Managing Obesity 2020

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Disclosures

I have no conflicts of interest.

Learning objectives

1. How to think about obesity in 2020
2. Updates on lifestyle changes
3. Current thinking about drug treatment
4. Update on bariatric surgery

How to talk to patients about obesity

- Systematic review of patients' perspectives: 21 studies of clinical encounters about obesity
- Overwhelming theme: interactions between patients and doctors about being overweight and weight loss were rare
- The meaning of NOT discussing weight: patients who were overweight felt stigmatized, assumed that the doctor was judging them negatively

Clinical Obesity 2019; e12347

Initiating the discussion about weight

- Patients want clinicians to initiate the discussion
- Use patient-centered language:
  - Person-first rather than condition-first: “patient with an unhealthy weight” rather than “overweight patient”
- Patient-preferred terminology can be motivating: “unhealthy weight” rather than “obese”

Clinical Obesity 2019; e12347

Clinicians' advice: unhelpful vs helpful

- **Unhelpful:** Recurrent theme: assuming that a person who was overweight must have an unhealthy diet
  - "Frequently they jump to conclusions: 'eat less, move more'. But nobody really asked me what I was eating and what my daily activities had been."
- **Helpful:**
  - Acknowledging weight loss efforts, reacting positively
  - Discussion of available weight loss options

Clinical Obesity 2019; e12347

Clinician factors

- Patients wanted clinicians to sound like they cared for them as a person
- Discussions about weight loss, overweight were easier with a clinician they trusted
- The amount of time allocated to weight discussion related to participant satisfaction

Clinical Obesity 2019; e12347

Update on the 5 A's model for weight management counseling

- Initially developed for smoking cessation, now adapted to weight management

1. Assess: Assess and screen for weight status.
   - A variant of the 1st A is "Ask": Ask permission before discussing weight: Most patients feel empowered by this
   - Assess prior weight loss attempts, current strategies and barriers, personal goals and motivations

Med Clin N Am 2018; 102:125-133

Advise and Agree

2. Advise about the benefits of small behavioral changes and moderate weight losses
   - E.g. Just 2-3% weight loss begins to improve glycemic control
3. Work with patients collaboratively to agree on a set of goals for behavior change
   - Goals should be specific, measurable, attainable

Med Clin N Am 2018;102: 125-133

Assist and Arrange

4. Assist patients to make progress toward their goals and to identify barriers that are limiting their progress
5. Arrange regular interaction with patients
   - One of most consistent predictors of weight loss progress is having regular interaction with a health care provider or group

Med Clin N Am 2018; 102:125-133

What is an evidence based way to help your patient lose weight?

Tell your patient to enroll in Weight Watchers	A
Motivate your patient to enroll in Weight Watchers	B
Tell your patient to increase her exercise to 150 minutes a week	C
Tell your patient to eat less	D

Stepwise approach to treatment

1. Self-directed lifestyle change
2. Professionally directed lifestyle change
3. Pharmacotherapy
4. Bariatric surgery
5. Post-surgery: add drugs if needed

1st step:
Self-directed lifestyle change

- Take a history about lifestyle factors that affect weight:
  - Diet
  - Physical activity
  - Drugs: On any that increase weight?
  - Stress
  - Sleep
  - Circadian rhythms

Diet Assessment

- 24 hour diet recall
- Check re problems:
  - high fat and sugar
  - high processed food
  - low fruit and vegetable intake
  - frequent eating out, buffets
  - rapid meal consumption

What to say about diet

- Recommend calorie-restricted diet
  - 1200-1500 kcal/day for women
  - 1500-1800 kcal/day for men
  - Small portions
- Refer to nutritionist

Circulation 2014; 129:S102

Find a diet that the patient will adhere to

- All of these diets can produce weight loss if reduced caloric intake is achieved
  - Low calorie diet
  - Mediterranean
  - DASH
  - Low glycemic load
  - High or mod protein diet
  - Vegetarian diet

Physical activity

- Ask re:
  - sedentary work and behavior
  - doing moderate intensity exercise less than 150 minutes per week
  - physical limitations to exercise
- Recommend:
  - moderate intensity exercise at least 150 minutes per week
- Exercise helps with frame of mind, weight maintenance

60 yo man with DM, HTN, OA, depression wants to lose wt. Meds: metformin, paroxetine, oxycodone. BMI 34, BP 130/72, A1c 7.4. What med change could you make?

Consider changing paroxetine to sertraline	A
Start naltrexone/bupropion	B
Consider adding liraglutide	C
Consider starting phentermine	D

Check drugs: on any that cause weight gain?

CNS	Weight GAIN	Weight LOSS or Neutral
Atypical antipsychotics	Clozapine, olanzapine	Ziprasidone
Anti-epileptics	Gabapentin, Valproic acid, carbamazepine	Topiramate, zonisamide, phenytoin
Bipolar rx	Lithium	Ziprasidone
Antidepressants	Paroxetine, amitriptyline, mirtazapine	Bupropion, sertraline

Drugs: Endocrine

Endocrine	Weight GAIN	Weight LOSS or neutral
Glucocorticoids	Prednisone	Immunosuppressive agents
Hormonal contraceptives	Medroxyprogesterone	OCPs, IUD, vaginal ring
Diabetes drugs	Insulin, sulfonylureas	Metformin, GLP-1 analogs, SGLT-2 inhibitors

Drugs: Misc.

Miscellaneous	Weight GAIN	Weight LOSS or neutral
Beta-blockers	Propranolol, metoprolol	Carvedilol, other anti-HTs
Anti-histamines	Diphenhydramine, cetirizine	Loratadine, fexofenadine
Sleep aids	Zolpidem, trazodone	Sleep hygiene, melatonin

Stress and sleep

- Ask about:
  - personal or work stress correlating with weight gain
  - stress interfering with healthy lifestyle
- Ask about:
  - sleep less than 6 hours
  - disturbed sleep due to frequent awakenings

Circadian patterns

- Ask about:
  - skipping meals
  - eating significant amount of food after dinner
  - frequent grazing between meals
  - night shift work

Step 2: If < 5% weight loss after 6 months, recommend a professionally directed lifestyle program

- Components
  - On-site treatment by trained interventionist
  - Reduced calorie diet: deficit of ≥ 500 kcal/d
  - Increased physical activity: ≥ 150 min/wk
  - Behavior therapy: regular self-monitoring of food intake, physical activity and weight

Circulation 2014; 129:**S102,**
JAMA 2018;320(11):1172-1191
JAMA 2018:320(11):1163-1171

Program intensity matters

- **Low intensity**
  - Less than monthly sessions -> no sig. wt loss
- **Moderate intensity**
  - 1-2 sessions per month: avg. loss of 3 kg in 6 months
- **High intensity: most effective**
  - ≥ 14 sessions in 6 months -> avg. loss of 8 kg in 6 months
  - Example: Diabetes Prevention Program
  - Evidence: high

Circulation 2014;129:S102

Commercial programs can be helpful

- Choose one that offers intensive comprehensive lifestyle interventions
- Choose one with peer-reviewed published evidence of safety, efficacy
  - Weight Watchers: $43/month
  - Jenny Craig: $570/month

Circulation 2014; 129:S102, Ann Intern Med 2015;162:501-512

Consider electronically delivered weight loss programs

- By internet or phone
- Includes personalized feedback from trained interventionist
- Smaller weight loss than face-to-face interventions
- Examples: Weight Watchers, TOPS

Circulation 2014; 129:S102

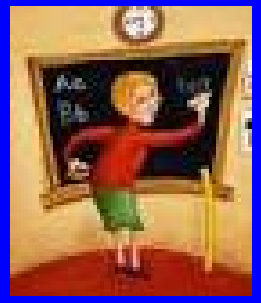
Very low calorie diet (VLCD) can help

- < 800 kcal/day
- Must be provided by trained practitioners in medical care setting where medical monitoring is provided

Circulation 2014; 129:S102

Step 3: Discuss pharmacotherapy

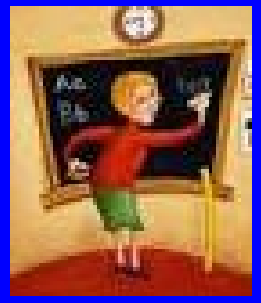
- If < 5% weight loss after 3-6 months of lifestyle management
- Appropriate candidates:
  - Patients with BMI ≥ 30
  - Patients with BMI ≥ 27 and 1 major co-morbidity like DM



How to use anti-obesity medications

1. Start after 3 months of weight stability
2. Choose a medication
3. Follow safe use protocol:
    - Baseline eval (relevant hx, pulse, BP)
    - Educate patient on med, side effects
4. Start med: use introductory dose, escalate as needed

J Clin Endocrinol Metab 2015; 100(2):342



How to use anti-obesity medications, continued

5. Evaluate for safety, effectiveness at 1 and 3 months
6. Goal: ≥ 5% weight loss after 3 months
7. If not successful, stop and consider switching meds
8. If successful: anticipate long-term use
9. CONTRAINDICATED in pregnancy

J Clin Endocrinol Metab 2015; 100(2):342

58 yo woman with BMI 33, BP 125/75, P 60. Tried Weight Watchers for 6 months, only lost 3 lbs. Always feels hungry. What medication might be best first choice?

Naltrexone/bupropion	**A**
Orlistat	**B**
Lorcaserin	**C**
Phentermine	**D**
Liraglutide	**E**

Approved Meds for Obesity

Name	Weight Loss	Mechanism	Side Effects	Dose	Cost (Good Rx)
Orlistat (Alli, Xenical)	3%	Lipase Inhibitor	Steatorrhea	60-120 mg TID	$590/month
Lorcaserin (Belviq)	3.5%	5-HT_{2c} receptor agonist	Headache	10 mg BID	$272/month
Naltrexone/ Buproprion (Contrave)	4%	CNS	Nausea Constipation Headache	8/90 mg: Titrate to 2 tabs BID	$235/month
Phentermine (approved for 3 month use)	5%	Adrenergic	↑P, ↑BP	15-37.5 mg QAM	$10/month
Phentermine/TopiramateER (Qsymia)	7-9%	Adrenergic/ CNS	↑P, ↑BP, Cognitive Teratogenic	Titrate to 7.5/46 mg QAM	$187-207/month
Liraglutide (Saxenda)	8-9%	GLP-1 agonist	Nausea, Diarrhea	3 mg *SC* QD	$1200/month

Picking a drug

- Consider
  - Patient co-morbidities
  - Patient preferences
  - Adverse effects
  - Insurance coverage
  - Cost

Orlistat (Xenical)

- Long-term safety record: 4 year data
- Mechanism: intestinal lipase inhibitor
  - increase in fecal fat excretion
- Dose: 120 mg po tid with meals

Orlistat: side effects and contraindications

- Side effects:
  - GI: 20% incidence of gas, fecal incontinence, subsides if decrease fat in diet. Suggest initial referral to nutritionist.
  - Calcium oxalate stones
- Contraindications:
  - Malabsorption syndromes
- Give multivitamin at bedtime

Lorcaserin (Belviq)

- Recent RCTs: decrease in risk of DM[1], no increase in CV events[2]
- Mechanism: Selective agonist of serotonin 2C receptor: reduces appetite
- Dose: 10 mg bid
- Use: safe in patients with CV disease or risk factors for CV disease

1. Lancet 2018;392:2269-79 2. N Engl J Med 2018;379:1107-17

Lorcaserin: side effects and contraindications

- Side effects:
  - Mild (common): headache, dizziness, nausea
  - Severe (rare): serotonin syndrome
- Contraindications:
  - Don’t use with SSRIs/SNRIs
  - Valvulopathy

Naltrexone/Bupropion (Contrave)

- CV safety not established: RCT terminated early. Not considered 1st line therapy
- Mechanism
  - Naltrexone: opioid antagonist, reduces food intake in animals
  - Bupropion: atypical antidepressant, causes modest weight loss in people
- Use: consider for obese smoker

JAMA 2016;315(10):990-1004

Naltrexone/Bupropion: dosing

- Comes as 12 hour tablet with 8 mg naltrexone/90 mg bupropion
- Week 1: 1 tablet q am

  Week 2: 1 tablet q AM and q eve

  Week 3: 2 tablets q AM and 1 q eve

  Week 4: 2 tablets q AM and q eve

Naltrexone/Bupropion: side effects and contraindications

- Side effects
  - Mild (common): nausea, constipation, headache, vomiting
  - Severe (rare): suicidal thoughts, seizures, HTN
- Contraindications
  - Seizure disorder, uncontrolled HTN, on opioids

Pharmacological Research 2014;84:1-11

Phentermine

- Most widely used weight loss drug
- Mechanism: sympathomimetic: can increase BP
- Dose: 15-37.5 mg po qd
- Use:
  - Only approved for 3 month use
  - Get informed consent if using longer

Br Med J 1968;1:352

Phentermine: side effects and contraindications

- Side effects:
  - Sympathomimetic: can increase pulse and BP, cause insomnia, dry mouth, constipation, nervousness
  - Schedule IV drug: low potential for abuse
- Contraindications: CAD, HTN, hyperthyroidism, h/o drug abuse

Endocrine Society Clinical Practice Guideline

- Reasonable to prescribe phentermine long-term as long as the patient has:
  - No evidence of serious CV disease
  - No significant increase in pulse or BP
  - No serious psychiatric disease or h/o substance abuse
  - Been informed that phentermine is not FDA approved for > 3 months use
  - Significant weight loss on drug

J Clin Endocrinol Metab 2015 (Feb); 100(2):342

Phentermine/Topiramate ER (Qsymia)

- Mechanism: sympathomimetic, enhances GABA
- Dose: start: 3.75/23 mg qd x 2 weeks,
  then standard dose: 7.5/46 mg qd x 12 weeks,
  then 11.25/69 mg qd x 2 weeks,
  then highest dose: 15/92 mg qd x 12 weeks
- Use: option for patients without HTN or CAD
- Safety of combining generic phentermine with generic topiramate not yet established

Phentermine/Topiramate ER: side effects and contraindications

- Side effects
  - Mild (common): dry mouth, constipation, paresthesias
  - Severe (rare): teratogenic: check HCG q month, tachycardia, cognitive impairment, acute angle-closure glaucoma
- Contraindications
  - HTN, CAD, glaucoma, hyperthyroidism

Liraglutide (Saxenda)

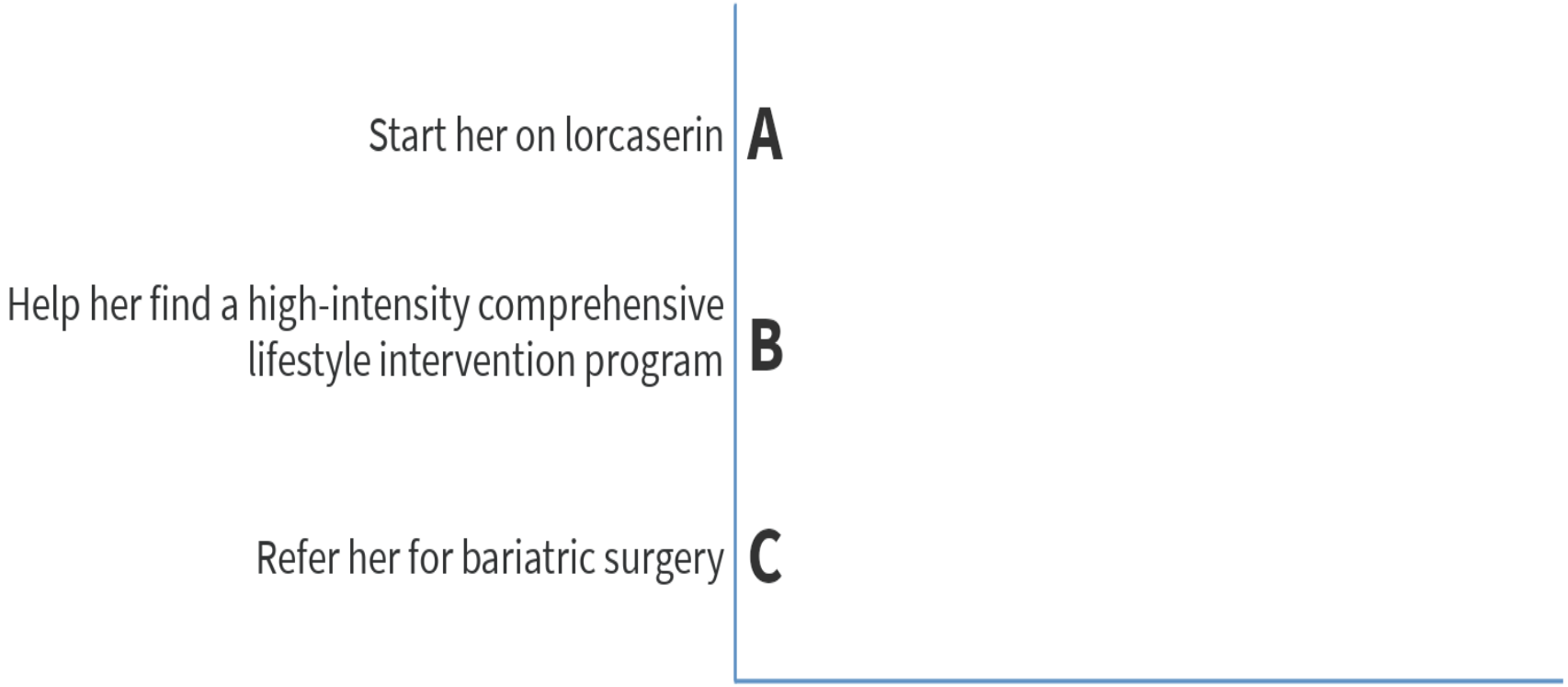
- Mechanism: Long-acting GLP-1 analog
  - stimulates glucose-dependent insulin secretion
- Developed for treatment of diabetes
- Reduces major CV events in adults with T2DM and preexisting CV disease
- Can use for weight loss in diabetics and non-diabetics
- Dose: titrate up to 3 mg sc injection qd

N Engl J Med 2016; 375:311

Liraglutide: side effects and contraindications

- Side effects
  - Mild (common): nausea, vomiting
  - Severe (rare): pancreatitis, thyroid C cell tumors
- Contraindications
  - Medullary thyroid carcinoma, multiple endocrine neoplasia

58 yo woman has gained weight since her 40's. BMI now 35, BP 145/88, A1c 6. In her 40's, she lost 10 lbs. when walked regularly with neighbor. Next best step?

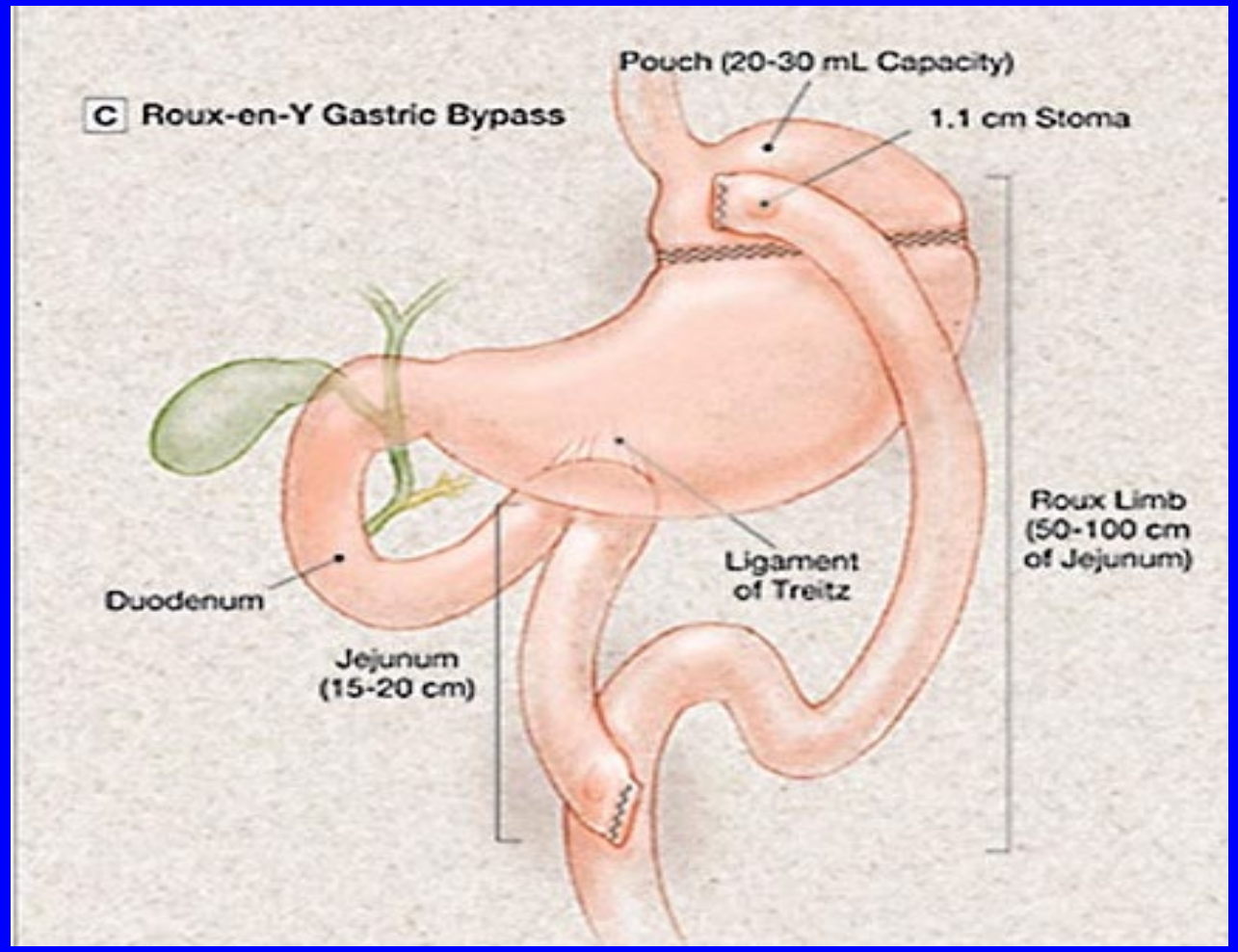


Step 4: Bariatric surgery

- Appropriate candidates:
  - Patients with BMI ≥ 40
  - Patients with BMI 35-39.9 with at least one serious comorbidity (e.g. DM)
  - Recent International Diabetes Organizations guideline: BMI 30-34.9 with inadequately controlled DM despite optimal medical treatment

JAMA 2017;317(6):635-636

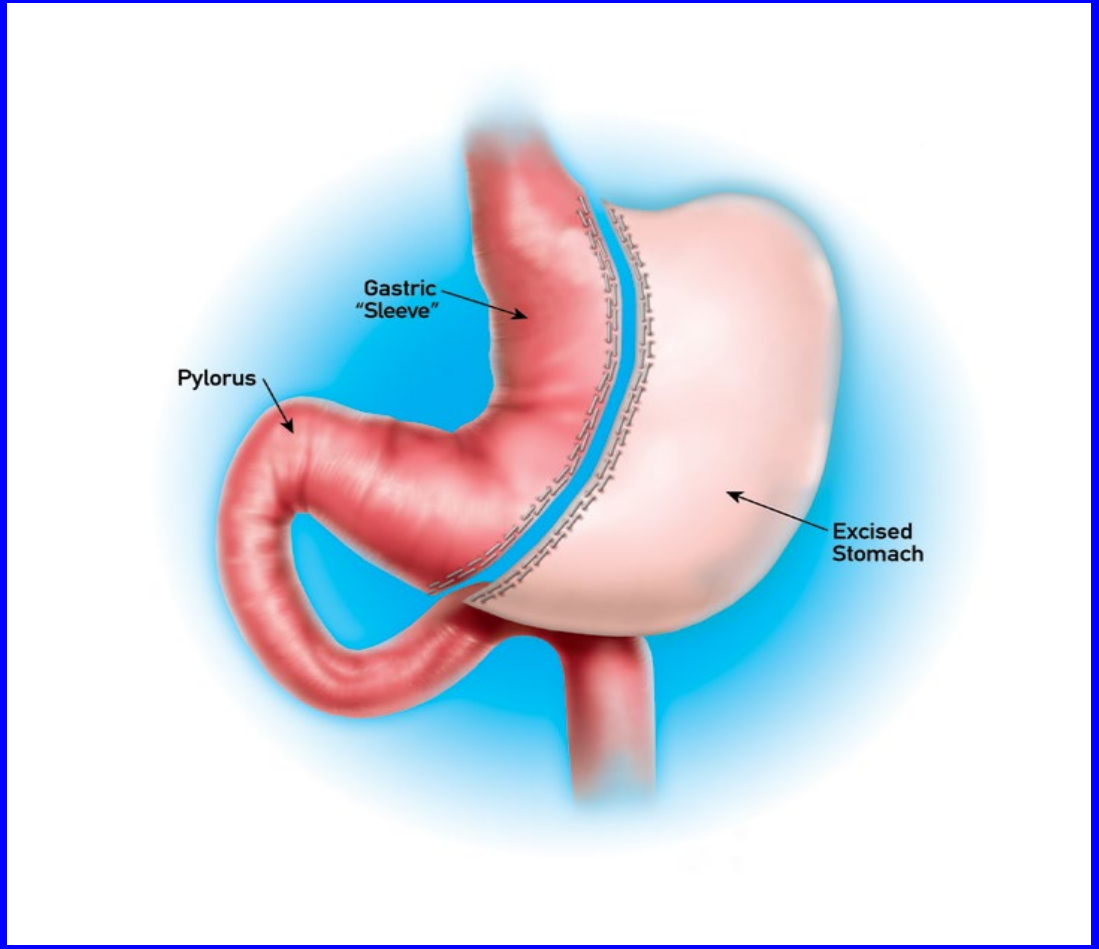
Roux-en-Y gastric bypass



Gastric bypass (GB) affects gut hormones

Hormone	Effect On Appetite	Level After GB
Ghrelin		
Peptide-YY		
GLP-1		

Sleeve Gastrectomy



Comparative effectiveness and safety of bariatric procedures

- **PCORnet Cohort Study**
  - Retrospective observational cohort study, 2005-2015
  - 65,093 patients from 41 health systems
  - 32,208 Roux-en-Y gastric bypass (RYGB), 29,693 sleeve gastrectomy (SG), 3192 adjustable gastric banding (AGB)

Ann Intern Med 2018;169:741-750

PCORnet study: comparative effectiveness of bariatric procedures

Procedure	1-year mean TWL	5-year mean TWL
RYGB	31.2%	25.5%
SG	25.2%	18.8%
AGB	13.7%	11.7%

TWL: total weight loss
RYGB: Roux-en-Y gastric bypass
SG: sleeve gastrectomy
AGB: adjustable gastric banding

Ann Intern Med 2018;169:741-750

PCORnet study: comparative safety of bariatric procedures

Procedure	30-day rate of major adverse events
RYGB	5.0%
SG	2.6%
AGB	2.9%

Ann Intern Med 2018;169:741-750

Systematic review: 2 yr f/u of bariatric surgery vs. non-surgical treatment

- Diabetes remission: RR of remission 5.3 (CI 1.8-15.8) after bariatric surgery
- Hypertension: decrease in antihypertensive drug use
- Hyperlipidemia: decrease in use of lipid lowering agents
- Quality of life: improved

BMJ 2013;347:15934

Microvascular and macrovascular outcomes in patients with diabetes after bariatric surgery

- Microvascular: matched cohort study
  - Lower incidence of neuropathy, nephropathy and retinopathy
- Macrovascular: observational study
  - Lower incidence of CAD: 1.6% vs 2.8%
- Recommendation: Discuss potential role of bariatric surgery in preventing microvascular and macrovascular events in patients with diabetes

JAMA 2018;320(15):1570-1582. Ann Intern Med 2018;169:300-310

Bariatric procedures: mortality

- Israeli retrospective cohort study of 8385 bariatric surgery patients and 25,155 matched nonsurgical patients

Procedure	All-cause mortality (median f/u 4.3 yrs)
RYGB	1.3%
SG	0.8%
AGB	1.7%
Usual care	2.3%

JAMA 2018;319(3):279-290

Newer procedures

- Intragastric balloon
- Vagal blockage
- Aspiration therapy
- None as successful or durable as RYGB and sleeve gastrectomy

Key points

- Patients respond positively to offers of support for weight loss
- Comprehensive lifestyle changes are essential
- Pharmacotherapy: try a drug; if not helpful, try another
- Bariatric surgery can be helpful

Next best steps

- Use the **5 A's** to assess and help increase your patient's motivation to lose weight
- Start with **comprehensive lifestyle changes**
- If your patient can't "do it on his own", refer to a **high intensity lifestyle management program**
- Feel comfortable adding **pharmacotherapy** and referring for **bariatric surgery** when appropriate
- Be kind and be confident that you can help