

New Strategies in Weight Loss

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Overview

- Treatments of Obesity
 - Behavioral Treatment
 - Dietary Treatment
 - Pharmacological Treatment
 - Surgery and Devices

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Rationale for treating obesity

- Many OSA patients are obese
- Reductions in weight are associated with improvements in SDB
- Reductions in weight improve many comorbidities that obesity and OSA share

Barriers

- Fatigue
- “One more thing to do”
- Multiple behavior changes

Guide for selecting obesity treatment

Treatment	BMI Category (kg/m ²)				
	25-26.9	27-29.9	30-34.9	35-39.9	≥40
Diet, Exercise, Behavior Tx	+	+	+	+	+
Pharmacotherapy		With co-morbidities	+	+	+
Surgery				With co-morbidities	+

Jensen MD, et al. Circulation 2013

Obesity guidelines for programs that work

	2012 USPSTF ¹ recommendations	2013 AHA/ACC/TOS ² guidelines
Intensive (12-26 sessions/yr ¹ , ≥ 14 sessions/6 months ²)	◆	◆
Multicomponent/Comprehensive	◆	◆
Behavioral counseling/management activities (setting weight-loss goals)	◆	◆
Improving diet or nutrition	◆	◆
Increasing physical activity	◆	◆
Self-monitoring	◆	◆
Strategies for maintain lifestyle changes	◆	◆
Individual or group sessions led by trained interventionist	◆	◆
Commercial program (provided peer-reviewed published evidence of safety and efficacy)	◆	◆

¹Moyer VA. Ann Intern Med.;2012

²Jensen MD et al. Circulation. 2013

Behavioral Treatment

Lifestyle Modification for Obesity

Key Components of a Comprehensive Lifestyle Modification Program to Achieve and Maintain a 7% to 10% Weight Loss at 1 Year or More

Components	Weight Loss	Weight Loss Maintenance
Frequency and duration of treatment contact	Weekly contact, in person or by telephone, for 20–26 wk. (Internet/e-mail contact yields smaller weight loss.)	Every-other-week contact for 52 wk (or longer). (Monthly contact may be adequate.)
Dietary prescription	Group or individual contact. Low-calorie diet (1200–1500 kcal for individuals <250 lb, 1500–1800 kcal for those ≥250 lb). Typical macronutrient composition: ≤30% fat (≤7% saturated fat), 15%–25% protein; remainder from carbohydrate. (Diet composition may vary based on individual needs or preferences.)	Group or individual contact. Consumption of a hypocaloric diet to maintain reduced body weight. Typical macronutrient composition: similar to that for weight loss.
Physical activity prescription	180 min/wk of moderately vigorous aerobic activity (eg, brisk walking); strength training also desirable.	200 to 300 min/wk of moderately vigorous aerobic activity (eg, brisk walking); strength training also desirable.
Behavior therapy prescription	Daily monitoring of food intake and physical activity by use of paper or electronic diaries. Weekly monitoring of weight. Structured curriculum of behavior change (eg, Diabetes Prevention Program). Regular feedback from an interventionist.	Occasional to daily monitoring of food intake and physical activity by use of similar diaries. Twice weekly to daily monitoring of weight. Curriculum of behavior change, including relapse prevention and individualized problem solving. Periodic feedback from an interventionist.

Wadden TA et al. Circulation 2012

Behavioral Management of Obesity

- **Consists of a set of principles and techniques to modify eating and activity habits**
- Management is designed to increase skills not psychological insights
- Management recognizes non-behavioral causes of obesity

Antecedent → Behavior → Consequence



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A Sample Behavior Chain



Brownell KD. *The LEARN Program for Weight Control*. 7th ed. American Health Publishing Co.

Self-monitoring in weight loss: a systematic review

Dietary Intake

15 studies found a significant association between dietary self-monitoring and weight loss

- Participants with the most complete food records lost significantly more weight than those who had less complete records

Physical Activity

5 studies discussed the use of records for tracking exercise behaviors

- Consistent self monitors of exercise achieved significantly greater weight loss and experienced fewer difficulties with exercise, and exercised more often

Weight

Weight self-monitoring increases participants' awareness of weight and related energy intake & expenditure

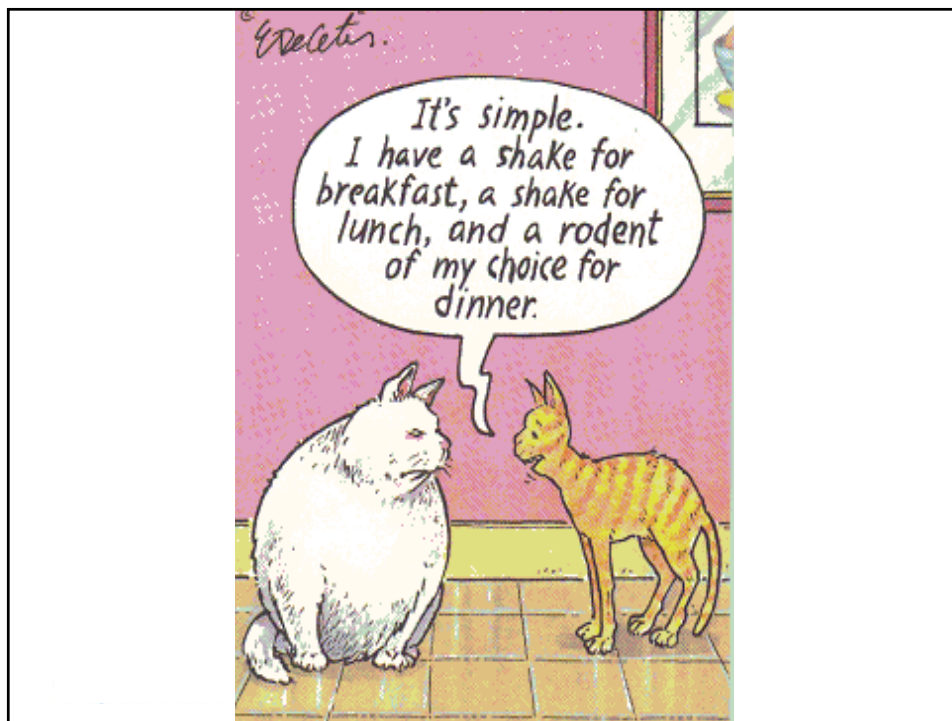
- More frequent weighing is associated with greater weight loss

Burke LE et al. JADA 2011.

Portion-controlled meals

- Provide fixed-portion and calorie amounts
- Reduce choices and contact with problem foods
- Are convenient to use
- Satisfy appetite (monotony and sensory specific satiety)
- Facilitate dietary adherence

Rolls B. IJO 2014.



Weight loss and dietary composition

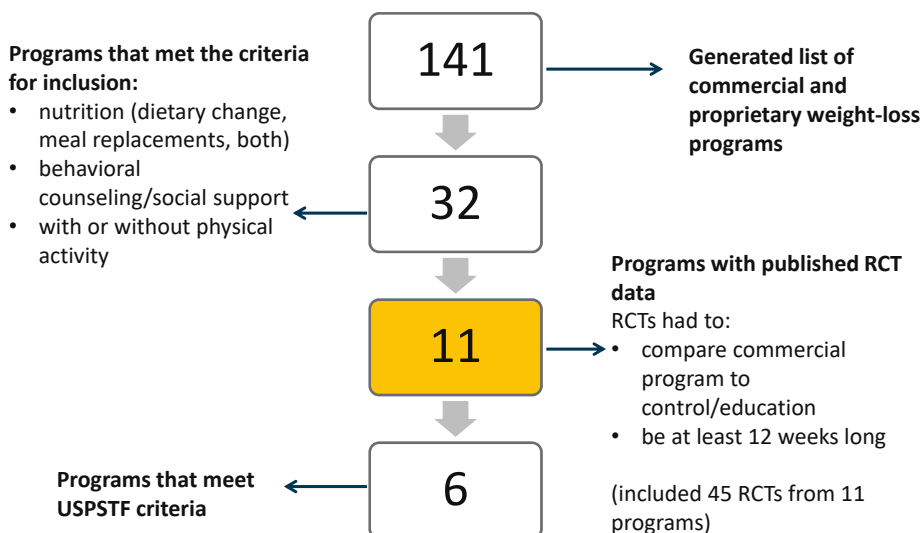
- People with obesity can lose weight (on average 7-10%) on diets that vary widely in macronutrient composition.
- **Calorie restriction, rather than macronutrient composition, is the key determinant of weight loss**
 - All diets have comparable short- and long-term safety
 - Choice of diet can be guided by:
 - Patient preference, ease of adherence
 - Desired control of comorbidities
- Need to explore additional means of adapting intensive lifestyle interventions to reach a large number of people
 - Electronic delivery modalities
 - Community settings

Weight loss at 24 months	
Foster et al. Ann Intern Med 2010	
Low-fat	-7.4 kg
Low-carb	-6.3 kg
Sacks et al. NEJM 2008	
Low-fat, avg protein (high carb)	-2.9 kg
Low-fat, high protein	-3.1 kg
High-fat, avg protein	-3.1 kg
High-fat, high protein (low carb)	-3.5 kg
Shai et al. NEJM 2008	
Low-fat	-2.9 kg
Mediterranean	-4.4 kg
Low-carb	-4.7 kg

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Wadden TA et al. Circulation 2012

Efficacy of Commercial Weight-loss programs



Gudzune KA et al. Annals Intern Med. 2015

Components of included programs with eligible RCTs

Program	Intensity	Support	Monthly cost	USPSTF Criteria	RCTs
Weight Watchers	High	Group sessions Online coaching Online community forum	43	Yes	8
Jenny Craig	High	1-on-1 counseling	570	Yes	3
Nutrisystem	High	1-on-1 counseling Online community forum	280	Yes	3
HMR	High	Group sessions Telephone coaching Medical supervision	682	Yes	4
Medifast	High	1-on-1 counseling Online coaching	424	Yes	1
OPTIFAST	High	1-on-1 counseling Group support Medical supervision	665	Yes	4
Atkins	Self-directed	Online community forum	10 for book	No	8
The Biggest Loser Club	Self-directed	Online community forum	20	No	1
EDiets	Self-directed	Online nutrient support Online community forum	10	No	1
Lose It!	Self-directed	Online community forum	Free	No	1
SlimFast	Self-directed	Online nutrition support Coaching text messages	70	No	8

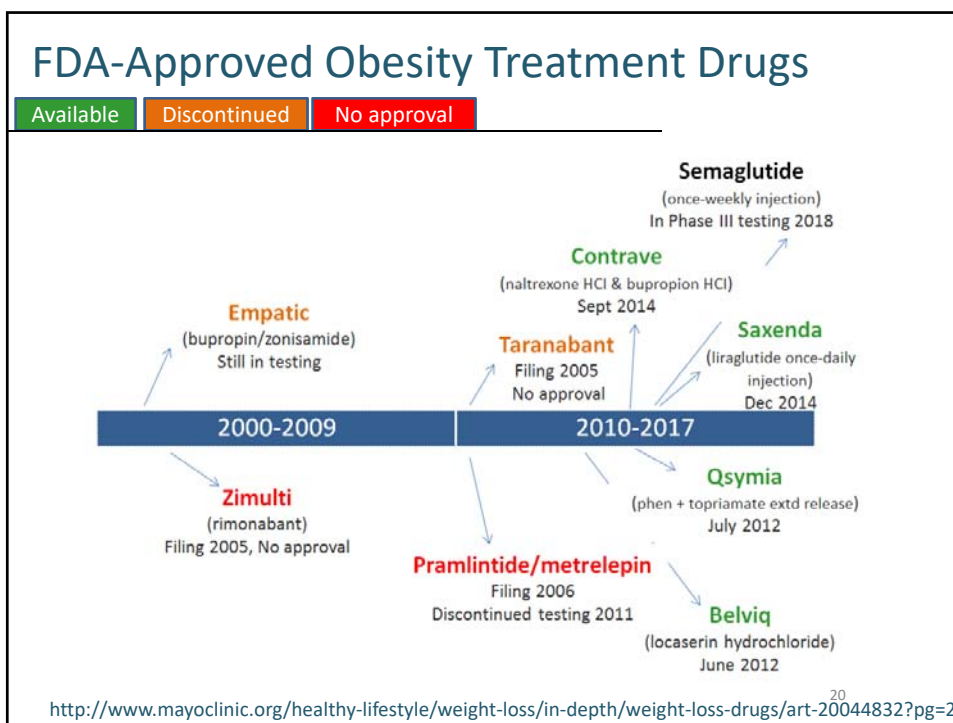
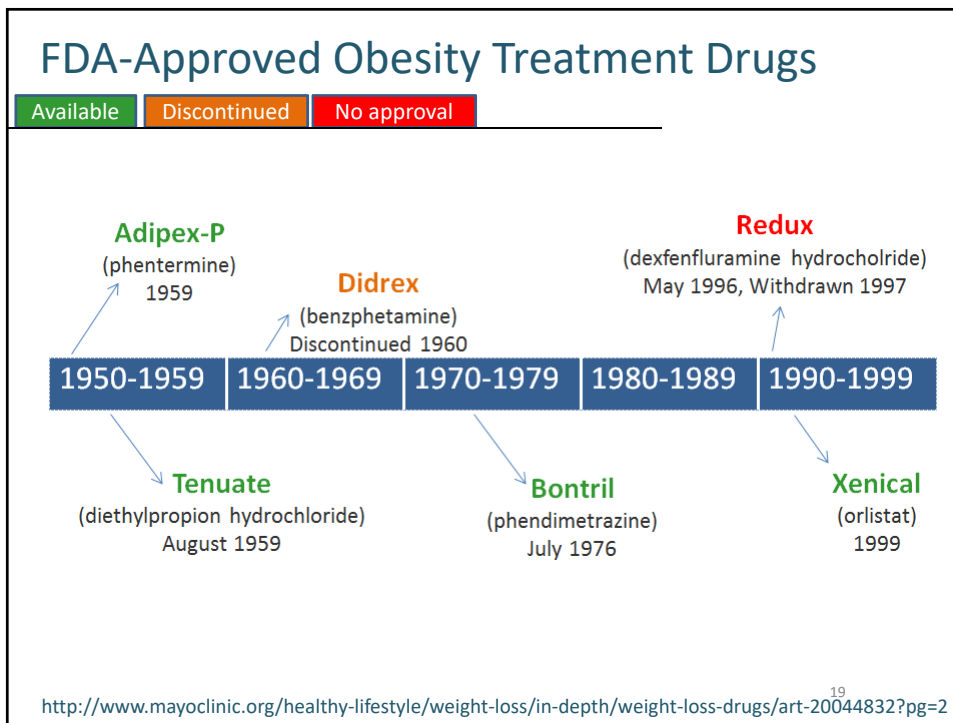
Gudzune KA et al. Annals Intern Med. 2015

Recommendation

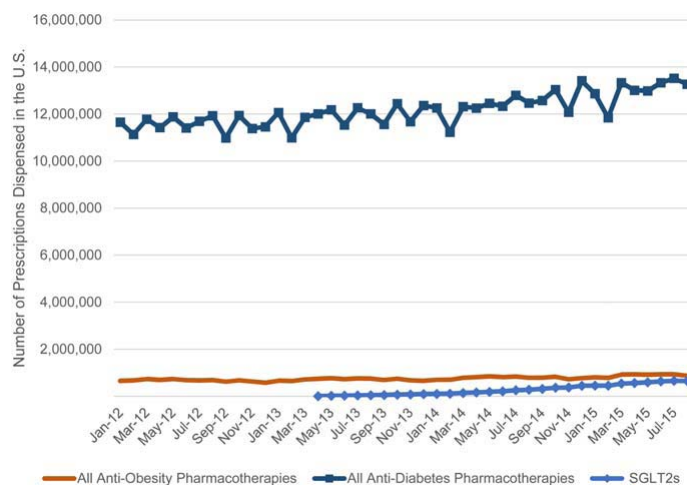
“Clinicians might consider prioritizing referral only for those commercial programs that have a substantial body of evidence showing a consistent, long-term effect.”

Gudzune KA et al. Annals Intern Med. 2015

Medications



Volumes of dispensed prescriptions



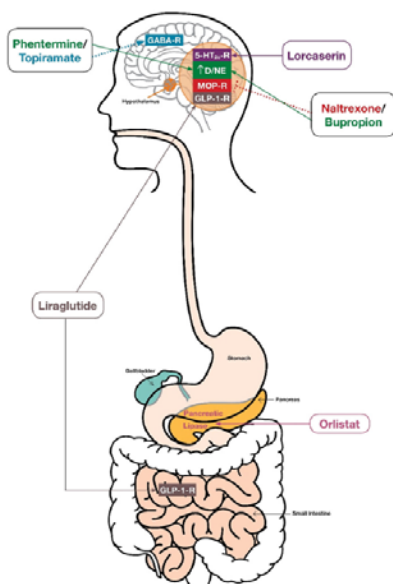
Thomas Obesity 2016

Drugs with FDA short-term approval

Generic Drug (Proprietary Name[s] Dose Frequency/d)	Mechanism Of Action	Wholesale Price/mo, \$	1-y Weight Change Relative to Placebo, Mean (95% CI), kg	Common Adverse Effects
Phentermine 15-37.5 mg (Adipex-P, Fastin, Oby-Cap, Ionamin, Others; 1x)	Noradrenergic causing appetite suppression	6-45	Not included	Insomnia, elevation in heart rate, dry mouth, taste alterations, dizziness, tremors, headache, diarrhea, constipation, vomiting, gastrointestinal distress, anxiety, and restlessness
Diethylpropion 25 mg or 75 mg, SR (Tenuate, Tenuate Dospan, Tepanil; low dose, 3x; SR dose, 1x)	Noradrenergic causing appetite suppression	47-120	Not included	Same as phentermine
Phendimetrazine 17.5-70 mg or 105 mg, SR (Bontril; lower doses, 2-3x; SR dose, 1x)	Noradrenergic causing appetite suppression	6-20	Not included	Same as phentermine
Benzphetamine 25-50 mg (Didrex; 1-3x)	Noradrenergic causing appetite suppression	20-50	Not included	Same as phentermine

Yanovski and Yanovski, JAMA, 2014

Drugs with FDA long-term approval



Patel Metabolism 2015

Drugs with FDA long-term approval

Table 1 – Summary of FDA-approved, long-term, anti-obesity pharmacotherapies available by prescription.

Generic name	Trade name	Year of approval	MOA	Dosage	Clinical trial(s)	Weight loss relative to baseline weight, drug vs. placebo	
						kg	%
Orlistat	Xerical®	1999	Gastrointestinal lipase inhibitor	120 mg TID	XENDOS	-5.8 vs. -3.0; 4 years	Not reported
Lorcaserin	Belviq®	2012	Serotonin 2C receptor agonist	10 mg BID	BLOOM BLOSSOM BLOOM-DM	-5.8 vs. -2.2; 1 year	-5.8 vs. -2.2; 1 year
						-7.2 vs. -2.9; 2 years	-7.0 vs. -3.0; 2 years
Phentermine/topiramate ER (extended release)	Qsymia®	2012	Sympathomimetic amine with anorectic effect/mechanism unknown	3.75 mg/23 mg (14 days) 7.5 mg/46 mg (thereafter)	CONQUER ^a EQUIP ^a SEQUEL ^a	-5.8 vs. -2.9; 1 year	-5.8 vs. -2.8; 1 year
						-4.7 vs. -1.6; 1 year	-4.5 vs. -1.5; 1 year
Naltrexone/bupropion	Contrave®	2014	Opioid receptor antagonist/aminoketone antidepressant	32 mg/360 mg (achieved after 4 weeks)	COR-I COR-II COR-BMOD COR-Diabetes	-10.2 vs. -1.4; 1 year	-9.8 vs. -1.2; 1 year
						Not reported	-10.9 vs. -1.6; 1 year
Liraglutide	Saxenda®	2014	GLP-1 receptor agonist	3 mg	SCALE Maintenance ^b SCALE Diabetes ^b SCALE Obesity and Prediabetes	-6.1 vs. -1.4; 1 year	-6.1 vs. -1.3; 1 year
						-6.2 vs. -1.3; 1 year	-6.4 vs. -1.2; 1 year
						Not reported	-9.3 vs. -5.1; 1 year

Weight loss related to baseline at 1 year ranges from 4.5%-10.9%

Greater weight loss relative to placebo at 1 year ranges from 0.2% -5.1%

Patel Metabolism 2015

Belviq (Lorcaserin):

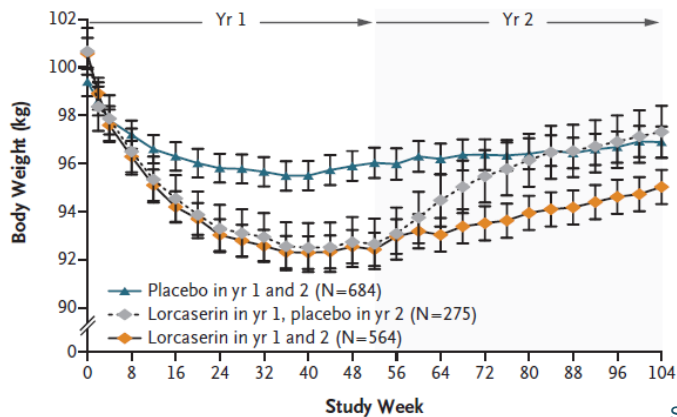
BLOOM study

2 year RCT with 3,182 adults

- mean age 43.5 y, 83.3% female, BMI 36.2 kg/m², 66.8% white, HbA1c 5.6%

Attrition at Year 2: 25.7% in Lorcaserin group, 27.3% in Placebo group

C Body Weight during Yr 1 and 2



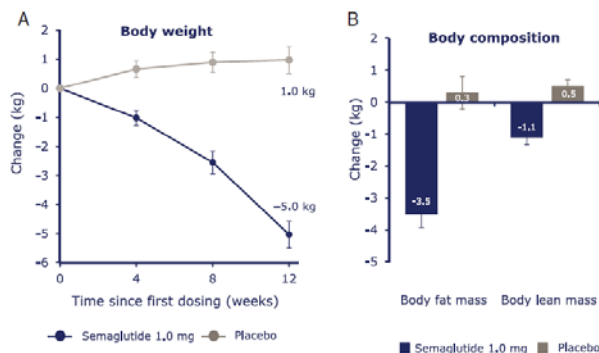
Semaglutide:

Once-weekly injection

12-week RCT with 30 adults randomized to once-weekly injections of semaglutide (GLP-1 antagonist) or placebo [two 12-week crossover treatment periods with randomization to placebo- semaglutide or semaglutide-placebo with 5-7 week wash out in between]

- Mean age 42 y, 33% female, BMI 33.8 kg/m²

Retention: 28 out of 30 completed the study



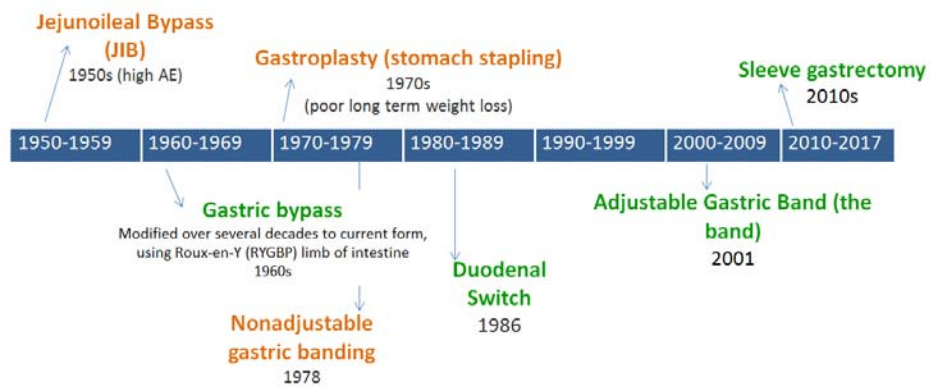
Blundell J et al. Diabetes, Obesity and Metabolism 2017

Surgery and Devices

Bariatric Surgery

Available

No longer recommended



<https://asmbs.org/resources/story-of-obesity-surgery>
<https://asmbs.org/patients/bariatric-surgery-procedures>

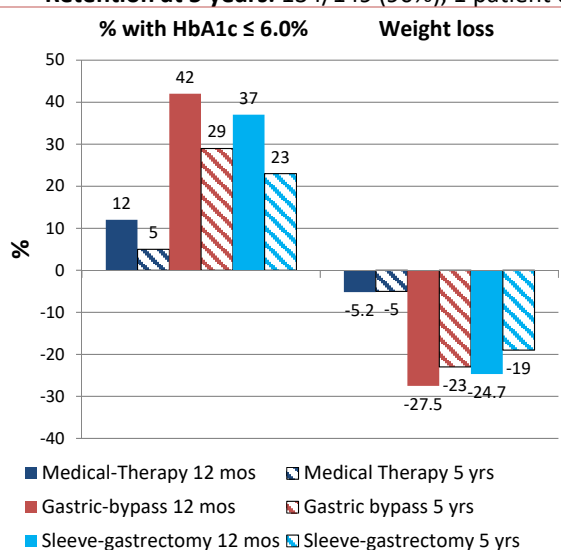
The STAMPEDE randomized clinical trial

- **Design:** randomized, nonblinded, single-center trial with a primary endpoint 12 months after treatment
- **Sample:** 150 patients, 66% female, 49 years, HbA1c 9.2%, BMI 27-43 (mean 36) kg/m², 73% white, all with type 2 diabetes
- **Randomization 1:1:1:**
 - Intensive medical therapy alone
 - Intensive medical therapy plus Roux-en-Y gastric bypass
 - Intensive medical therapy plus sleeve gastrectomy
- **Intensive medical therapy:** medical management as defined by the ADA, included lifestyle counseling, weight management (encouraged to participate in Weight Watchers), home glucose monitoring, and the use of newer drug therapies (incretin analogues), medications to control hypertension and hyperlipidemia, and visits with a diabetes specialist every 3 months for the first 12 months

Schauer PR et al. NEJM 2012 ²⁹

5-year follow-up results

Retention at 5 years: 134/149 (90%), 1 patient died during follow-up period



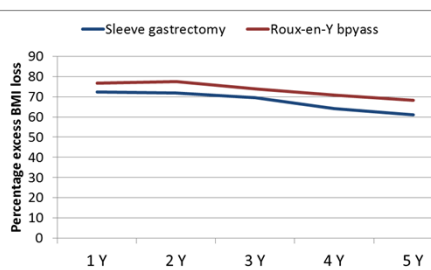
At 5 yr, significantly more patients in the surgical groups met the primary endpoint (HbA1c ≤ 6.0%) and achieved significantly greater weight loss compared to the medical therapy group

Conclusion: In patients with uncontrolled type 2 diabetes (HbA1c > 7.0%) and obesity, bariatric surgery plus intensive medical therapy was more effective than intensive medical therapy alone in decreasing, or in some cases resolving, hyperglycemia.

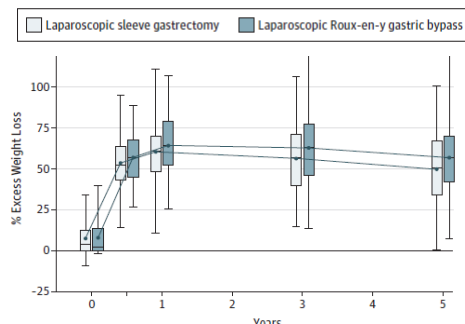
Schauer PR et al. NEJM 2017 ³⁰

RCTs: Bypass or Sleeve studies

SM-BOSS RCT with 217 Swiss adults
(72% female, 45.5 y, BMI 43.9 kg/m²)



SLEEVEPASS RCT with 240 Finnish adults
(69.9% female, 48 y, BMI 45.9 kg/m²)



In both studies, although sleeve gastrectomy produced slightly greater weight loss than Roux-en-Y bypass, the difference was not statistically significant

The two bariatric surgeries also had similar morbidity and reoperation rates

Peterli R. et al. JAMA 2018; Salminen et al. JAMA 2018 31

Conclusions

Data-based recommendations for physicians

Behavioral lifestyle modification: referral to commercial providers that meet expert panel guidelines and have a substantial body of evidence

Medications: no new medications in 2017, reasonable safety, modest efficacy (< 10%)

Surgery: most effective and intensive treatment