BMI:

Bariatric Medicines In-Depth

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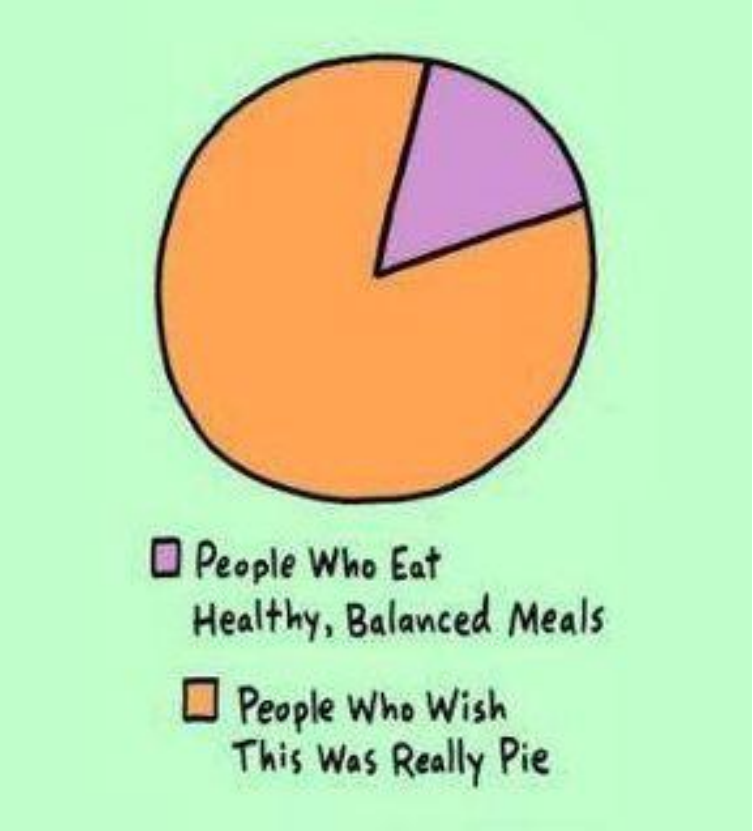
AMERICAN BOARD of OBESITY MEDICINE
CERTIFIED DIPLOMATE

Disclosures

- Nothing to report



Learning Objectives

- To better understand the current vital statistics of the obesity epidemic
- To review impediments to starting anti-obesity drugs (both patients and providers)
- To understand pharmacologic options to assist patients in meaningful weight loss
- To understand the role of prescriptions in long-term weight management

Case Study

- 54 year old female for weight loss consultation
- Past Medical History: T2DM, HTN, Hyperlipidemia, Asthma and Allergies
- Family History: Father d.55 MI, HTN. MGF –CAD and CVA, PGM-CAD.
- Meds: Losartan-HCTZ 50-12.5mg, Amlodipine 5mg, Jentadueto 2.5-1000mg BID, Pioglitazone 30mg, Pravastatin 20mg, Zyrtec 10mg, Dulera 200-5mcg – 2 puffs BID, Ventolin-HFA prn

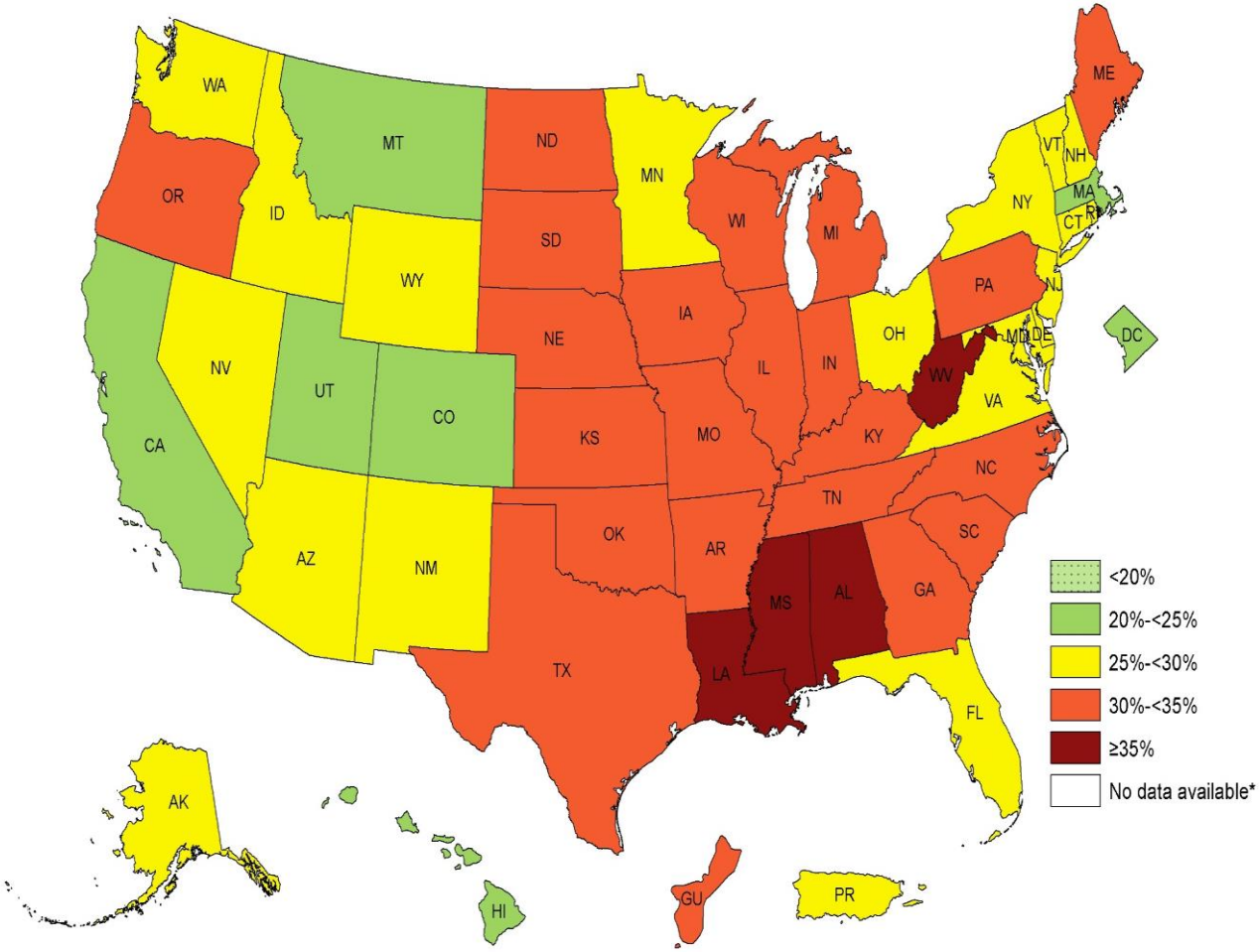
Case Study

- No Known Drug Allergies
- Labs: Glc-99, A1c 6.6, Cr-0.9, eGFR>60, Microalb ratio 9, TC160, TG116, HDL 48, LDL89
- Full Weight Loss History – #attempts & success, weight through years, 3-day food diary, PHQ-2, STOP-BANG, family weight hx, trauma hx, etc.
- Vitals: Ht-62in, Wt-176.5#, BMI-33, BP 124/72, Body fat% 36.3 (nl 23-35%), TBW% 46.5 (nl 40-60%), RMR-1456cal.

Case Study

- Is this patient a candidate for weight loss medications?

Obesity Affects Millions of People in the United States: Obesity Today

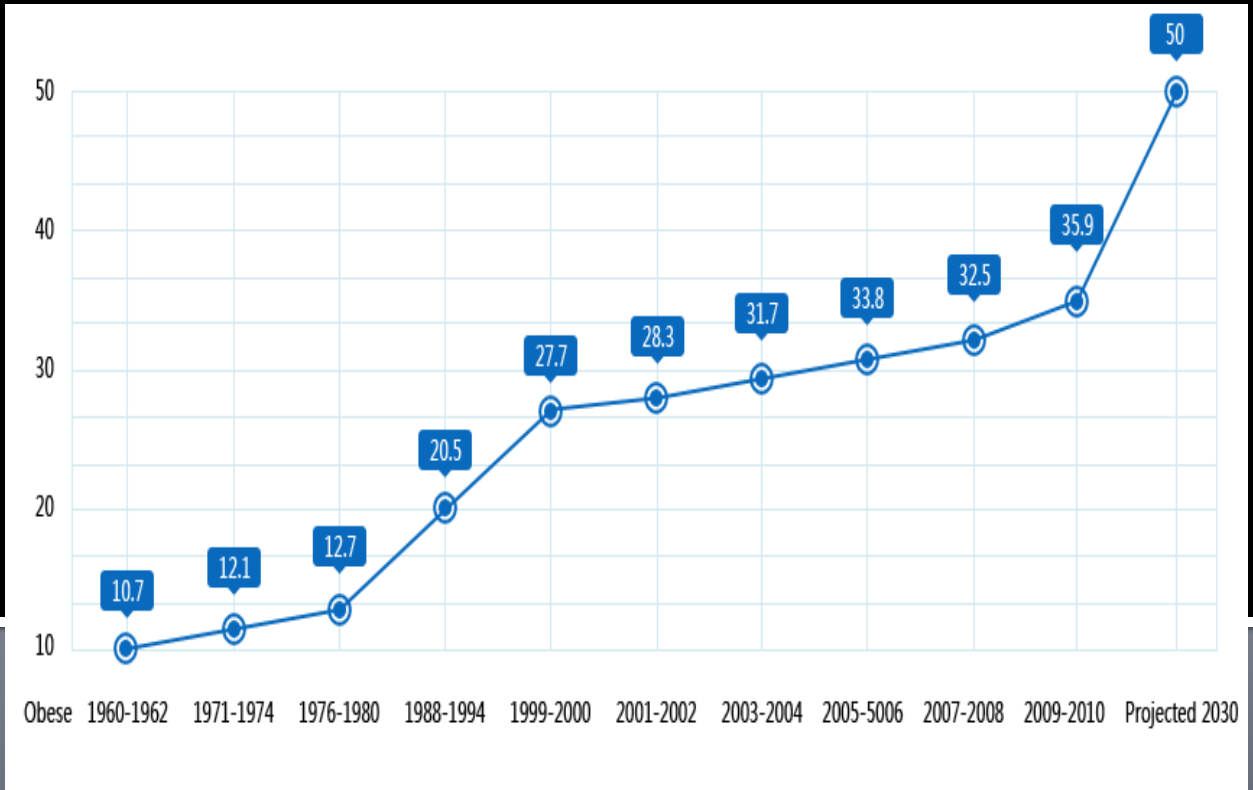


- No state has a prevalence of obesity less than 20%.
- 6 states and the District of Columbia have a prevalence of obesity between 20% and 25%.
- 19 states and Puerto Rico have a prevalence of obesity between 25% and 30%.
- 21 states and Guam have a prevalence of obesity between 30% and 35%.
- 4 states (Alabama, Louisiana, Mississippi, and West Virginia) have a prevalence of obesity of 35% or greater.

Prevalence reflects Behavioral Risk Factor Surveillance System (BRFSS) methodological changes started in 2011, and these estimates should not be compared to those before 2011. Centers for Disease Control and Prevention. Obesity Prevalence Maps. https://www.cdc.gov/obesity/data/prevalence-maps.html. 2015 Obesity Prevalence map. Accessed September 12, 2016.

Is This Our Future… Obesity of Tomorrow?

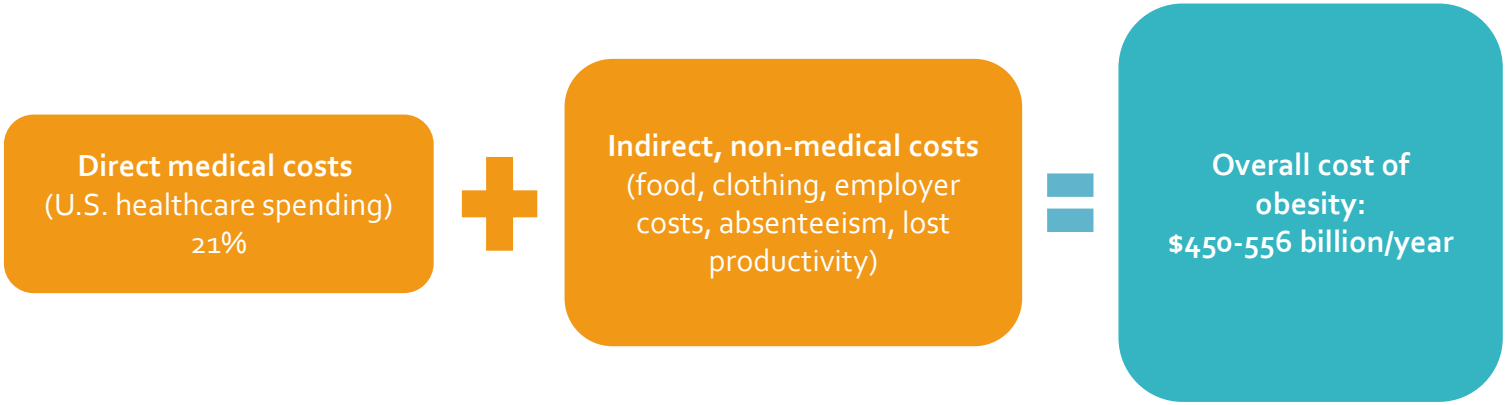
Prevalence of Obesity Among U.S. Adults Ages 20-74



Derived from NHANES data (http://www.cdc.gov/nchs/data/hestat/obesity_adult_09_10/obesity_adult_09_10.html#table1)

The Economic Burden of Obesity in the U.S.

- Direct medical spending due to obesity and its comorbidities is estimated to be **$210-$316 billion** annually: **21-28%** of total U.S. healthcare spending
- When also accounting for the indirect, non-medical costs of obesity, the overall annual cost is estimated to be **$450-$556 billion**



Brill. The Long-Term Returns of Obesity Prevention Policies (2013). Available at: http://www.rwjf.org/content/dam/farm/reports/reports/2013/rwjf405694 ; Cawley *et al. PharmacoEconomics* 2014: Nov 9.

The Good News? Modest Weight Loss Can Reduce Disease Risk

- Potential impact of 5% average BMI reduction in the U.S. by 2020:
  - 3.5 million cases hypertension avoided
  - 0.3 million cases cancer avoided
  - 2.9 million cases heart disease and stroke avoided
  - 3.6 million cases diabetes avoided
  - 1.9 million cases arthritis avoided

Levi *et al.* F as in fat: how obesity threatens America's future, 2012. Available at: http://healthyamericans.org/assets/files/TFAH2012FasInFatFnlRv.pdf

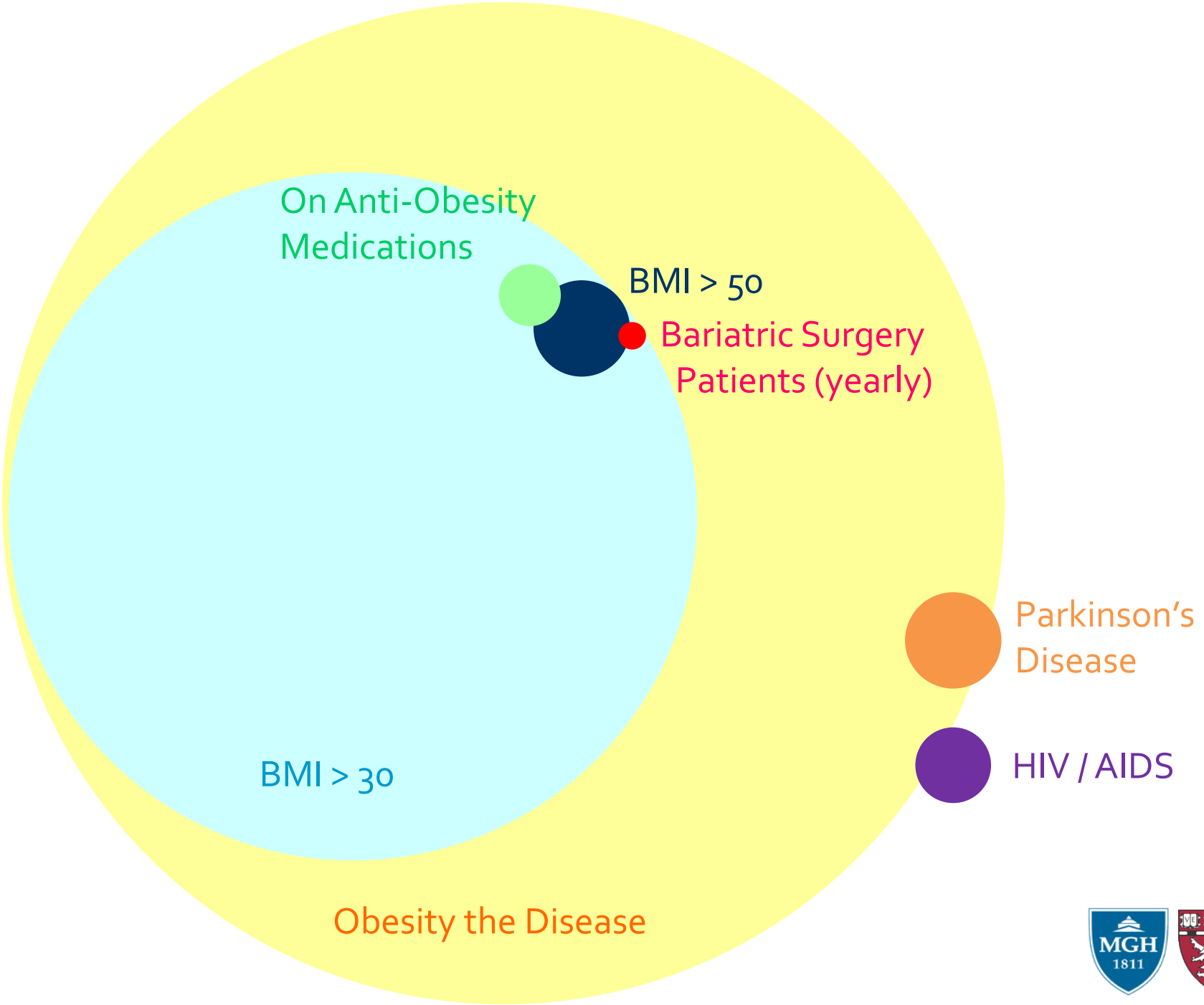
Few People with Obesity are Treated in the U.S.

~80 million adults with obesity in the U.S.

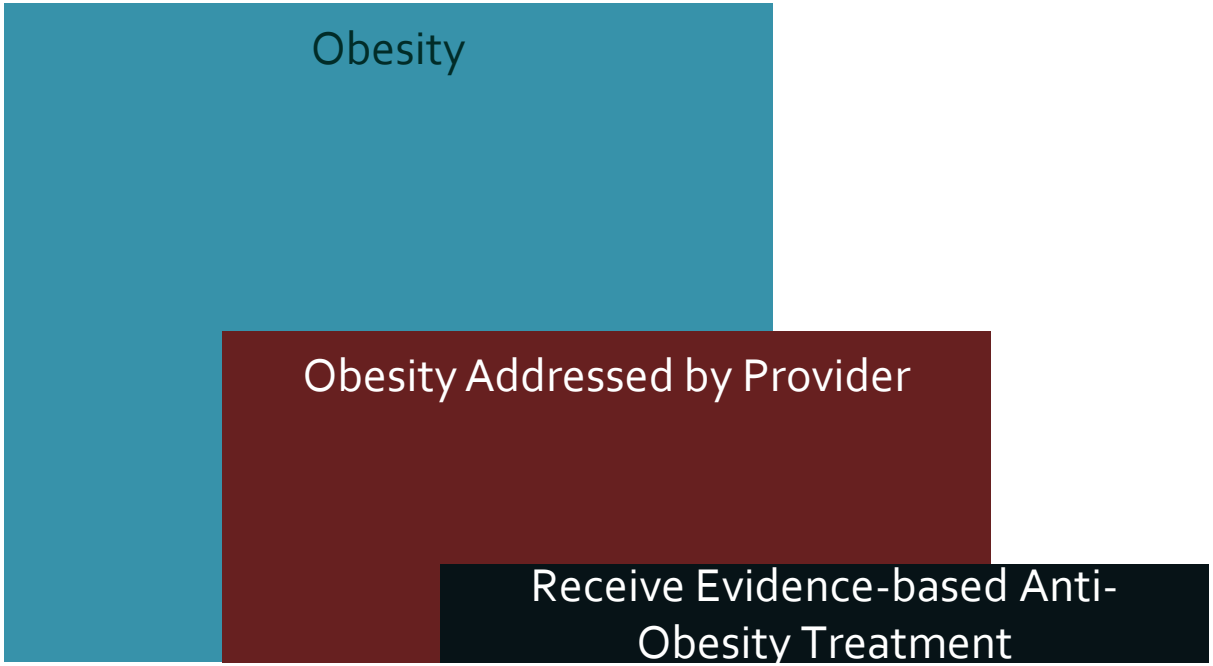
<1% receive a prescription for an anti-obesity medication in a given month

~195,000 people per year receive bariatric surgery

Sources: CDC 2014 (adults is defined as >20yrs. American Heart Association. Statistical Fact Sheet 2013 Update: Overweight and Obesity. http://www.heart.org/idc/groups/heart-public/@wcm/@sop/@smd/documents/downloadable/ucm_319588.pdf. Accessed June 9, 2014. Understanding the Treatment Dynamics of the Obesity Market, IMS Database (NPA) Aug 31, 2014; ASMBS website, estimated number of bariatric surgeries, published July 2016; asmbs.org


On Anti-Obesity Medications
BMI > 50
Bariatric Surgery Patients (yearly)
Parkinson's Disease
HIV / AIDS
BMI > 30
Obesity the Disease

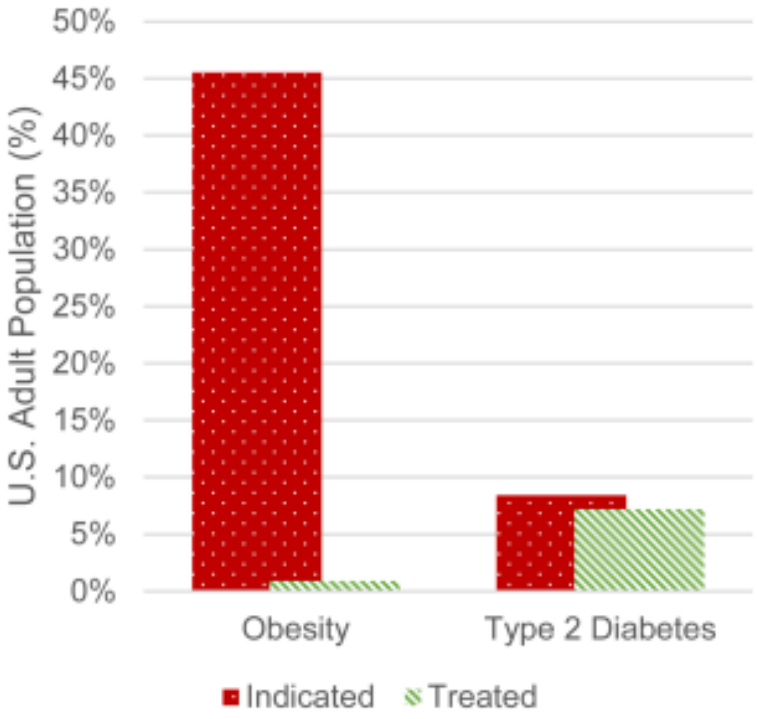
Obesity Remains Underdiagnosed and Undertreated

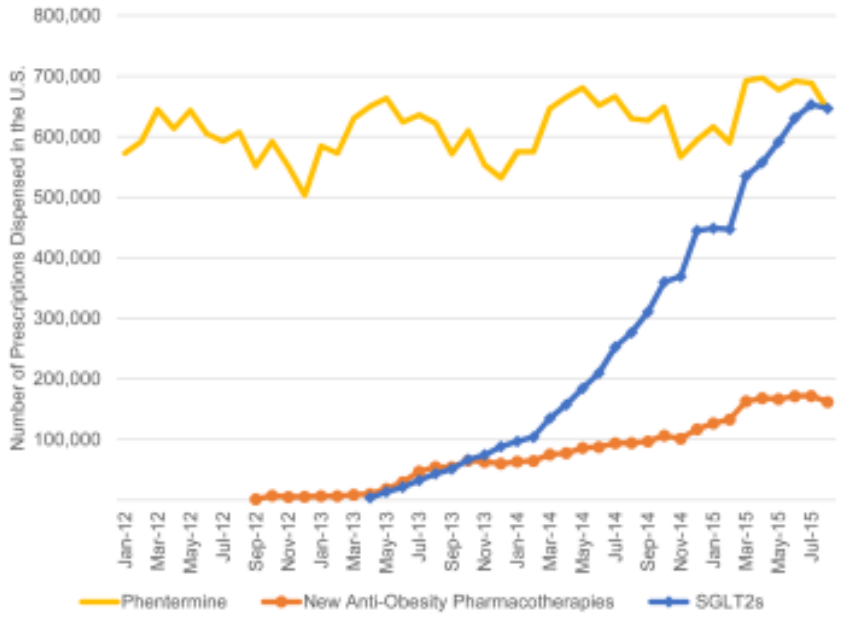


Xia Y *et al. Obesity 2015; 23:1721*

Low adoption of weight loss medications:

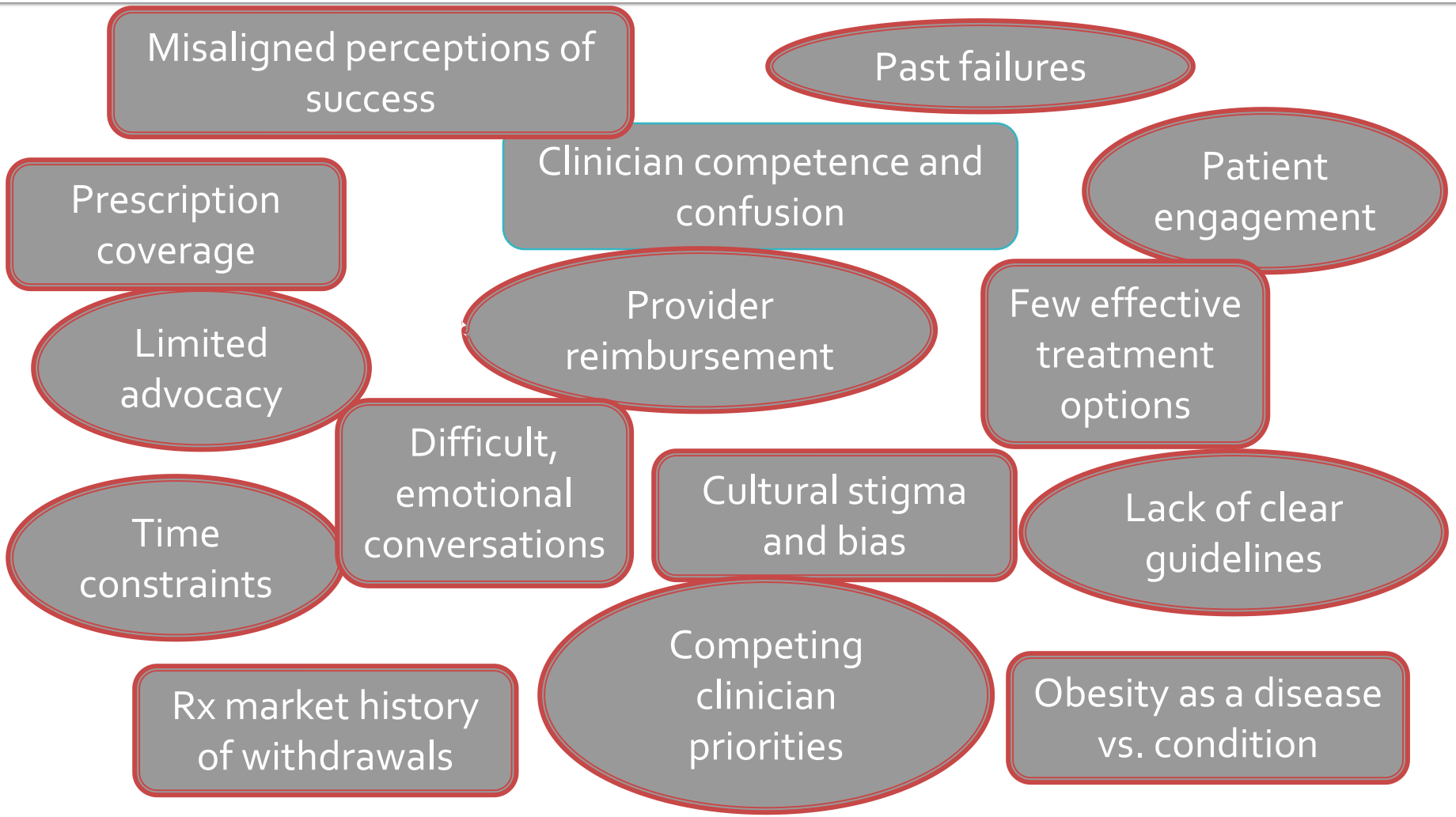
A comparison of prescribing patterns of antiobesity pharmacotherapies and SGLT2s





Obesity
Volume 24, Issue 9, pages 1955-1961, 29 AUG 2016 DOI: 10.1002/oby.21533
http://onlinelibrary.wiley.com/doi/10.1002/oby.21533/full#oby21533-fig-0001

What Drives the Large Care Gap in Obesity? Challenges and Barriers to Care

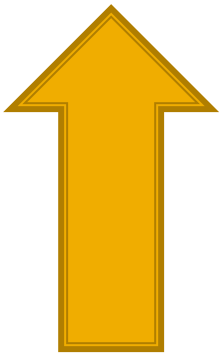


STOP Obesity Alliance. Available at: www.stopobesityalliance.org/wp-content/assets/2010/03/STOP-Obesity-Alliance-Primary-Care-Paper-FINAL.pdf. Forman-Hoffman V et al. *BMC Family Practice*. 2006;7:35.

Treatment of Adult Patients with Overweight or Obesity

Medical Management and Coordination

- Nutrition
- Physical Activity
- Behavior Therapy
- Pharmacotherapy
- Bariatric Surgery



Reference/s: [1]

Anti-obesity Medications

Adjunct to nutritional, physical activity, and behavioral therapies.

Objectives:

- Treat disease
  - Adiposopathy or sick fat disease (SFD)
  - Fat mass disease (FMD)
- Facilitate management of eating behavior
- Slow progression of weight gain/regain
- Improve the health, quality of life, and body weight of the patient with overweight or obesity

5-10 percent weight loss may improve both metabolic and fat mass disease.

Reference/s: [239]

Food and Drug Administration (FDA) Principles

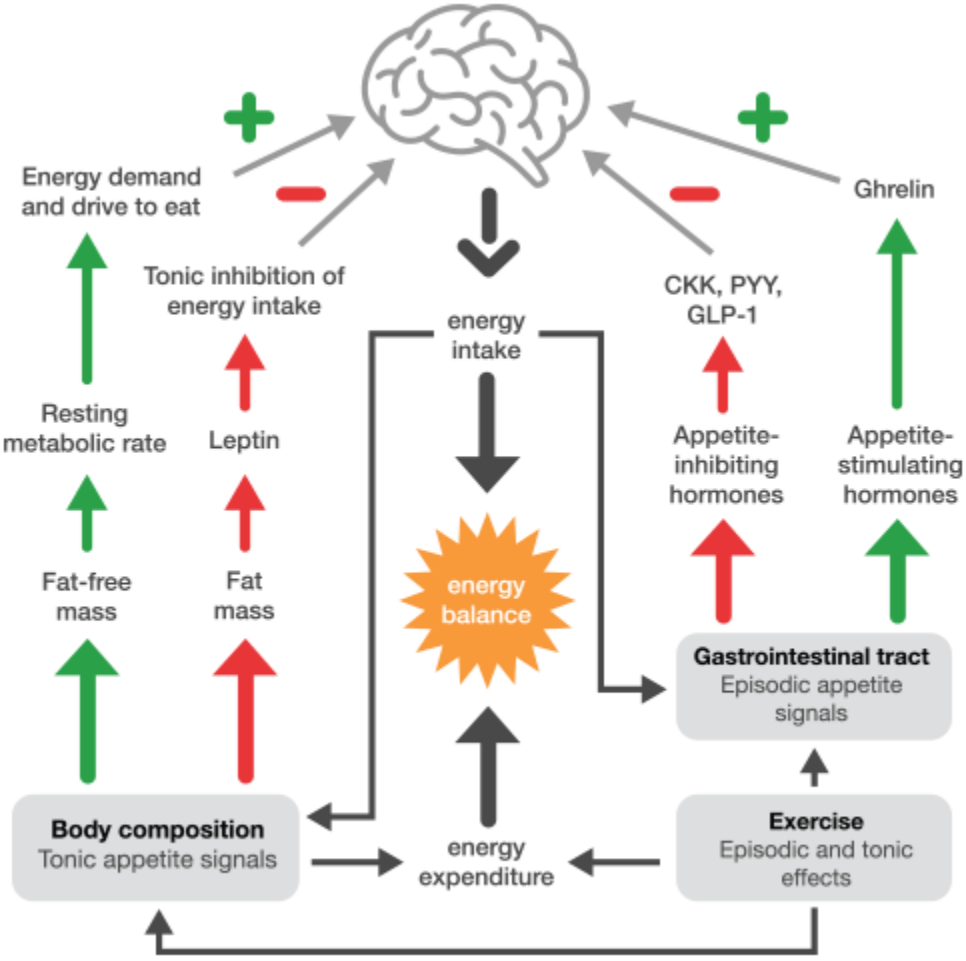
FDA-approved Anti-obesity Medication Indications:

- Patients with obesity (e.g., BMI $\geq$ 30kg/m^2)*
- Patients who are overweight (e.g., BMI $\geq$ 27kg/m^2) with presence of increased adiposity complications (e.g., type 2 diabetes mellitus, hypertension, dyslipidemia)*

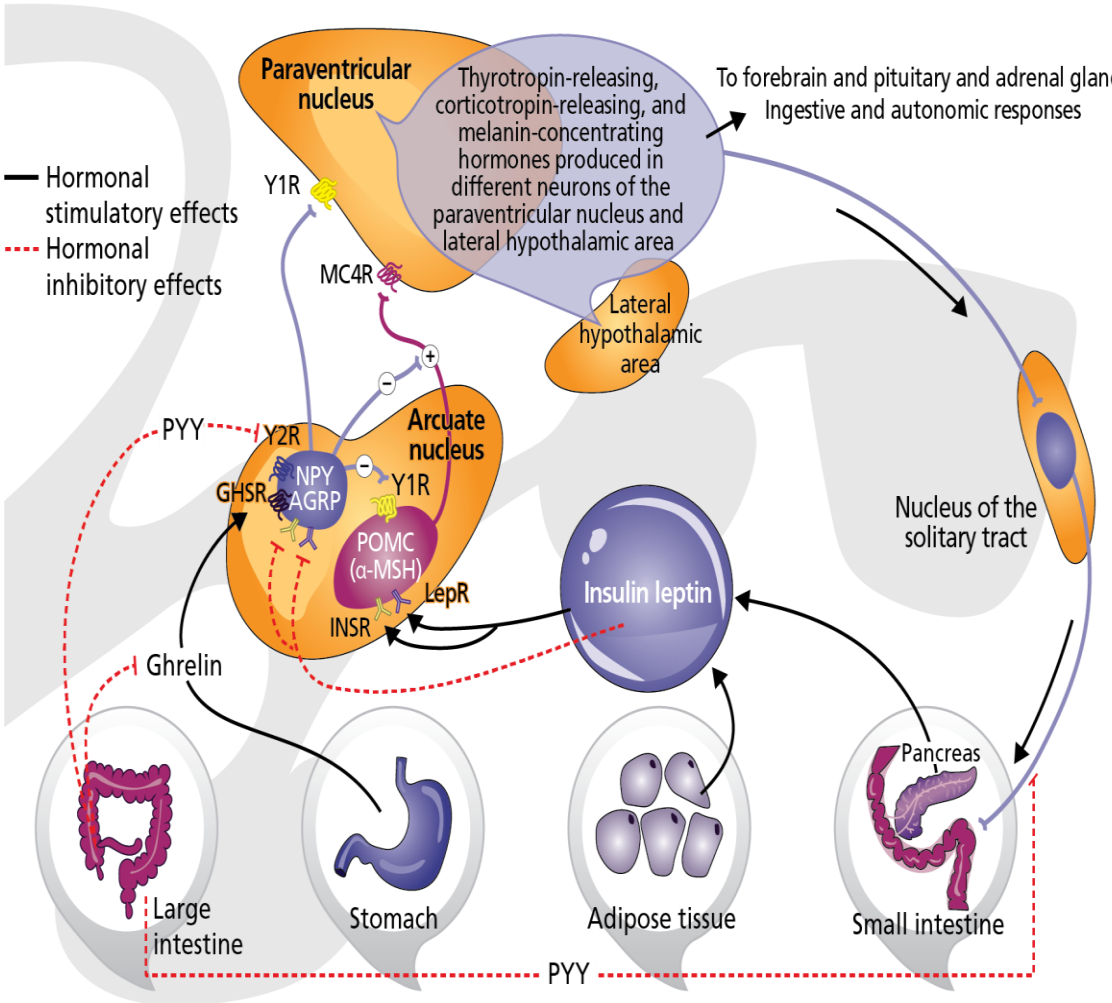
If no clinical improvement after 12-16 weeks with one anti-obesity medication, consider alternative anti-obesity medication or increasing anti-obesity medication dose (if applicable).

*While body mass index (BMI) is the only measure listed in the prescribing information for anti-obesity medications, BMI has limitations. Especially in muscular individuals or those with sarcopenia, overweight and obesity are more accurately assessed by other measures.

Complicated Energy Balance



Complicated Energy Balance



AGRP: agouti-related peptide; α-MSH: α-melanocyte-stimulating hormone; GHSR: growth hormone secretagogue receptor; INSR: insulin receptor; LepR: leptin receptor; MC4R: melanocortin-4 receptor; NPY: neuropeptide Y; POMC: proopiomelanocortin; PYY: peptide YY; Y1R; neuropeptide Y1 receptor; Y2R: neuropeptide Y2 receptor. Apovian CM, Aronne LJ, Bessesen D et al. *J Clin Endocrinol Metab*. 2015;100:342-362.

Pharmacotherapy

Examples of Anti-obesity Medications Approved in 1999 or Before

- Phentermine
- Diethylpropion
- Phendimetrazine
- Benzphetamine
- Orlistat

Examples of Anti-obesity Medications Approved in 2012 and Beyond

- Lorcaserin
- Phentermine HCL/topiramate extended release
- Naltrexone HCL/bupropion HCL extended release
- Liraglutide

Reference/s: [243]

Phentermine (Adipex, Loraira)

- Centrally acting sympathomimetics (amphetamine derivatives)
- Decreases appetite and food intake by release of catecholamines in hypothalamus

- FDA Approval 1959 – short term 12-week use
- Rx dosing: 15, 30, 37.5mg --- Lomaira 8mg TID dosing

- Little data in RCT and none since 1999
  - 12.2kg Phentermine vs. 4.8kg Placebo (P<0.001)
  - Meta analysis (2-24wks) – 3.6kg loss on Phentermine above Placebo

- SE: dry mouth, insomnia, palpitations, tachycardia, elevated BP

Orlistat (Xenical, Alli)

- Inhibits pancreatic and gastric lipases, thereby reducing fat absorption in gut by 30% (Bergstrom, 1988) – LIPASE INHIBITORS

- FDA Approval 1998 / OTC version 2007
- Rx Dosing: 120mg three times daily / during or up to 1 hr after the meal

- RCTs up to 4 years
  - Meta-Analysis -2.59kg (6mo), -2.9kg (12 months) over placebo
- Improved cardio-metabolic parameters
  - Decreases in total cholesterol (11mg/dL), LDL levels (8mg/dL) over 2 yrs
  - Reduced T2DM 9.0% to 6.2% (HR 0.63, CI, 0.46-0.86)

- SE: diarrhea, fecal incontinence, oily spotting, flatulence, bloating and dyspepsia (?early, avoid fat-rich diets).
- May 2010 – product label revision to add warning of severe liver injury (1999-2008 – 32 reports, 6 liver failure – review was 13 cases in 40 million users)

Lorcaserin (Belviq)

- Selective serotonin 2C agonist
- Decreases food intake and increases satiety by activation of PMC neurons in hypothalamus

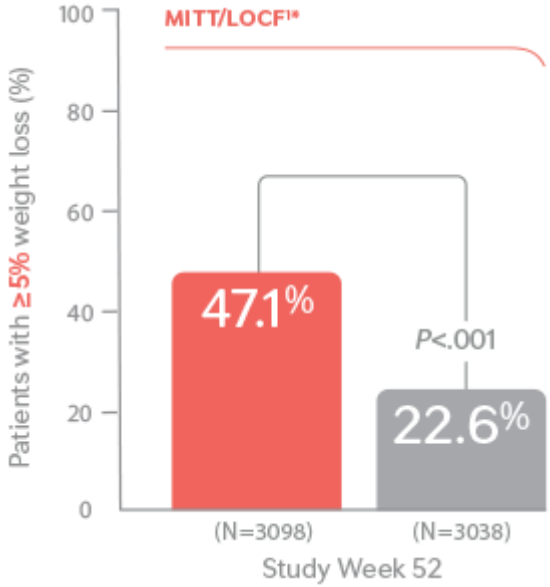
- FDA Approval June 2012
- Dosing: 10mg twice daily OR 20mg-once daily

- Safety – psychiatric symptoms rare with recommended doses but seen in 19% taking 40-60mg
- Contraindicated – avoid with other serotonin syndrome causing medications, ?valvular heart disease (2.4%B vs. 2.0% placebo)
- SE – headache, nausea, dizziness, nasopharyngitis

- Pregnancy-CatX, Lactation-unknown
- Not approved for use in children

BELVIQ® 10 mg Twice Daily - Proven More Than 2X as Effective as Diet and Exercise Alone (Placebo) at Helping Patients Lose ≥5% of Body Weight

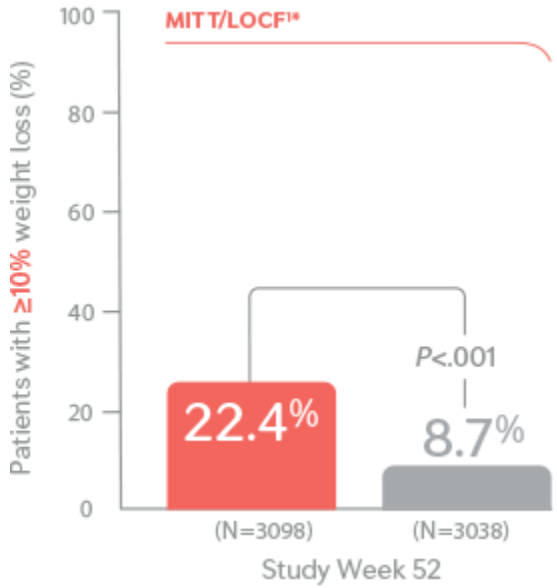
- At Week 52, the mean weight loss was 5.8% with BELVIQ vs 2.5% with placebo (*P*<.001)[1]



NNT=4

BELVIQ® 10 mg Twice Daily - Proven More Than 2X as Effective as Diet and Exercise Alone (Placebo) at Helping Patients Lose ≥10% of Body Weight

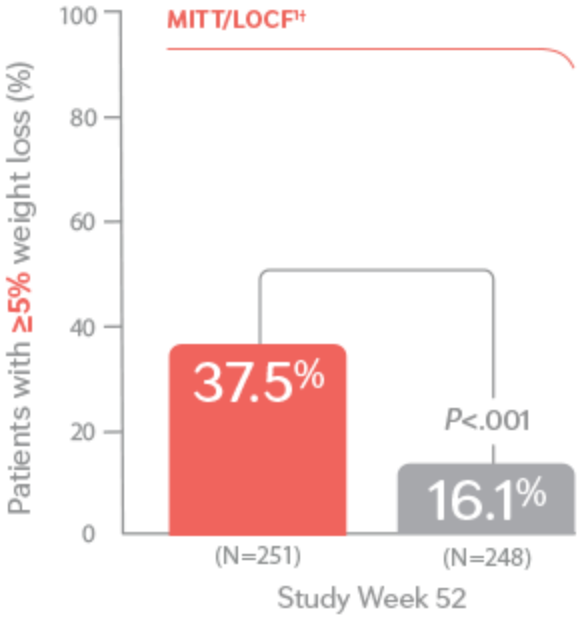
- At Week 52, the mean weight loss was 5.8% with BELVIQ® vs 2.5% with placebo (*P*<.001)[1]



NNT=7

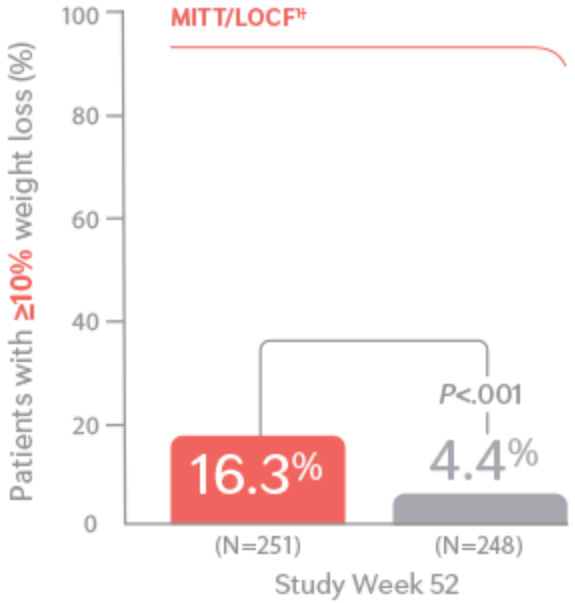
BELVIQ® 10 mg Twice Daily - More Than 2X as Effective as Placebo at Helping Patients in the MITT Population Lose ≥5% of Body Weight

- At Week 52, the mean weight loss was 4.5% with BELVIQ vs 1.5% with placebo (*P*<.001)[1]



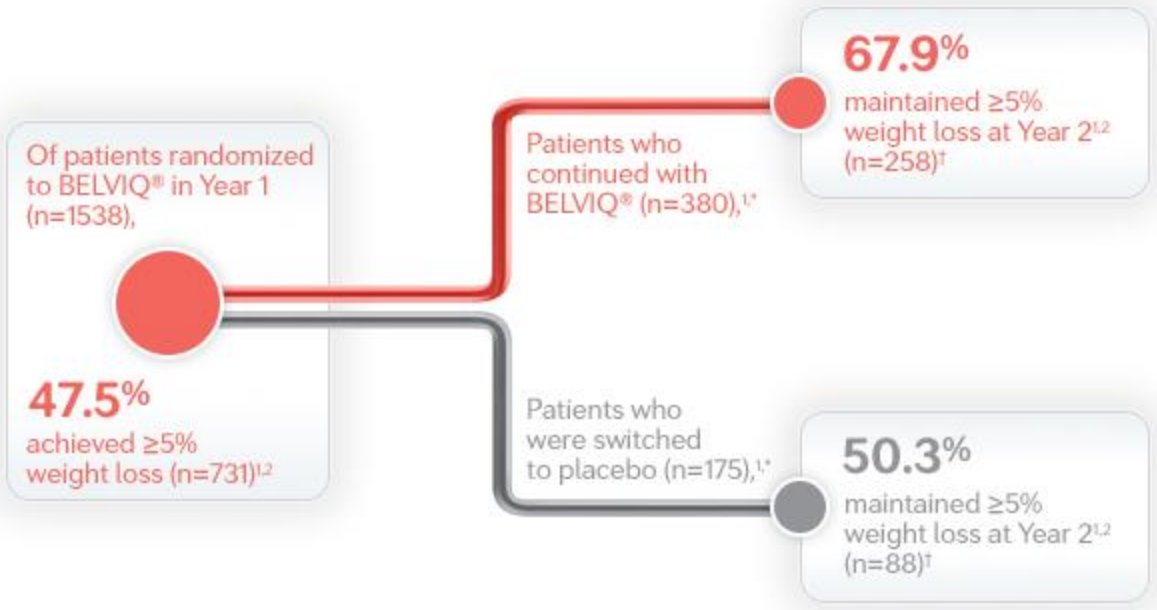
BELVIQ® 10 mg Twice Daily - More Than 3X as Effective as Placebo at Helping Patients in the MITT Population Lose ≥10% of Body Weight

- At Week 52, the mean weight loss was 4.5% with BELVIQ vs 1.5% with placebo (*P*<.001)[1]



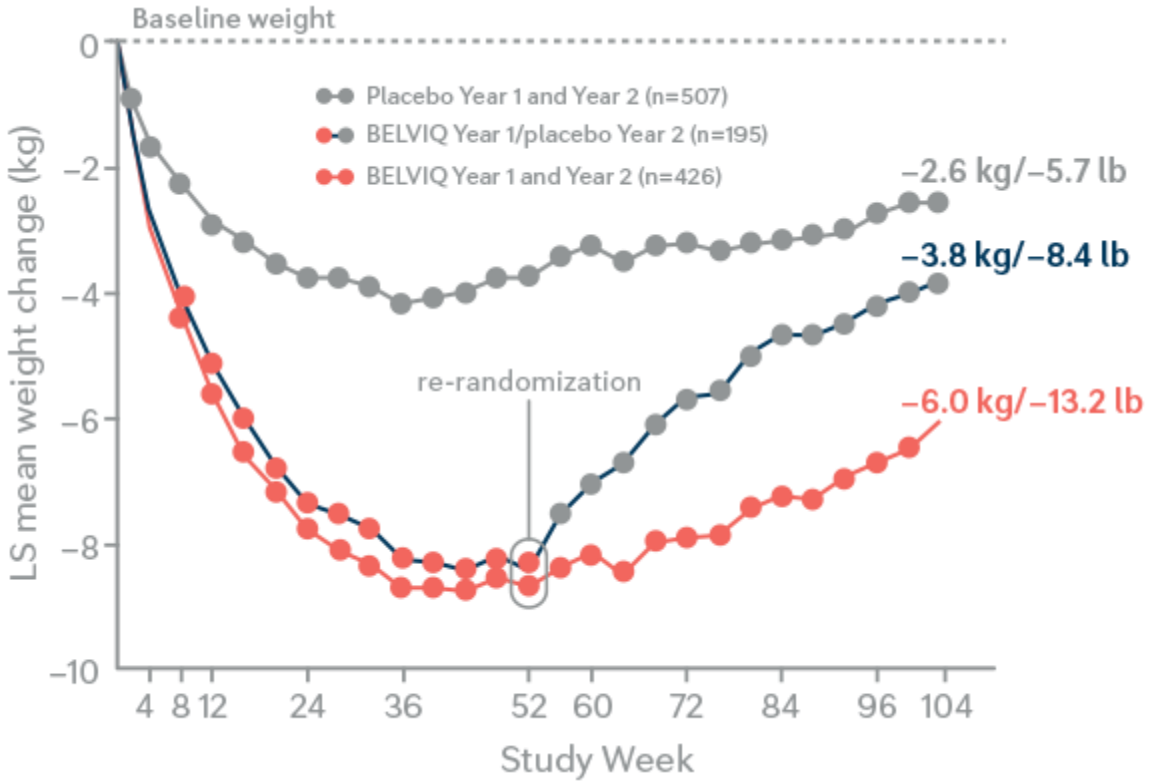
BELVIQ® ≥ 5% Weight Loss Attained and Maintained[1]

Weight loss maintenance in BLOOM: patients on BELVIQ who maintained ≥5% weight loss from Year 1 to Year 2

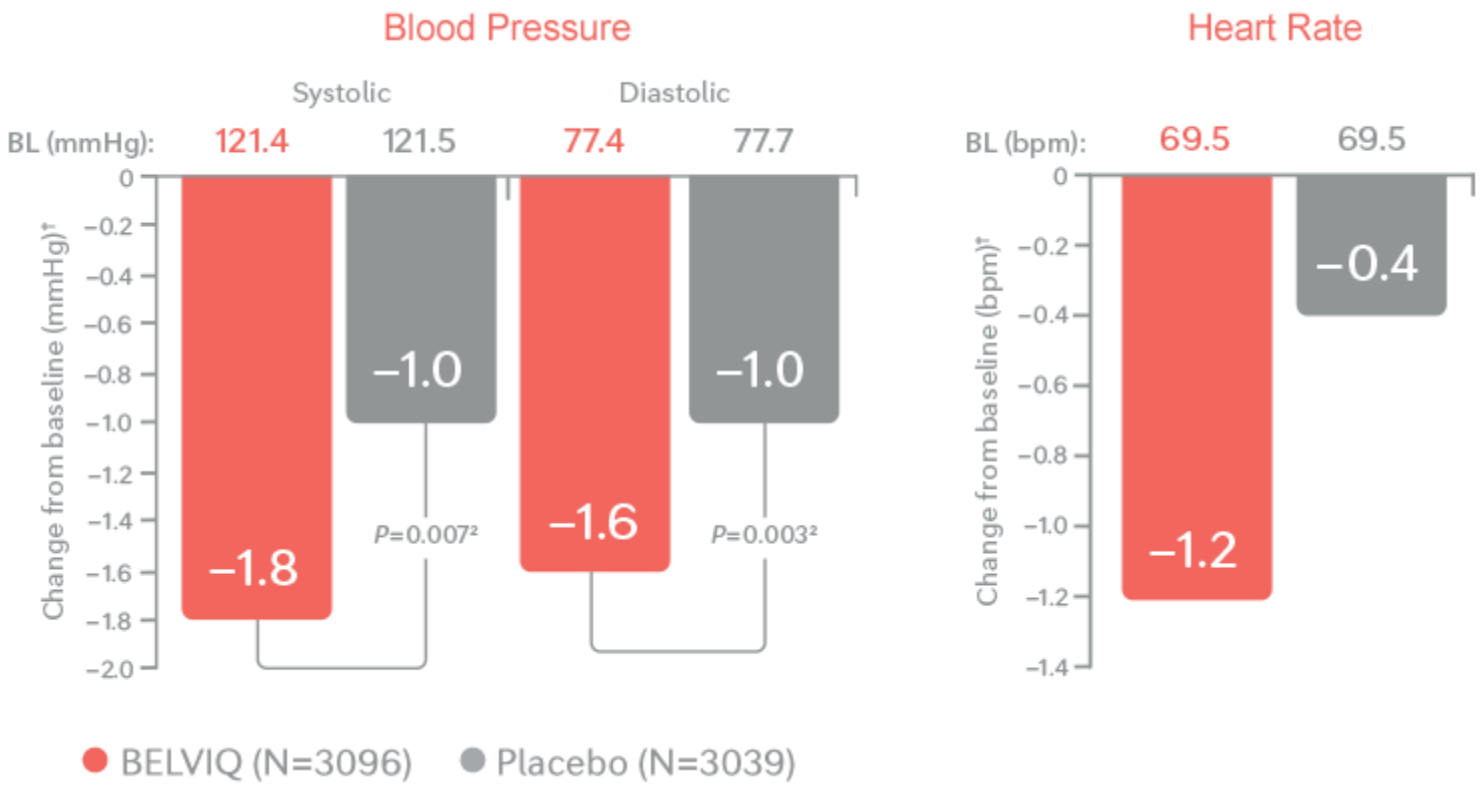


Continued BELVIQ® Treatment Supported Patients' Weight Loss[3]

- **Mean weight change over time:** all patients who completed the study



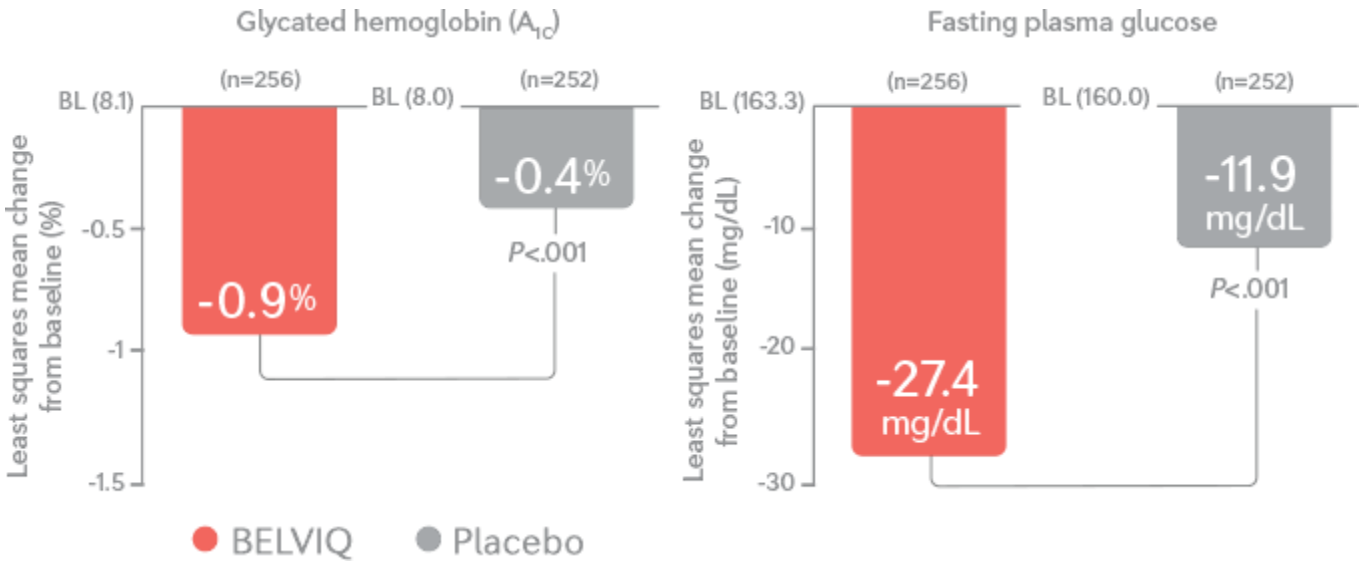
Impact on Blood Pressure and Heart Rate



Changes in Lipid Profile[1]

	BELVIQ® n=3096		Placebo n=3039	
	Baseline	Least squares mean change from baseline (%)	Baseline	Least squares mean change from baseline (%)
Total Cholesterol (mg/dL)	194.4	-0.9‡	194.8	0.4
LDL Cholesterol (mg/dL)	114.3	1.6‡	114.1	2.9
HDL Cholesterol (mg/dL)	53.2	1.8‡	53.5	0.6
Triglycerides (mg/dL)	135.4	-5.3‡	137.0	-0.5

BELVIQ®- Significant Improvement in Glycemic Control



Phentermine/Topiramate ER (Qsymia)

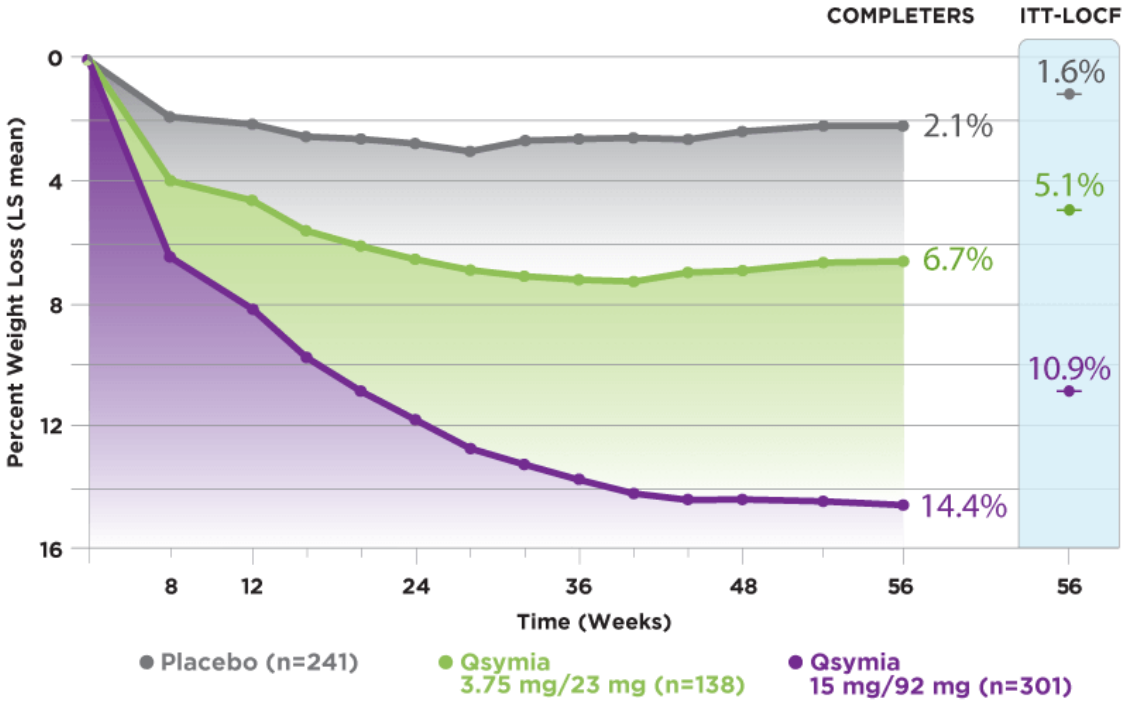
- Sympathometic amine + anti-epileptic
- P:Decreases appetite and food intake by release of catecholamines in hypothalamus
- T:Glutamate receptor, GABA-A, volt-dep Na-channels

- FDA Approval July 2012
- Dosing – 3.75/23mg for 2 weeks then 7.4/46mg daily - OTHERS

- Contraindicated – Active CV disease, Uncontrolled HTN, Hyperthyroidism, Glaucoma, Kidney stones, Avoid with MAOI
- SE-P:Dry mouth, restlessness, insomnia, palpitations, HA, constipation
- SE-T:Parasthesias, Dysgeusia, Somnolence, Cognitive impairment

- Pregnancy-CatX (cleft lip, palate), Lactation-unknown
- Not approved for use in children

QSYMIA® (phentermine and topiramate extended-release) capsules CIV vs placebo for 1 year of treatment (P<0.0001)[1,2,†]



STUDY 1—EQUIP: Treatment difference‡ from placebo in risk factors following 1 year of treatment[1]

STUDY 1 (OBESITY)	PLACEBO (N=498)	QSYMIA 7.5 mg/46 mg (N=234)	QSYMIA 15 mg/92 mg (N=498)	QSYMIA 7.5 mg/46 mg	QSYMIA 15 mg/92 mg
HEART RATE, BPM					
Baseline Mean (SD)	73.2 (8.8)	72.3 (9.2)	73.1 (9.6)	+1.1	+1.8
LS Mean Change (SE)	-0.8 (0.5)	+0.3 (0.6)	+1.0 (0.5)		
SYSTOLIC BLOOD PRESSURE, mmHg					
Baseline Mean (SD)	121.9 (11.5)	122.5 (11.1)	121.9 (11.6)	-2.8	-3.8
LS Mean Change (SE)	+0.9 (0.6)	-1.8 (0.8)	-2.9 (0.6)		
DIASTOLIC BLOOD PRESSURE, mmHg					
Baseline Mean (SD)	77.2 (7.9)	77.8 (7.5)	77.4 (7.7)	-0.5	-1.9
LS Mean Change (SE)	+0.4 (0.4)	-0.1 (0.6)	-1.5 (0.4)		

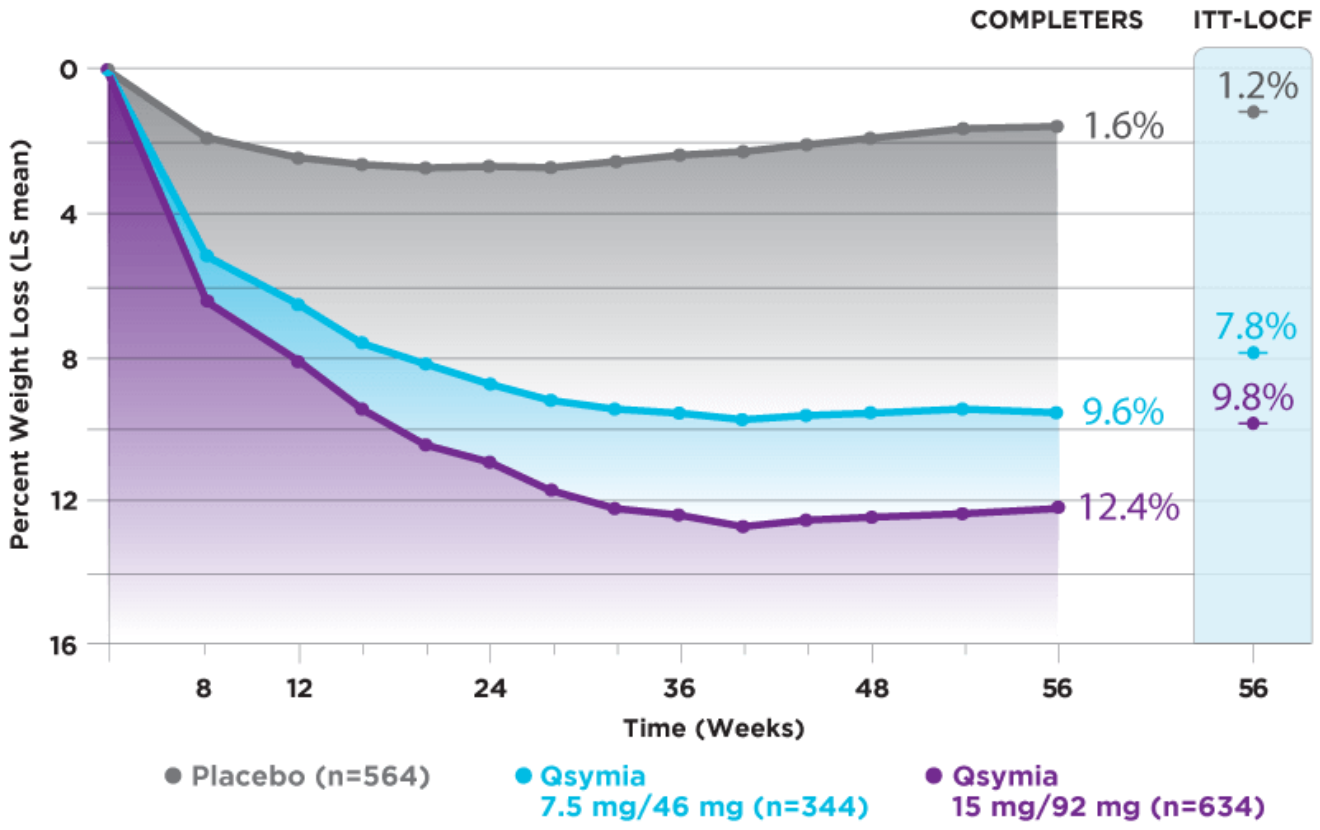
STUDY 1—EQUIP: Treatment difference‡ from placebo in risk factors following 1 year of treatment[1]

STUDY 1 (OBESITY)	PLACEBO (N=498)	QSYMIA 7.5 mg/46 mg (N=234)	QSYMIA 15 mg/92 mg (N=498)	QSYMIA 7.5 mg/46 mg	QSYMIA 15 mg/92 mg
TOTAL CHOLESTEROL, %					
Baseline Mean (SD)	194.3 (36.7)	196.3 (36.5)	192.7 (33.9)	-1.9	-2.5
LS Mean Change (SE)	-3.5 (0.6)	-5.4 (0.9)	-6.0 (0.6)		
LDL-CHOLESTEROL, %					
Baseline Mean (SD)	120.9 (32.2)	122.8 (33.4)	120.0 (30.1)	-2.2	-2.8
LS Mean Change (SE)	-5.5 (1.0)	-7.7 (1.3)	-8.4 (0.9)		
HDL-CHOLESTEROL, %					
Baseline Mean (SD)	49.5 (13.3)	50.0 (11.1)	49.7 (11.7)	+0.5	+3.5
LS Mean Change (SE)	+0.0 (0.8)	+0.5 (1.1)	+3.5 (0.8)		

STUDY 1—EQUIP: Treatment difference‡ from placebo in risk factors following 1 year of treatment[1]

STUDY 1 (OBESITY)	PLACEBO (N=498)	QSYMIA 7.5 mg/46 mg (N=234)	QSYMIA 15 mg/92 mg (N=498)	QSYMIA 7.5 mg/46 mg	QSYMIA 15 mg/92 mg
TRIGLYCERIDES, %					
Baseline Mean (SD)	119.0 (39.3)	117.5 (40.3)	114.6 (37.1)	-3.9	-14.3
LS Mean Change (SE)	+9.1 (2.3)	+5.2 (3.1)	-5.2 (2.2)		
FASTING GLUCOSE, mg/dL					
Baseline Mean (SD)	93.1 (8.7)	93.9 (9.2)	93.0 (9.5)	-1.2	-2.5
LS Mean Change (SE)	+1.9 (0.5)	+0.8 (0.7)	-0.6 (0.5)		
WAIST CIRCUMFERENCE, cm					
Baseline Mean (SD)	120.5 (14.0)	121.5 (15.2)	120.0 (14.7)	-2.5§	-7.8§
LS Mean Change (SE)	-3.1 (0.5)	-5.6 (0.6)	-10.9 (0.5)		

QSYMIA® (phentermine and topiramate extended-release) capsules CIV vs placebo for 1 year of treatment (P<0.0001)[1,2,†]



STUDY 2—CONQUER: Treatment difference‡ from placebo in risk factors following 1 year of treatment[1]

STUDY 2 (OVERWEIGHT AND OBESE WITH COMORBIDITIES)	PLACEBO (N=979)	Qsymia® 7.5 mg/46 mg (N=488)	Qsymia 15 mg/92 mg (N=981)	Qsymia 7.5 mg/46 mg	Qsymia 15 mg/92 mg
HEART RATE, BPM					
BASELINE MEAN (SD)	72.1 (9.9)	72.2 (10.1)	72.6 (10.1)	+0.6	+1.7
LS MEAN CHANGE (SE)	-0.3 (0.3)	+0.3 (0.4)	+1.4 (0.3)		
SYSTOLIC BLOOD PRESSURE, mmHg					
BASELINE MEAN (SD)	128.9 (13.5)	128.5 (13.6)	127.9 (13.4)	-2.3	-3.2
LS MEAN CHANGE (SE)	-2.4 (0.48)	-4.7 (0.63)	-5.6 (0.5)		
DIASTOLIC BLOOD PRESSURE, mmHg					
BASELINE MEAN (SD)	81.1 (9.2)	80.6 (8.7)	80.2 (9.1)	-0.7	-1.1
LS MEAN	-2.7 (0.3)	-3.4 (0.4)	-3.8 (0.3)		

STUDY 2—CONQUER: Treatment difference‡ from placebo in risk factors following 1 year of treatment[1]

STUDY 2 (OVERWEIGHT AND OBESE WITH COMORBIDITIES)	PLACEBO (N=979)	Qsymia® 7.5 mg/46 mg (N=488)	Qsymia 15 mg/92 mg (N=981)	Qsymia 7.5 mg/46 mg	Qsymia 15 mg/92 mg
TOTAL CHOLESTEROL, %					
BASELINE MEAN (SD)	205.8 (41.7)	201.0 (37.9)	205.4 (40.4)	-1.6	-3.0
LS MEAN CHANGE (SE)	-3.3 (0.5)	-4.9 (0.7)	-6.3 (0.5)		
LDL-CHOLESTEROL, %					
BASELINE MEAN (SD)	124.2 (36.2)	120.3 (33.7)	123.9 (35.6)	+0.4	-2.8
LS MEAN CHANGE (SE)	-4.1 (0.9)	-3.7 (1.1)	-6.9 (0.9)		
HDL-CHOLESTEROL, %					
BASELINE MEAN (SD)	48.9 (13.8)	48.5 (12.8)	49.1 (13.8)	+4.0	+5.6
LS MEAN CHANGE (SE)	+1.2 (0.7)	+5.2 (0.9)	+6.8 (0.7)		

STUDY 2—CONQUER: Treatment difference‡ from placebo in risk factors following 1 year of treatment[1]

STUDY 2 (OVERWEIGHT AND OBESE WITH COMORBIDITIES)	PLACEBO (N=979)	Qsymia® 7.5 mg/46 mg (N=488)	Qsymia 15 mg/92 mg (N=981)	Qsymia 7.5 mg/46 mg	Qsymia 15 mg/92 mg
TRIGLYCERIDES, %					
BASELINE MEAN (SD)	163.5 (76.3)	161.1 (72.2)	161.9 (73.4)	-13.3	-15.3
LS MEAN CHANGE (SE)	+4.7 (1.7)	-8.6 (2.2)	-10.6 (1.7)		
FASTING INSULIN, QIU/mL					
BASELINE MEAN (SD)	17.8 (13.2)	18.0 (12.9)	18.4 (17.5)	-4.2	-4.7
LS MEAN CHANGE (SE)	+0.7 (0.8)	-3.5 (1.1)	-4.0 (0.8)		
FASTING GLUCOSE, mg/dL					
BASELINE MEAN (SD)	106.6 (23.7)	106.2 (21.0)	105.7 (21.4)	-2.4	-3.6
LS MEAN CHANGE (SE)	+2.3 (0.6)	-0.1 (0.8)	-1.3 (0.6)		

STUDY 2—CONQUER: Treatment difference‡ from placebo in risk factors following 1 year of treatment[1]

STUDY 2 (OVERWEIGHT AND OBESE WITH COMORBIDITIES)	PLACEBO (N=979)	Qsymia® 7.5 mg/46 mg (N=488)	Qsymia 15 mg/92 mg (N=981)	Qsymia 7.5 mg/46 mg	Qsymia 15 mg/92 mg
WAIST CIRCUMFERENCE, cm					
BASELINE MEAN (SD)	113.4 (12.2)	112.7 (12.4)	113.2 (12.2)	-5.2§	-6.8§
LS MEAN CHANGE (SE)	-2.4 (0.3)	-7.6 (0.4)	-9.2 (0.3)		

Phentermine/Topiramate ER (Qsymia)

EQUIP trial	5%-weight loss	10%-weight loss
Qsymia 15/92mg	67%	47%
Qsymia 3.75/23mg	45%	19%
Placebo	17%	7%

CONQUER trial (comorb2)	5%-weight loss	10%-weight loss
Qsymia 15/92mg	70%	48%
Qsymia 7.5/46mg	62%	37%
Placebo	21%	7%

Naltrexone ER/Bupropion (Contrave)

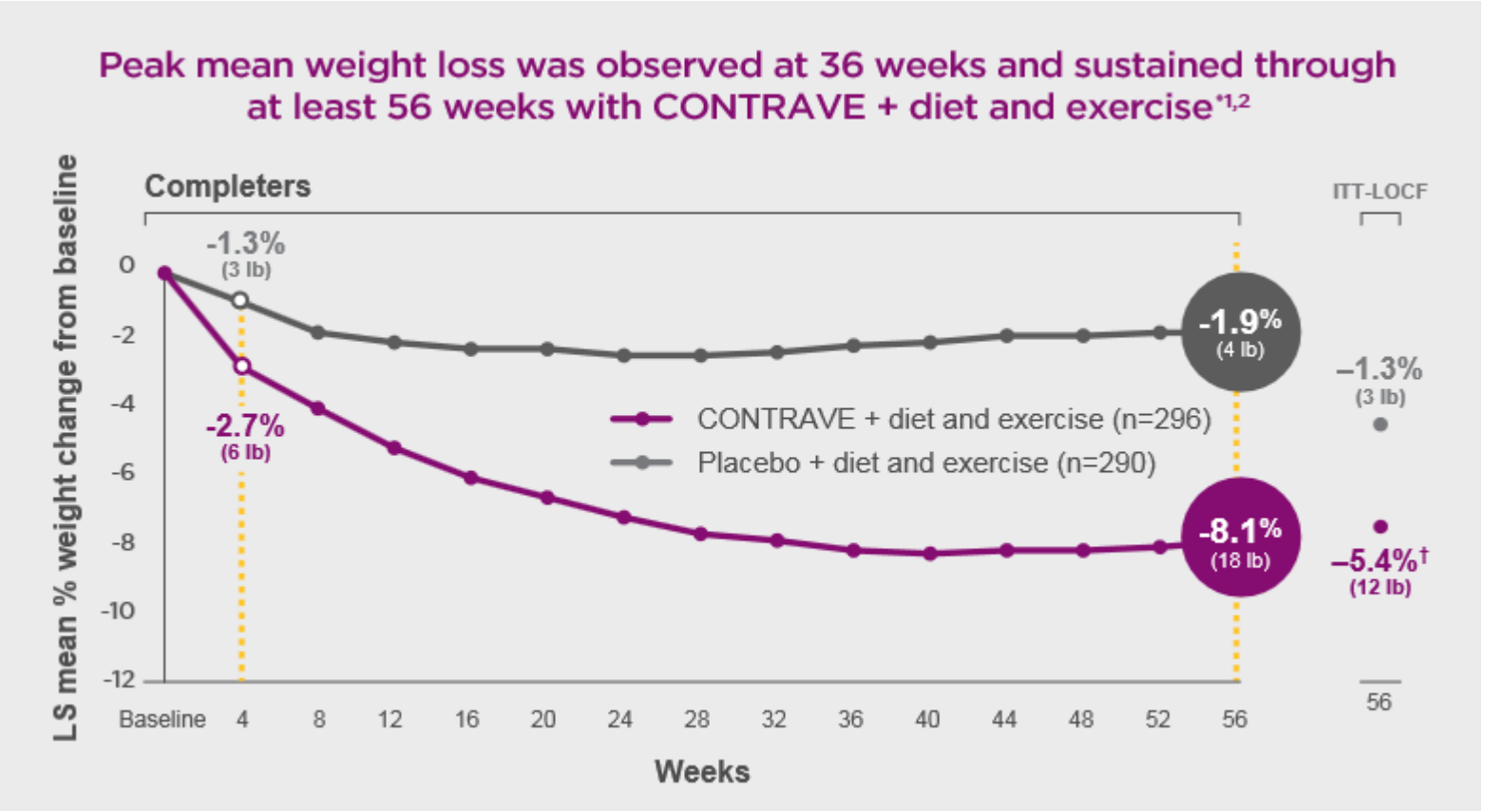
- Stimulates POMC, Blocks suppression of alpha-MSH
- Exerts effect on appetite regulatory center and the reward system to regulate appetite and reduce cravings

- FDA Approval Sept 2014
- Dosing – Titration (8/90mg tabs) – 2 tabs twice daily goal

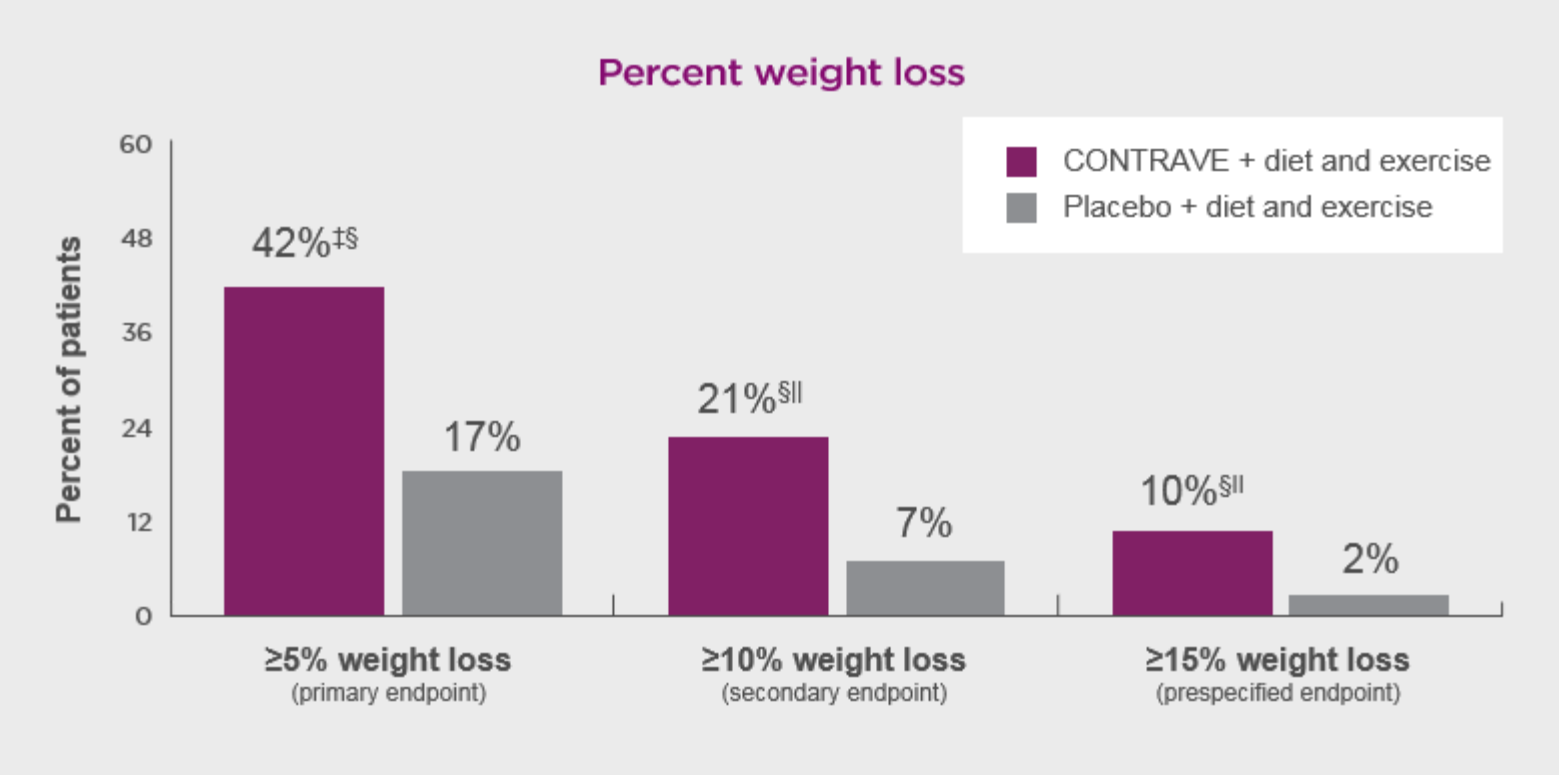
- Safety – neuropsychiatric reactions, suicidal thoughts / behavior
- Contraindicated – Seizures, uncontrolled HTN, Bulimia, chronic opioid use
- SE – nausea, HA, insomnia, dizziness, dry mouth

- Pregnancy-CatX, Lactation-avoid
- Not approved for use in children

CONTRAVE + diet and exercise produced statistically significant mean weight loss as early as 4 weeks[1,2]

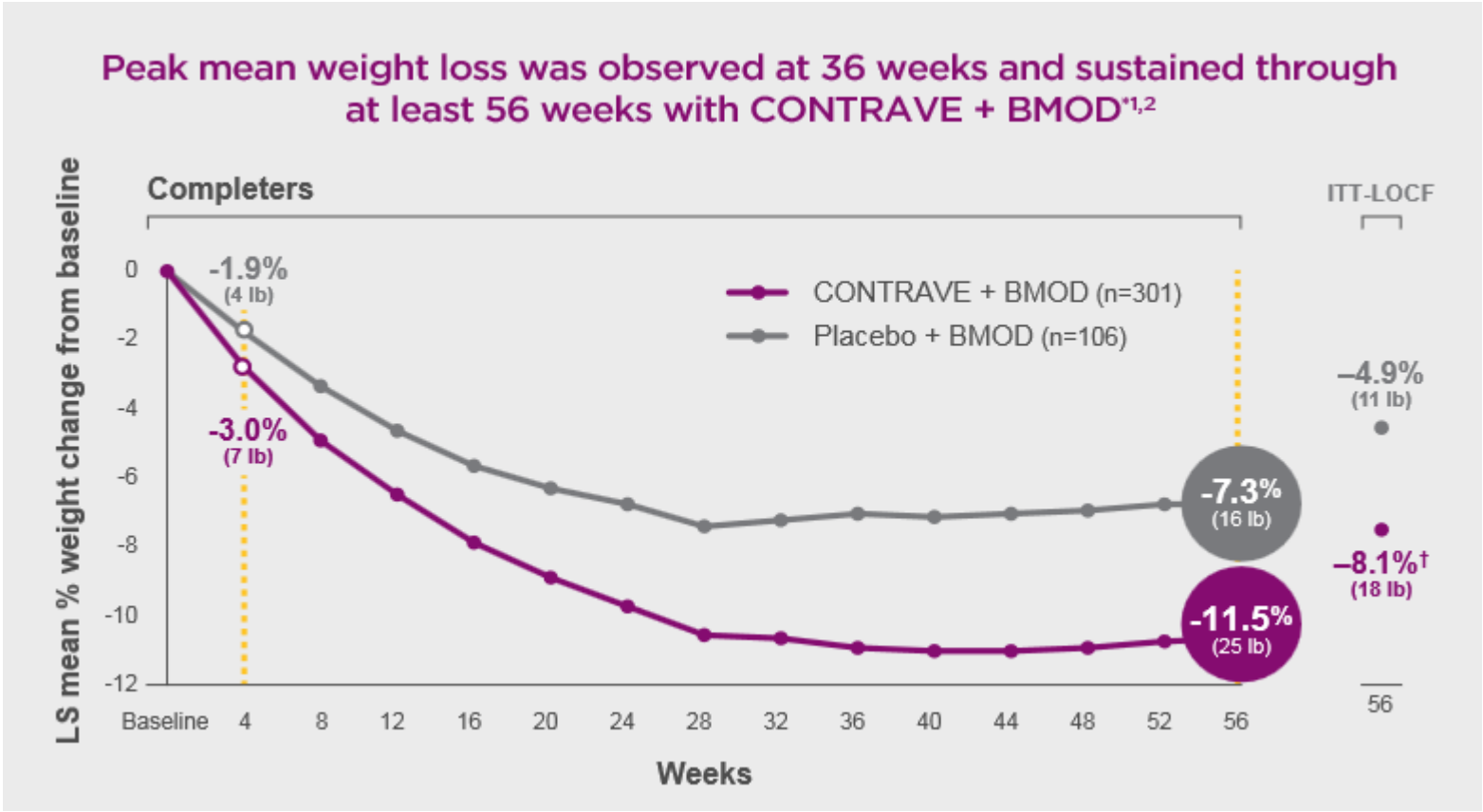


Significantly more patients achieved reductions in percent body weight with CONTRAVE at Week 56[1,2]



NNT=5 (5%)

(BMOD) program lost an average of 25 pounds CONTRAVE + BMOD produced statistically significant results as early as 4 weeks[1,2]



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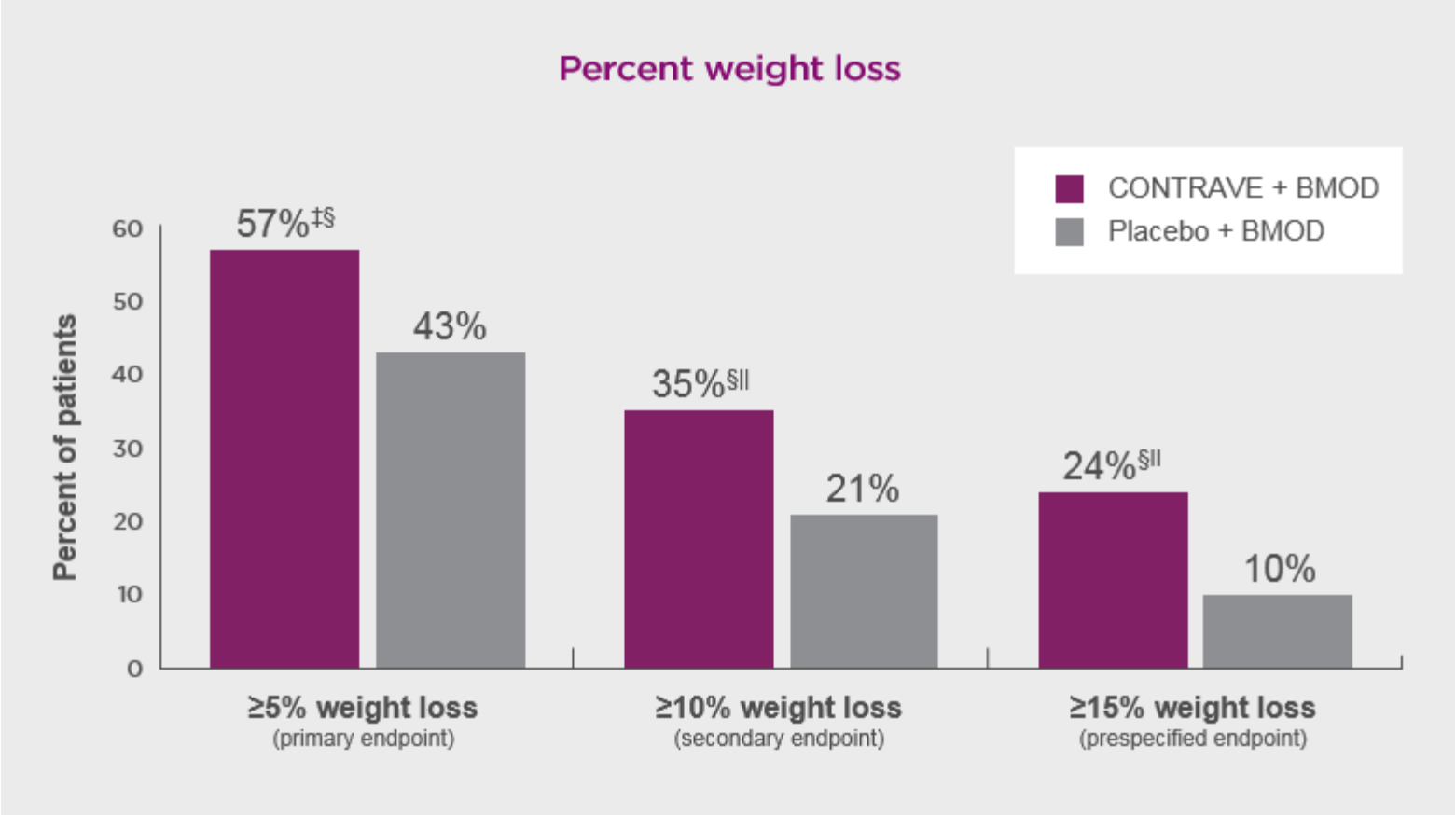
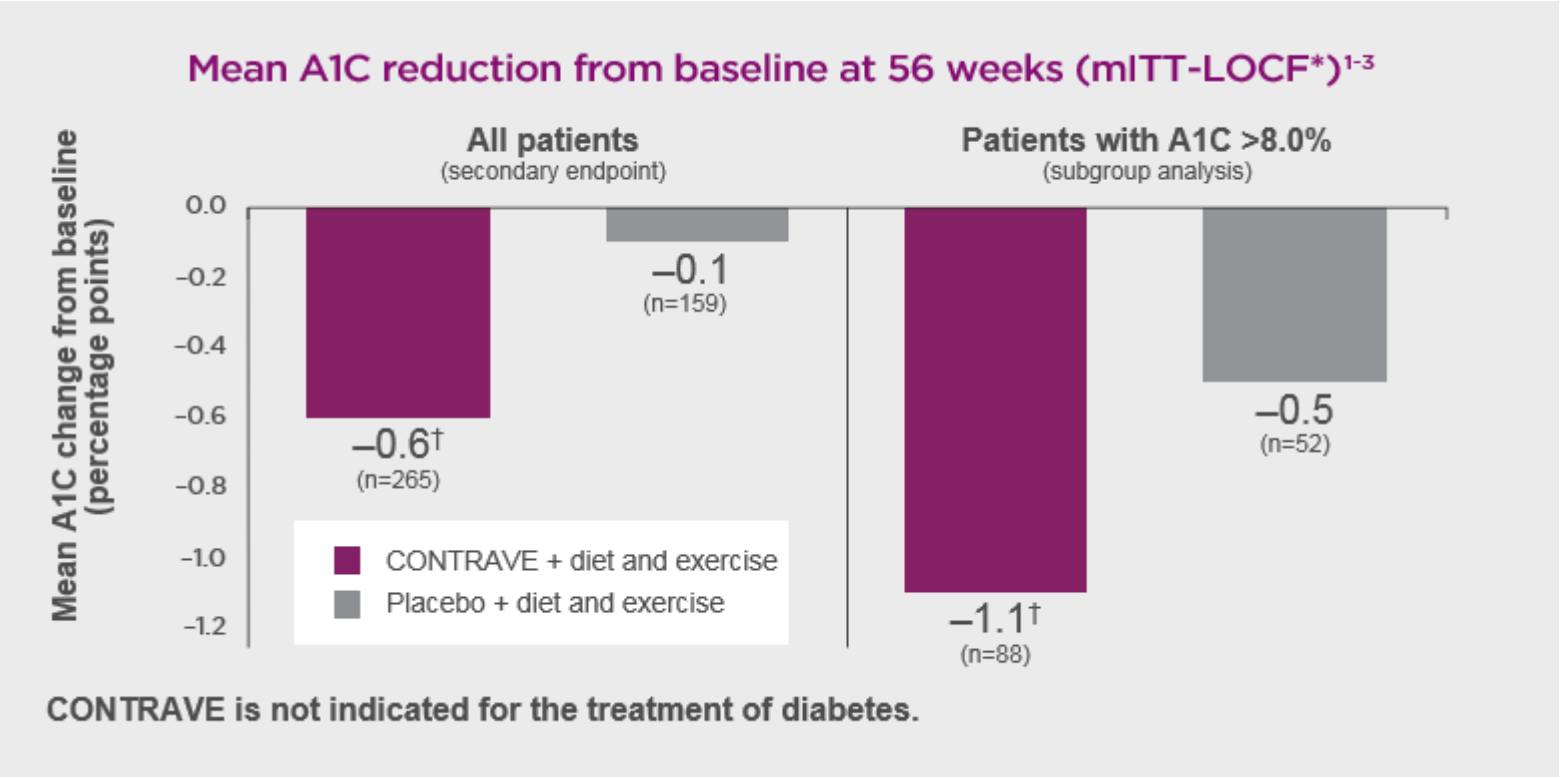


CONTRAVE significantly improved A1C in patients with type 2 diabetes



Changes in cardiometabolic risk factors were observed (secondary endpoint)[1,2]

Parameter	COR-BMOD[‡§]		COR-I[§‖]	
	CONTRAVE (n=482)	Placebo (n=193)	CONTRAVE (n=471)	Placebo (n=511)
Triglycerides (Median % change)	–17.8	–7.4	–11.6	+1.7
HDL-C (LS mean % change)	+9.4	+2.8	+8.0	+0.8
LDL-C (LS mean % change)	+7.1	+10.0	–2.0	–0.5
Heart rate (LS mean change, bpm)	+1.1	+0.2	+1.0	–0.2
Systolic blood pressure (LS mean change, mmHg)	–1.3	–3.9	–0.1	–1.9
Diastolic blood pressure (LS mean change, mmHg)	–1.4	–2.8	0.0	–0.9
Waist circumference (LS mean change, in)	–3.9	–2.7	–2.4	–1.0

Standard dosing for CONTRAVE®[2]

	Morning	Evening
Week 1	1	
Week 2	1	1
Week 3	2	1
Week 4 and maintenance	2	2

Maximum Daily Dose[2]	
Moderate or severe renal impairment	2 tablets (1 in the AM, 1 in the PM)
End-stage renal disease	Not recommended for use in these patients
Hepatic impairment	1 tablet in the AM

Liraglutide (Saxenda)

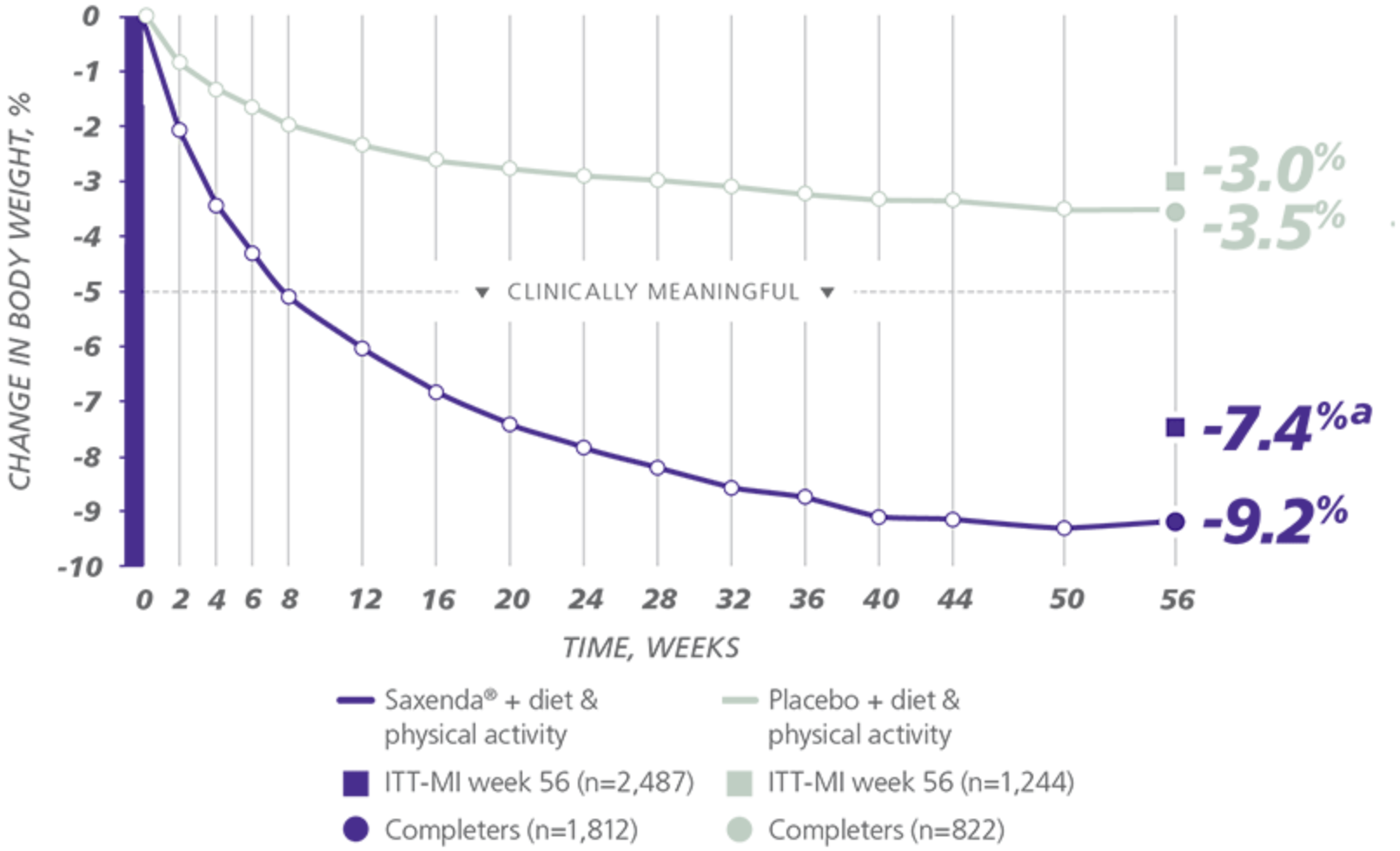
- GLP-1 (glucagon-like peptide-1) receptor agonist
- Stimulates insulin release and inhibits glucagon secretion
- Slows gastric emptying and increases satiety after eating

- FDA Approval December 2014
- Dosing: 3mg daily goal – Titration by 0.6mg weekly

- Safety – GB disease (NNH=100) and Cholecystitis (NNH=250). Pancreatitis – 0.3%
- Contraindicated – Family/Personal history of thyroid cancers and MEN-syndrome Type 2
- SE – 10% discontinuation rate due to GI side effects

- Pregnancy-CatX, Lactation-unknown
- Not approved for use in children

Observed mean change in body weight from baseline[2]



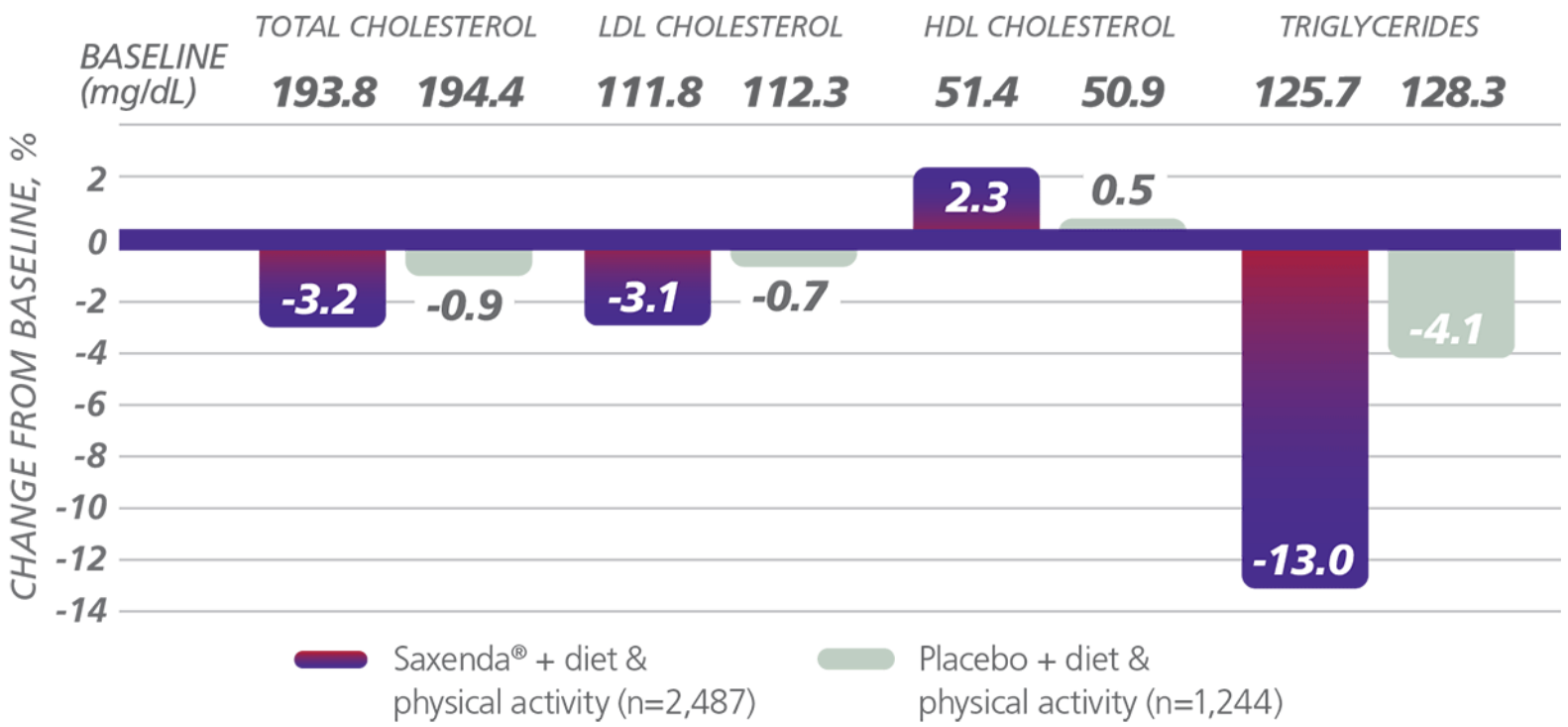
Study 1: Effect of Saxenda® on achieving weight loss

Placebo 34%

Placebo 15%

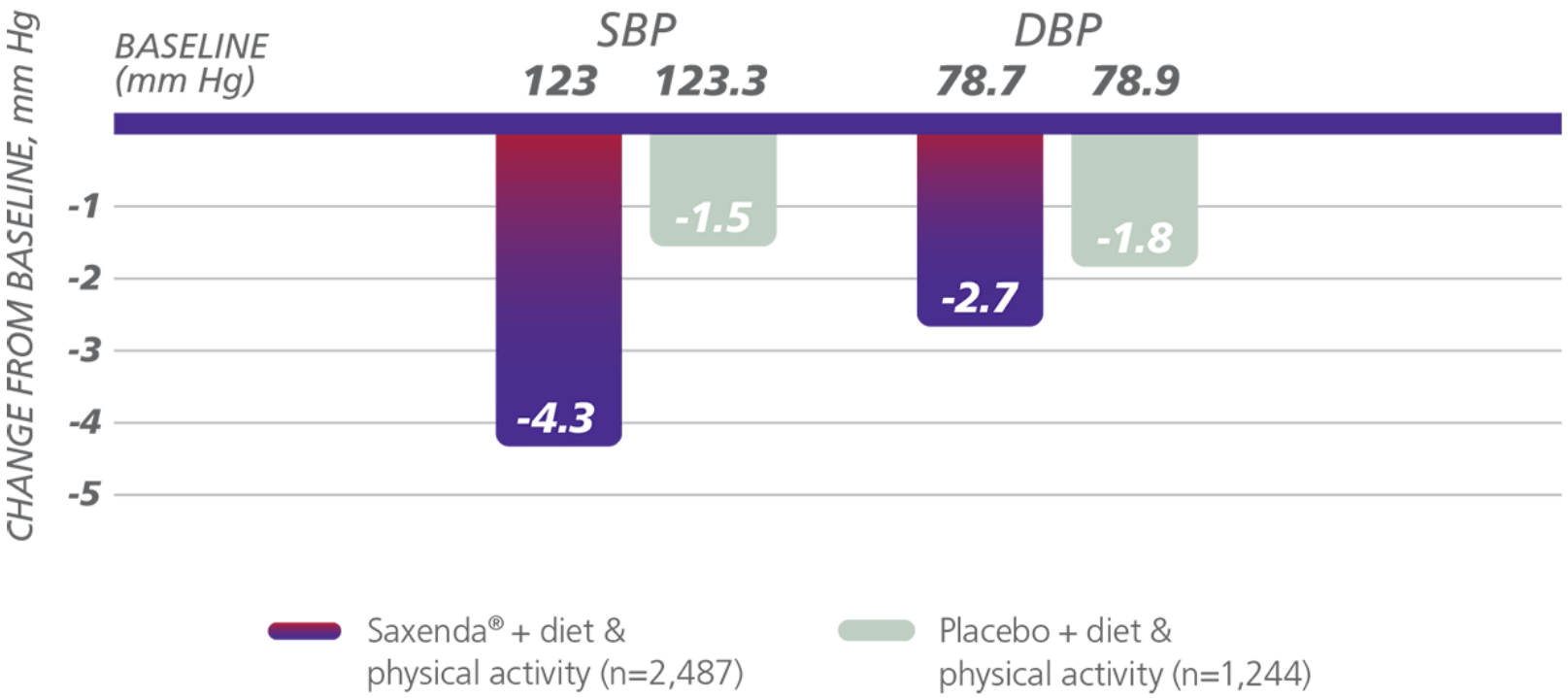
NNT=3 (5%), NNT = 5 (10%) --- Sustained weight loss up to 2 years

Change in cardiometabolic risk factors: Improved overall lipid profile[a]



LEADER Trial – 13% reduction (p=0.01) ARR 1.9% (NNT-53)

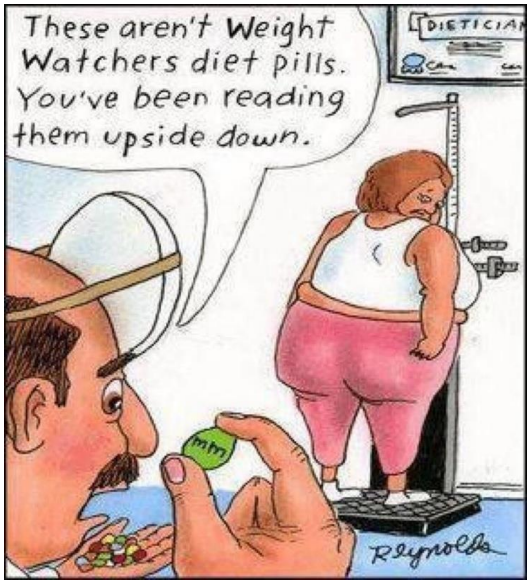
Change in cardiometabolic risk factor: Reduction in blood pressure vs placebo[a]



LEADER Trial – 13% reduction (p=0.01) ARR 1.9% (NNT-53)

How do they compare?

- All achieved clinically significant weight loss over placebo, each improved cardiometabolic parameters
- Numbers vary based on study inclusion criteria: such as risk factors (DM or CVD) or the addition of behavioral modification
- ***SO*** which to use and why? And is there another we are 'forgetting'?



Lisdexamfetamine (Vyvanse)

- Stimulates CNS sympathomimetic activity
- Moderate to Severe BED in adults

- FDA Approval January 2015 (BED)
- Dosing – Start 30mg and titrate to 70mg max

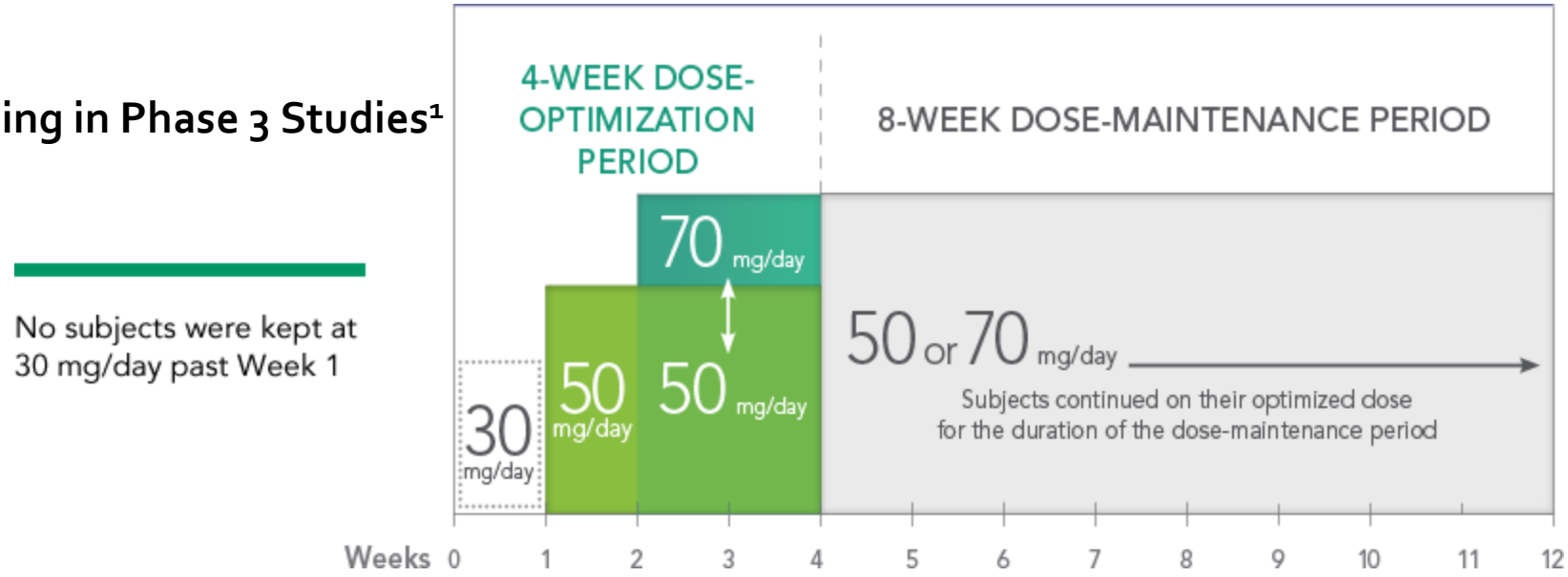
- Pregnancy-CatX, Lactation-avoid
- Approved for use in children as ADHD mediation

- BINGE EATING – most common eating disorder in US Adults 25.4%, BN 19.7%, AN 18.9%
- 19% NL weight, 36% overweight, 45% obese

Lisdexamfetamine (Vyvanse)

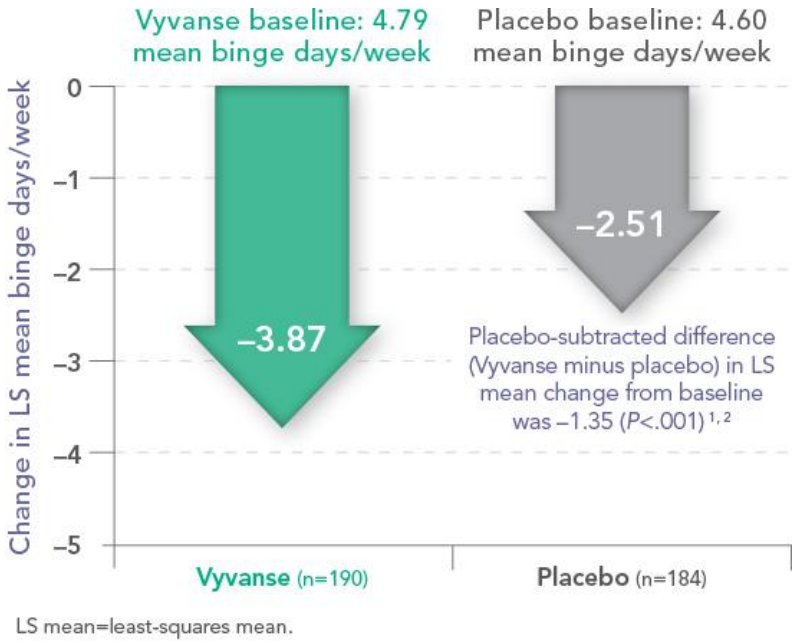
- Both studies were 12-week, randomized, double-blind, parallel-group, placebo-controlled, dose-optimization studies of adults aged 18 to 55 years (N=374 and N=350) with protocol-defined moderate to severe B.E.D.[1]

Dosing in Phase 3 Studies[1]



STUDY 1: Vyvanse® (lisdexamfetamine dimesylate) Significantly Reduced Mean Binge Days per Week[1]

- REDUCTION IN LS MEAN BINGE DAYS PER WEEK FROM BASELINE **AT WEEK 12**[1]

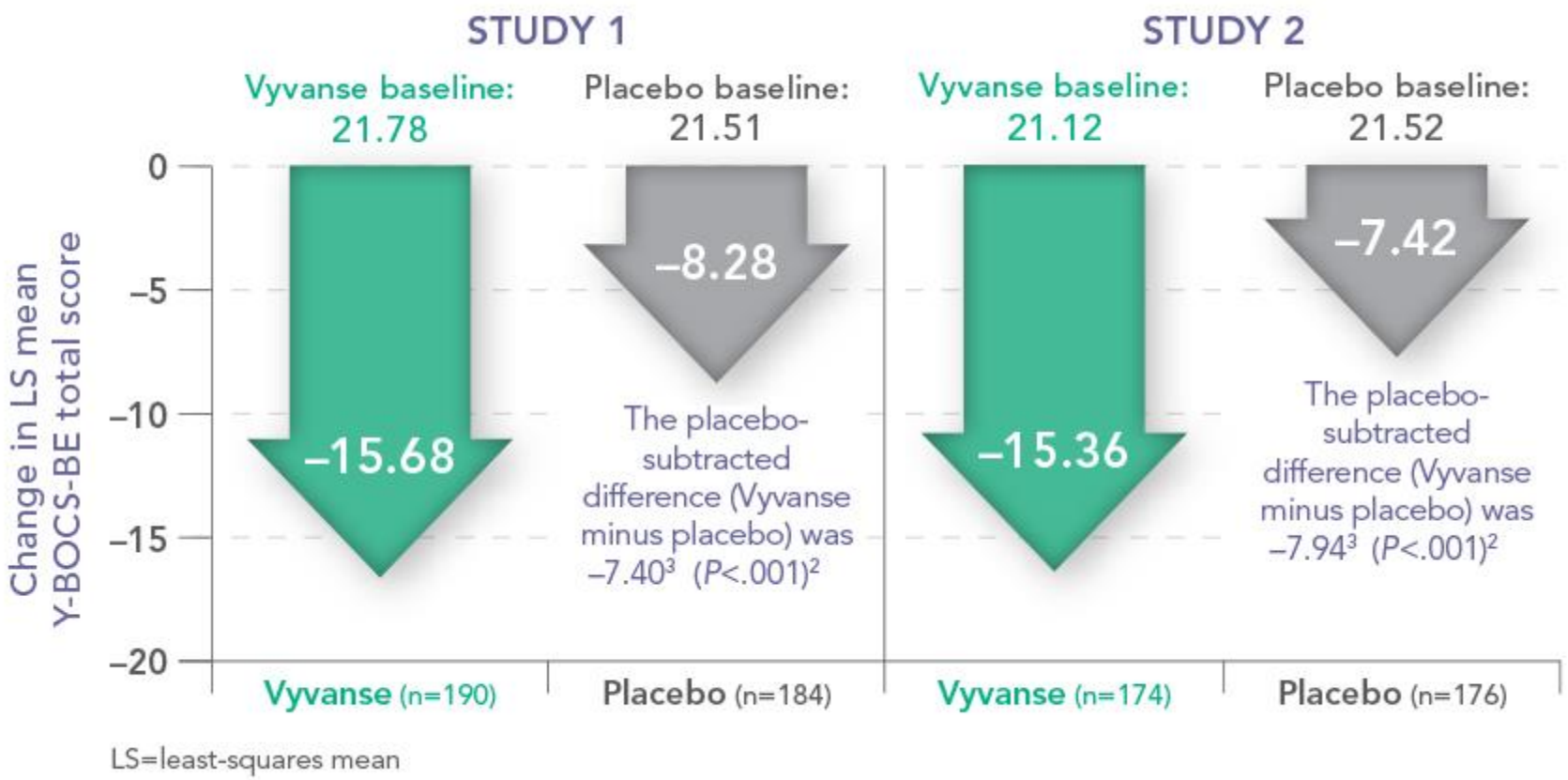


LS mean=least-squares mean.

MEAN BINGE DAYS PER WEEK AT BASELINE AND WEEK 12[2]

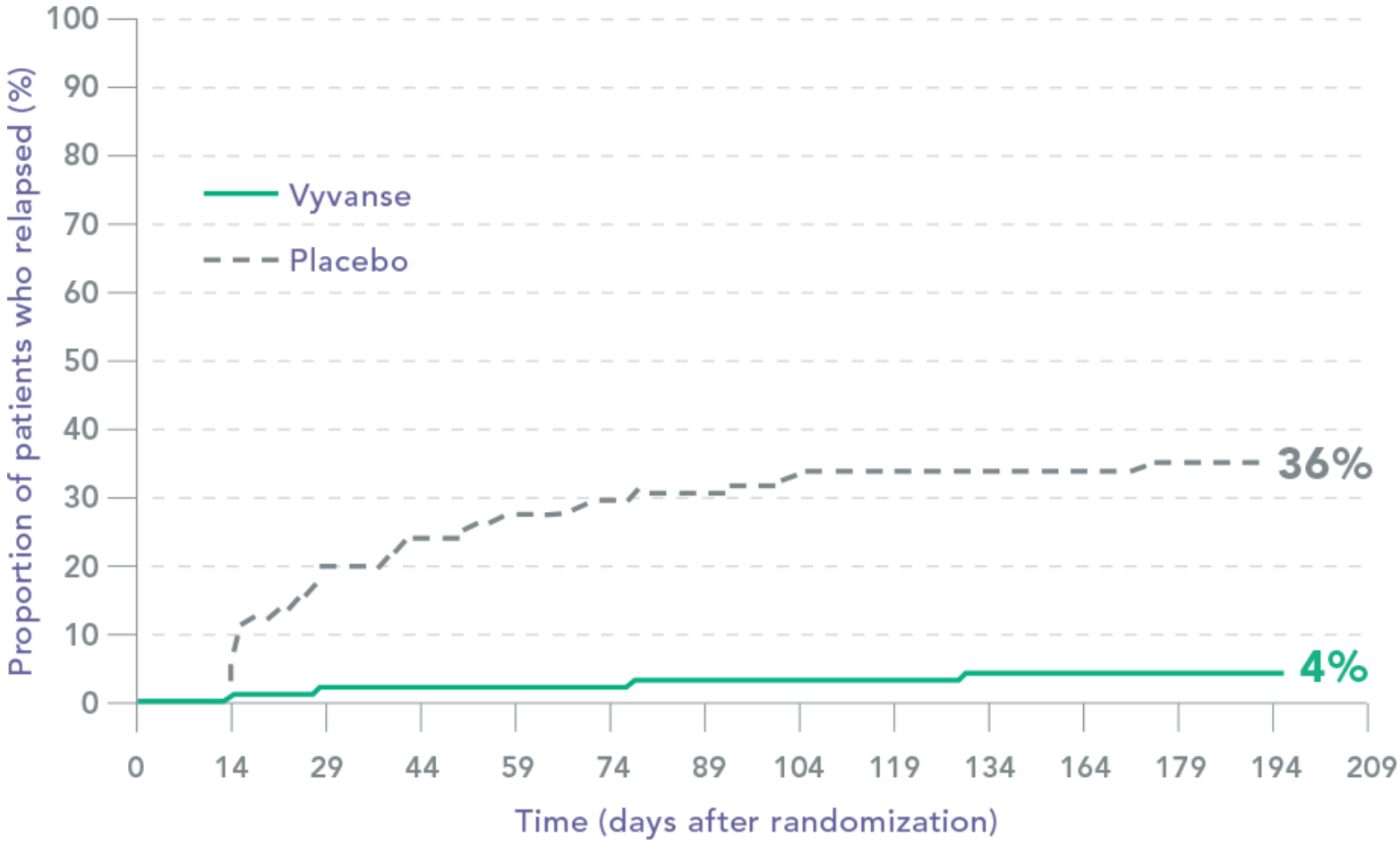
	BASELINE	WEEK 12
Vyvanse (n=190)	4.79	0.78
Placebo (n=184)	4.60	2.22

Vyvanse® (lisdexamfetamine dimesylate) Reduced Obsessive Thoughts and Compulsive Behaviors Related to Binge Eating, Using Y-BOCS-BE



LS=least-squares mean

Vyvanse Was Superior To Placebo Based on Time to Relapse in Adult Patients With Moderate to Severe B.E.D.[1]



MY CLINICAL APPROACH

HUNGER / SATIETY

- Phentermine
- Qsymia (phentermine/topiramate-ER)
- Belviq (lorcaserin)
- Saxenda (liraglutide)

BEHAVIORAL EATING

- Contrave (naltrexone/bupropion-ER)
- Vyvanse (lisdexamfetamine dimesylate)

*REVIEW other chronic medications for weight gain
*START when 'obstacles' to weight loss / maintenance
*TITRATE dose whenever possible before changing
*CONSIDER combination medications, when appropriate
*DON'T forget about post-surgical patients needs

Clinical Pearls

- Medication in an evidence-based tool to support the physiologic & behavioral changes necessary for sustained weight loss
- As with other chronic diseases, medications for the treatment of obesity should be used long-term
- An individualized treatment plan is important in addition to anti-obesity medications

Case Study

- 54 year old female with PMHx of T2DM, HTN, Hyperlipidemia, Asthma and Allergies
- Family History: Father d.55 MI, HTN. MGF –CAD and CVA, PGM-CAD.
- Meds: Losartan-HCTZ 50-12.5mg, Amlodipine 5mg, Jentadueto 2.5-1000mg BID, Pioglitazone 30mg, Pravastatin 20mg, Zyrtec 10mg, Dulera 200-5mcg – 2 puffs BID, Ventolin-HFA prn (NKDA)
- Labs: Glc-99, A1c 6.6, Cr-0.9, eGFR>60, Microalb ratio 9, TC160, TG116, HDL 48, LDL89.
- Vitals: Ht-62in, Wt-176.5#, BMI-33, BP 124/72, Body fat% 36.3 (nl 23-35%), TBW% 46.5 (nl 40-60%), RMR-1456cal.

What would you do???

Pediatric obesity medications

Pharmacology

Orlistat (Xenical)

- FDA-approved for children ≥ 12 years
- Weight loss is small
- Side effects preclude usage in most patients
- May cause oily stools

Metformin

- FDA-approved for children with T2DM ≥ 10 years
- Weight loss is small
- Useful for elevated serum insulin levels
- May prolong duration of time before onset of T2DM
- May cause gastrointestinal upset, especially in first few weeks

Topiramate

- Not FDA-approved for weight loss in children
- Has been used for seizure control in children for years
- May control cravings
- Can cause cleft palate in fetus
- May cause paresthesias of extremities, cognitive disruption (confusion, difficulty concentrating)

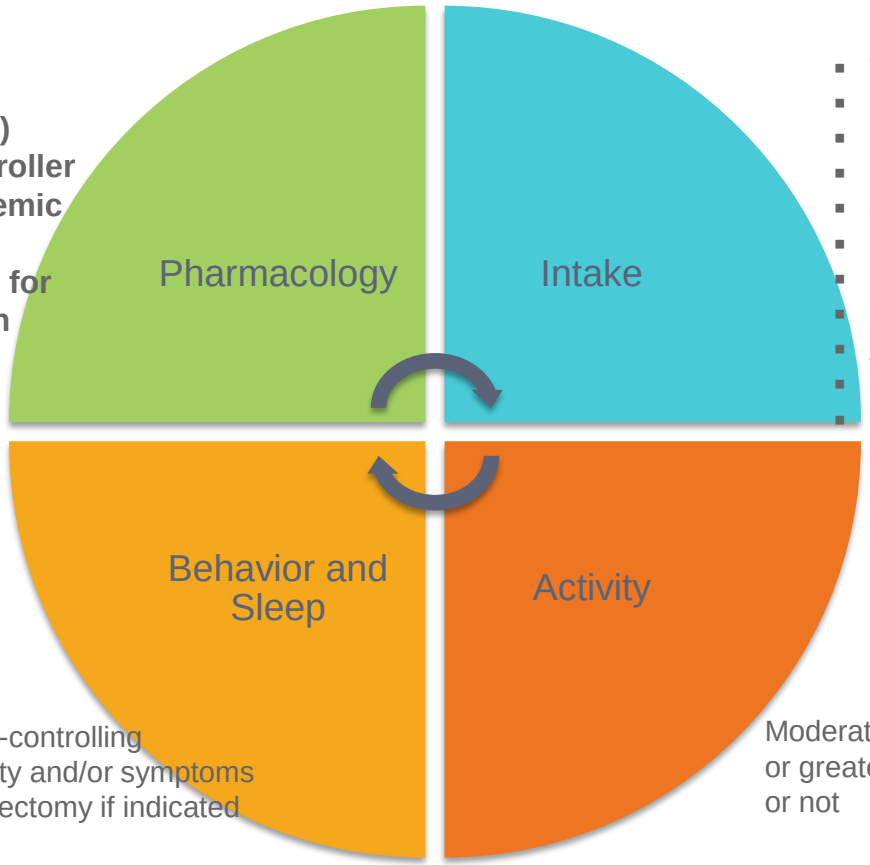
Phentermine

- FDA-approved for weigh loss in children ≥ 16 years
- Has been used in adolescents
- Weight loss is small to moderate
- May cause anxiety, tremors, slightly increased blood pressure

[33] [64] [65] [66]

Management of the Young Child with Obesity: 5-9 Years

- **Minimize obesogenic medications especially second-generation antipsychotics (SGAPs)**
- **Treat asthma with controller meds to minimize systemic steroid use**
- **Consider ACE inhibitor for persistent hypertension**



- Three meals; 1-2 snacks
- 3 servings of protein/day
- 2-3 servings of dairy/day
- 1.5-2 servings of fruit/day
- 4-5 servings non-starchy vegetables
- Dessert only on special occasion
- NO sugar-sweetened beverages
- NO fast food
- Age-appropriate portion sizes
- Praise for trying new foods
- Consider LGI/reduced-CHO diet

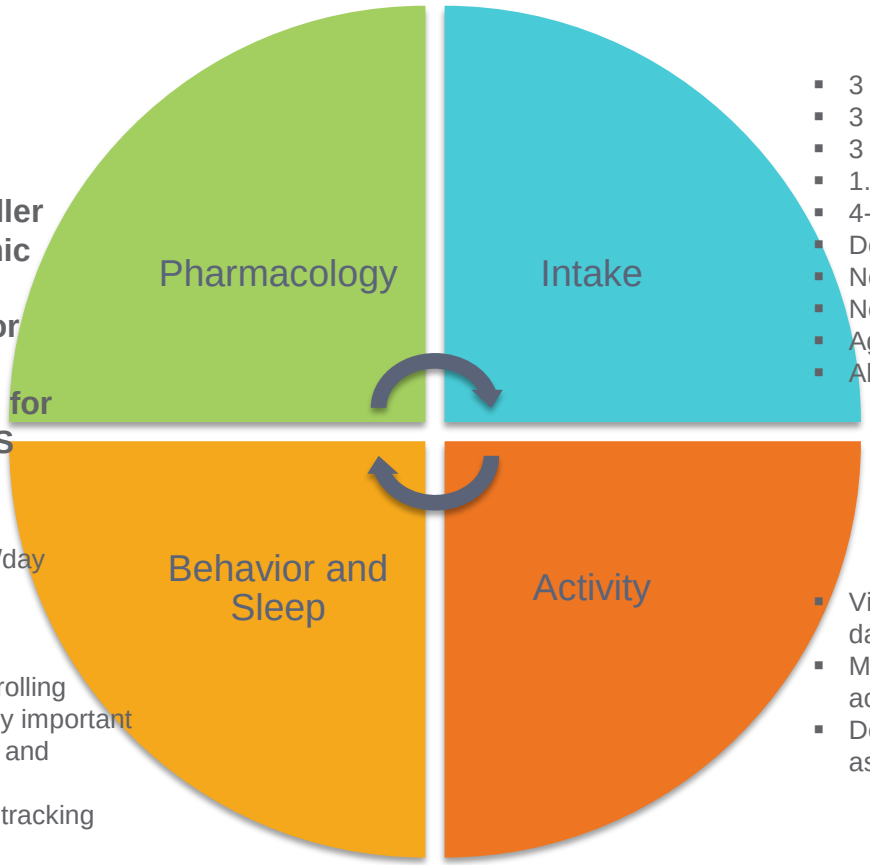
- Screen time < 1-2 hours
- Routine sleep pattern
- No TV in bedroom
- 11-14 hours of sleep
- All meals at the table
- Parents as role models
- Parents should not be over-controlling
- Sleep study if severe obesity and/or symptoms
- Tonsillectomy and adenoidectomy if indicated

Moderate to vigorous activity for 60 minutes or greater each day; can be organized or not

[16] [17] [18] [19]

Management of the Pubertal Child with Obesity: 10-14 Years

- **Orlistat (Xenical) FDA-approved for ≥ age 12**
- **Minimize obesogenic medications, especially SGAPs**
- **Treat asthma with controller meds to minimize systemic steroid use**
- **Consider ACE inhibitor for persistent hypertension**
- **Metformin FDA-approved for T2DM ≥ age 10 and PCOS**



- 3 meals; 1-2 nutritious snacks
- 3 servings of protein/day
- 3 servings of dairy/day
- 1.5-2 servings of fruit/day
- 4-5 servings of non-starchy vegetables
- Dessert only on special occasion
- No sugar-sweetened beverages
- No fast food
- Age-appropriate portion sizes
- Allow child to leave food on plate

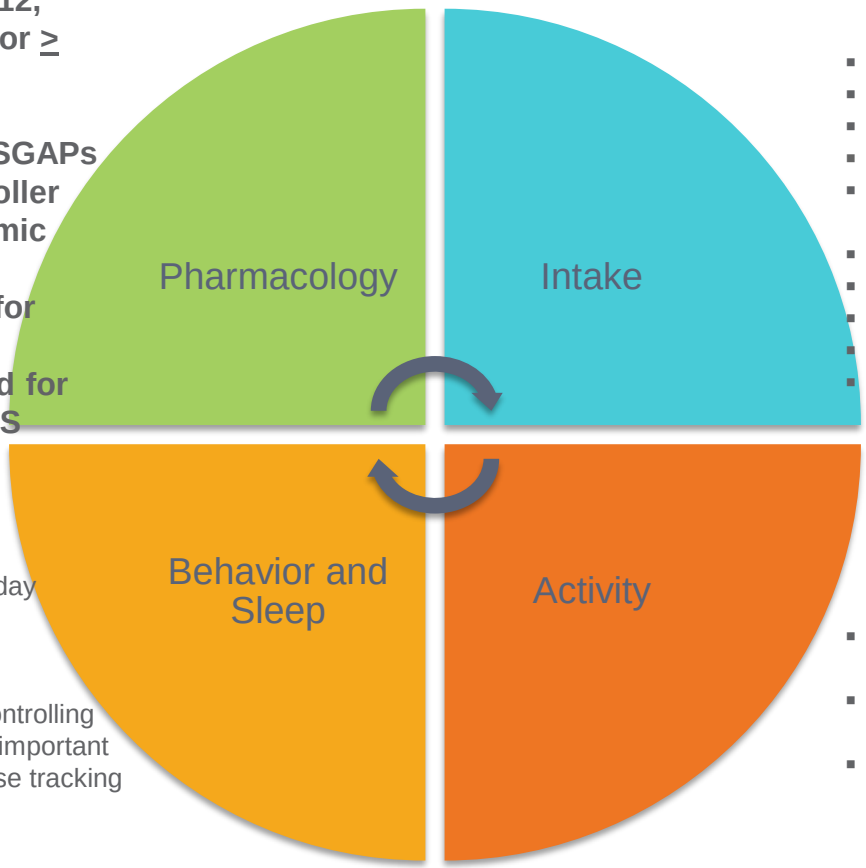
- Screen time less than 1-2 hours/day
- 10-12 hours of sleep
- Routine sleep pattern
- No TV in bedroom
- Parents should not be over-controlling
- Peer groups become increasingly important
- All meals at the table with family and encourage socialization
- Recommend meal and exercise tracking

- Vigorous activity for 60 minutes or more daily; can be organized or not
- Monitor for changes in decreased activity level
- Decrease non-academic sedentary time as much as possible

[16] [17] [18] [19]

Management of the Adolescent with Obesity: 15-18 Years

- **Orlistat (Xenical) ≥ age 12, Phentermine approved for ≥ age 16**
- **Minimize obesogenic medications especially SGAPs**
- **Treat asthma with controller meds to minimize systemic steroid use**
- **Consider ACE inhibitor for persistent hypertension**
- **Metformin FDA-approved for T2DM ≥ age 10 and PCOS**



- 3 meals; nutritious snacks
- 3 servings of protein/day
- 3 servings of dairy/day
- 1.5-2 servings of fruit/day
- 4-5 servings of non-starchy vegetables
- Dessert only on special occasion
- No sugar-sweetened beverages
- No fast food
- Age-appropriate portion sizes
- Allow adolescent to leave food on plate

- Screen time less than 1 hour/day
- 10-12 hours of sleep
- Routine sleep pattern
- No TV in bedroom
- Parents should not be over-controlling
- Friends and relationships are important
- Recommend meal and exercise tracking or monitoring

- Vigorous activity for 60-90 minutes or more daily
- Planned intervention with structured physical activity
- Decrease non-academic sedentary time as much as possible

[16] [17] [18] [19]

QUESTIONS?

"I tried some of those diet pills, but unfortunately my results were typical."

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