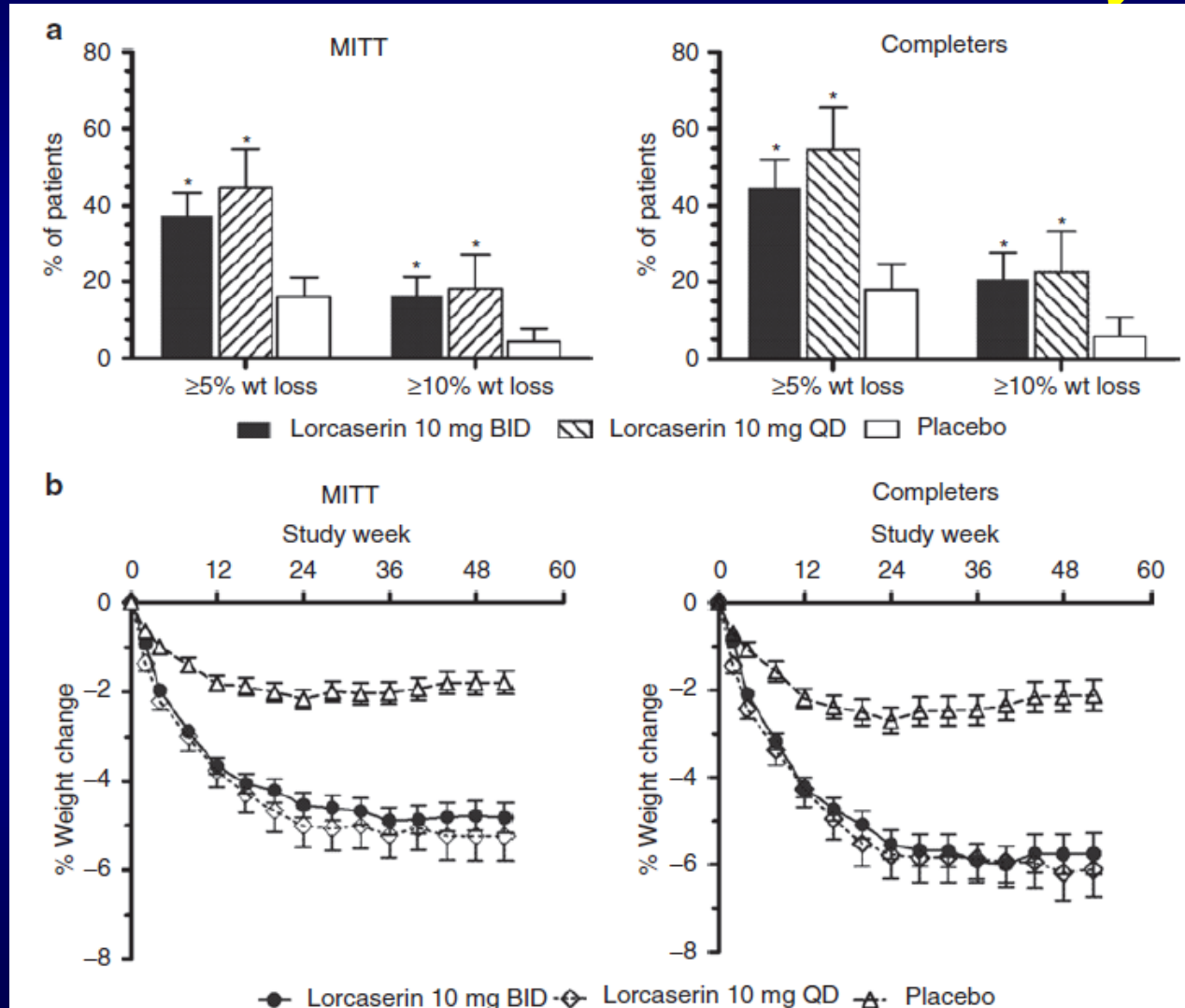
# Lorcaserin (Belviq)

- Serotonin 2C receptor agonist, activates POMC neurons which leads to  $\alpha$ -MSH activation of MC4R leading to satiety
- Previous serotonin agonists fenfluramine and dexfenfluramine caused cardiac valve disease
- 2C receptor only in the brain not in heart
- Studies in 1-2,000 people for up to 2 years do not show evidence of valvulopathy with lorcaserin.

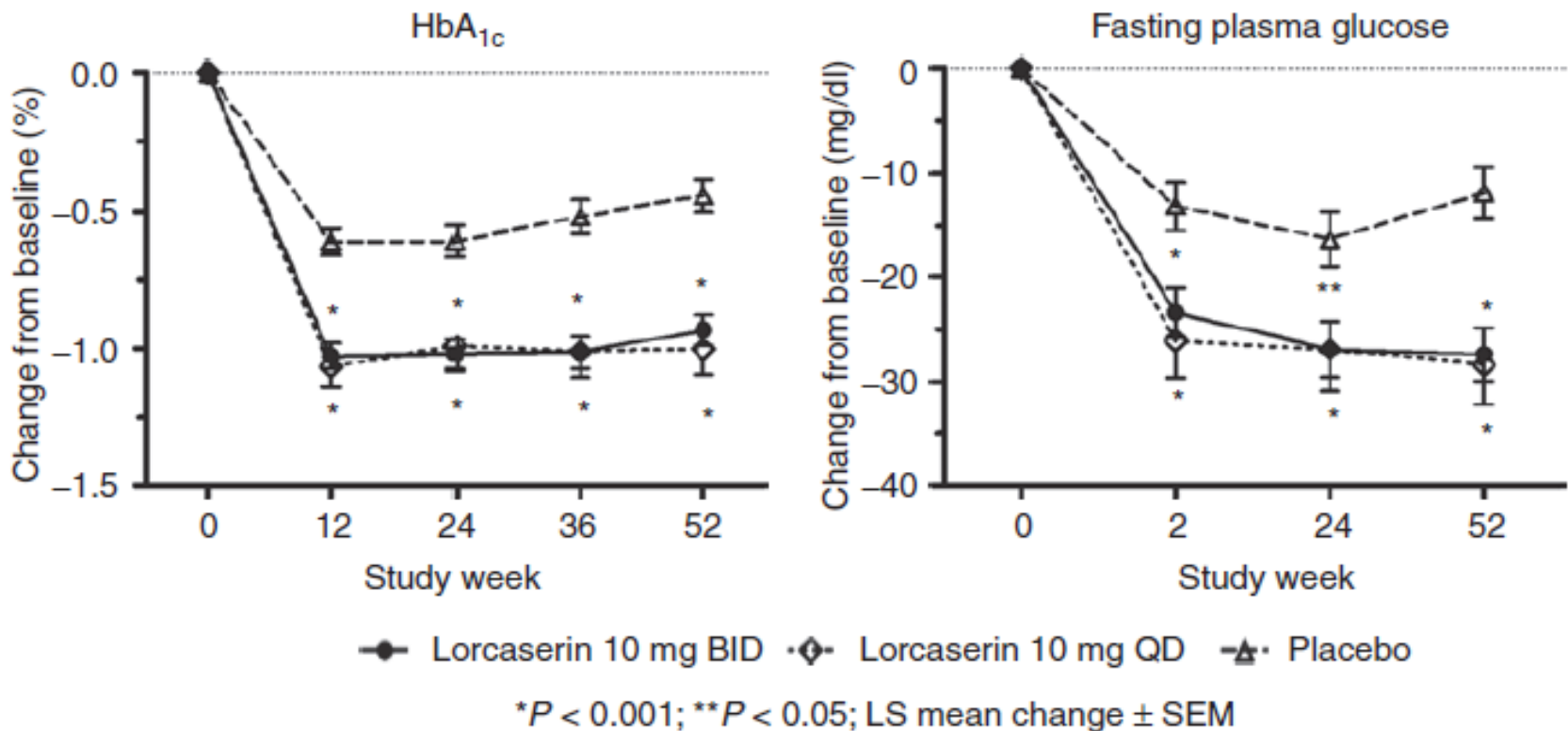
# Lorcaserin (Belviq)

- Weight loss: 4-5% not much better than phentermine or orlistat
- Side effects: minimal, headache, dizziness and nausea (rare priapism, monitor for depression)
- Cost: about \$200/mo
- Unclear if physicians will prescribe with phentermine (no safety/efficacy data)

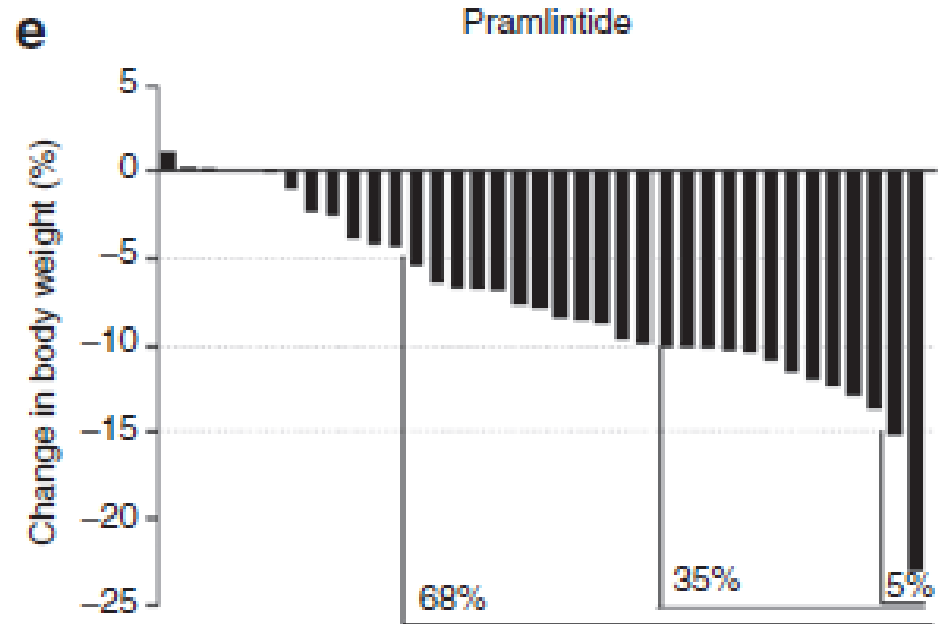
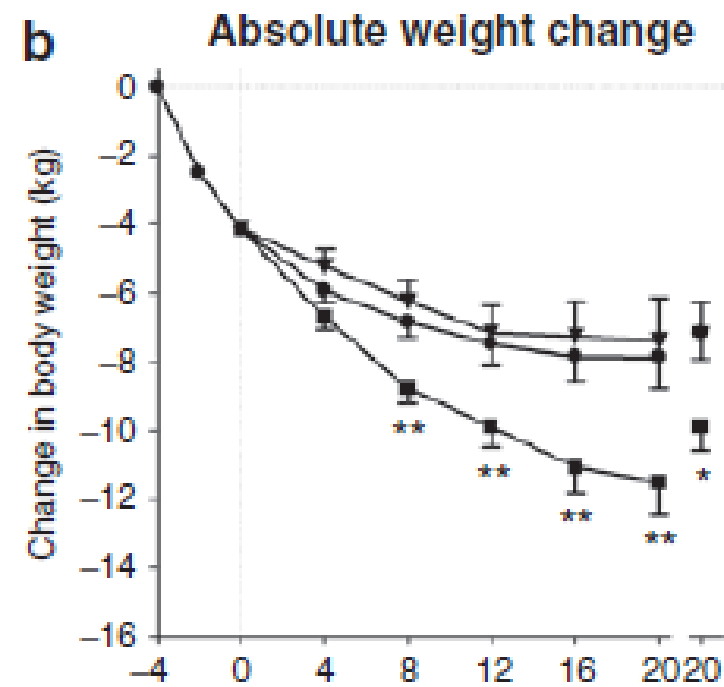
# Lorcaserin: Weight Effects BLOOM Diabetes Study



# Lorcaserin (Belviq): Glucose, A1C Effects

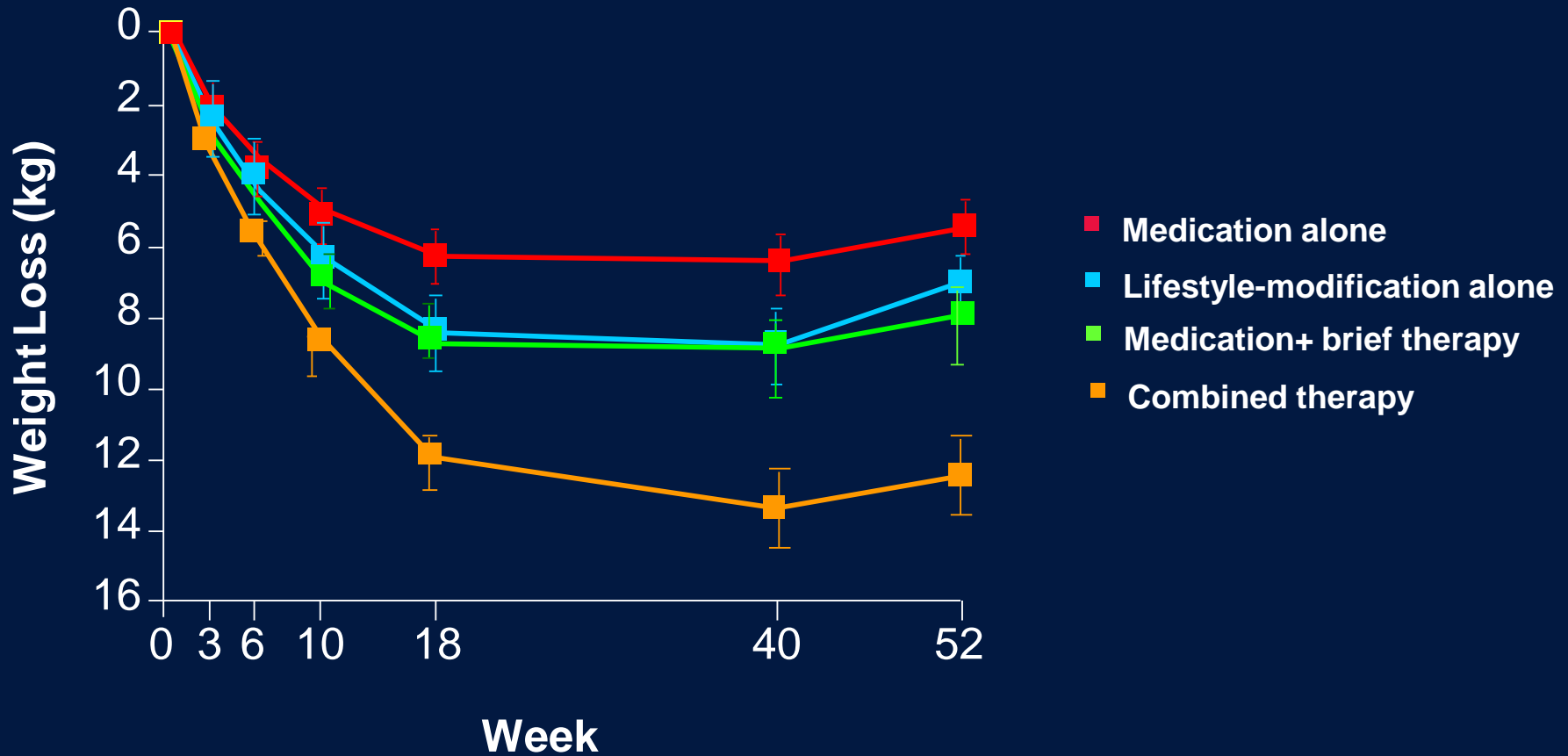


# Variability in Response to a Weight Loss Medication





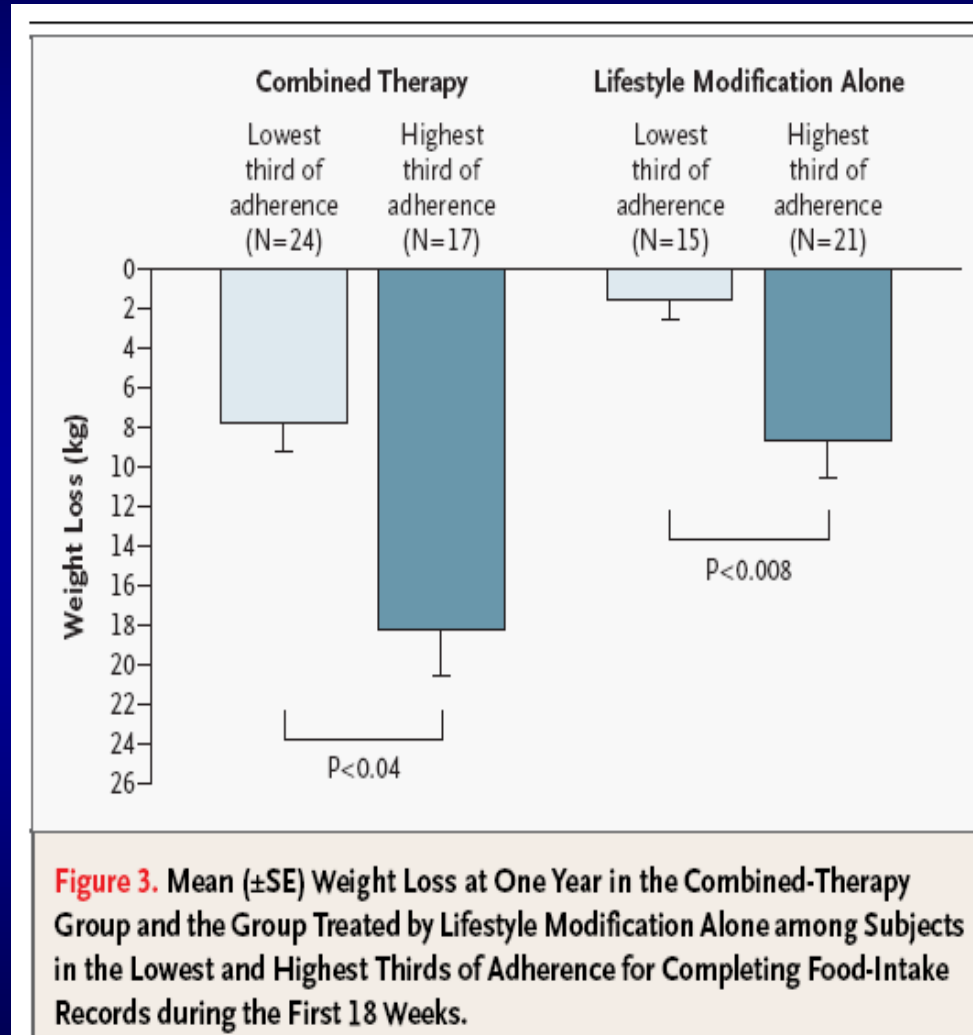
# Diet plus Medication is Better than Either Alone



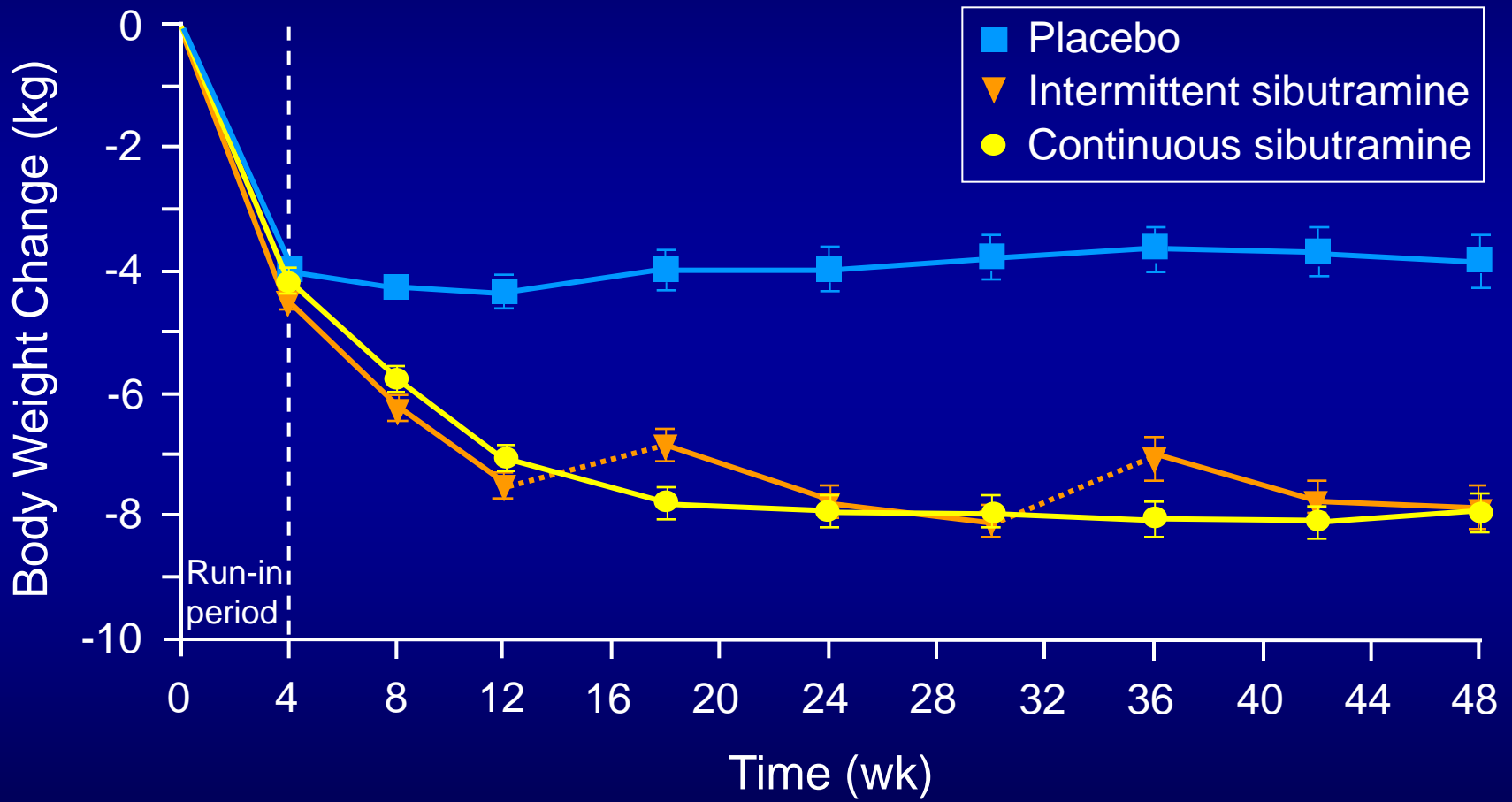
Wadden TA, et al. *NEJM*. 2005;353:2111-2120.

\*Study was with Sibutramine, which is no longer available

# Adherence correlates with weight loss when combining diet and medications



# Effect of Continuous vs Intermittent Sibutramine Therapy on Body Weight



Sibutramine dose=15 mg/d.

# Summary

- Weight loss medications are an appropriate form of treatment that is often not discussed with patients.
- Newer medications have greater efficacy (phen/top) and fewer side effects (lorcasarin) than older agents
- If a patient asks about a weight loss medication I hope you will feel comfortable discussing risks and benefits.