

Medications and Surgery for Treatment of Obesity



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NOT SO SIMPLE!

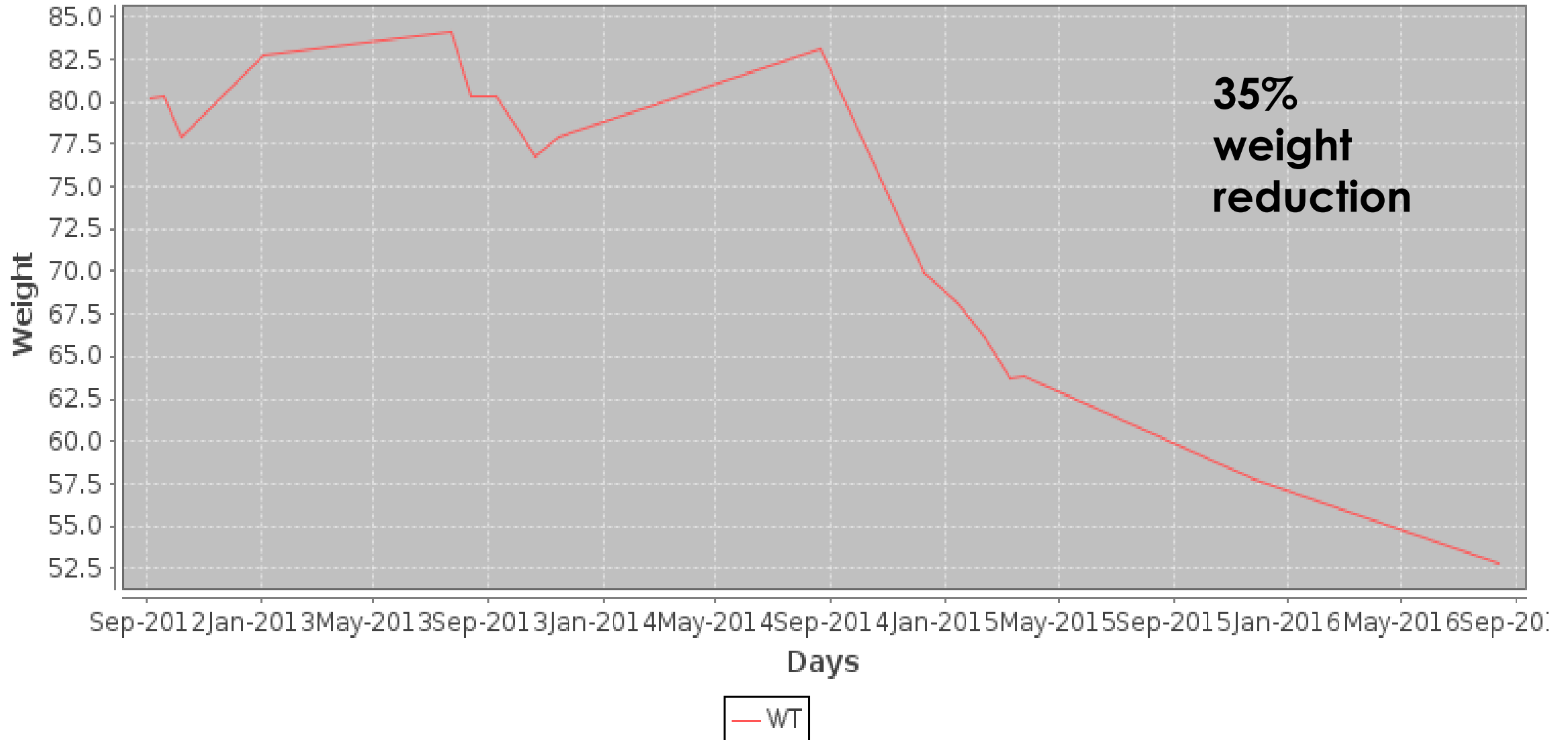




“Set Point”

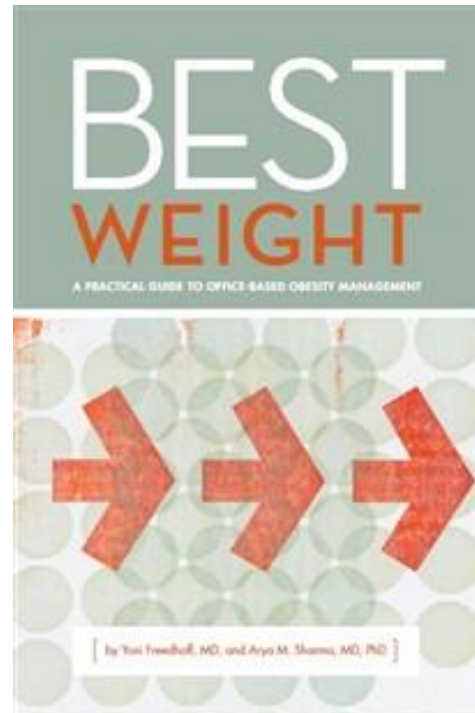


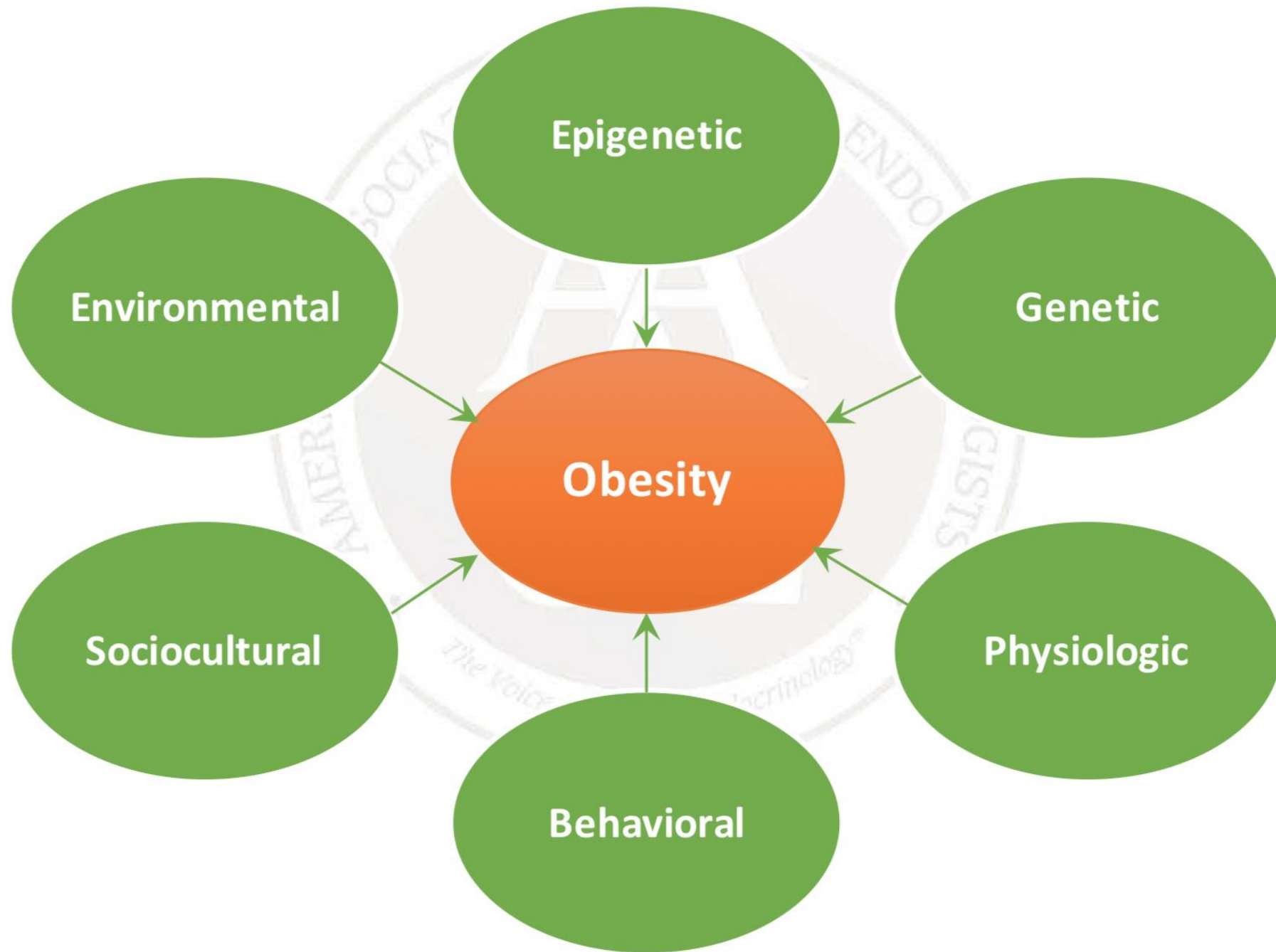
Real Life Weight Management



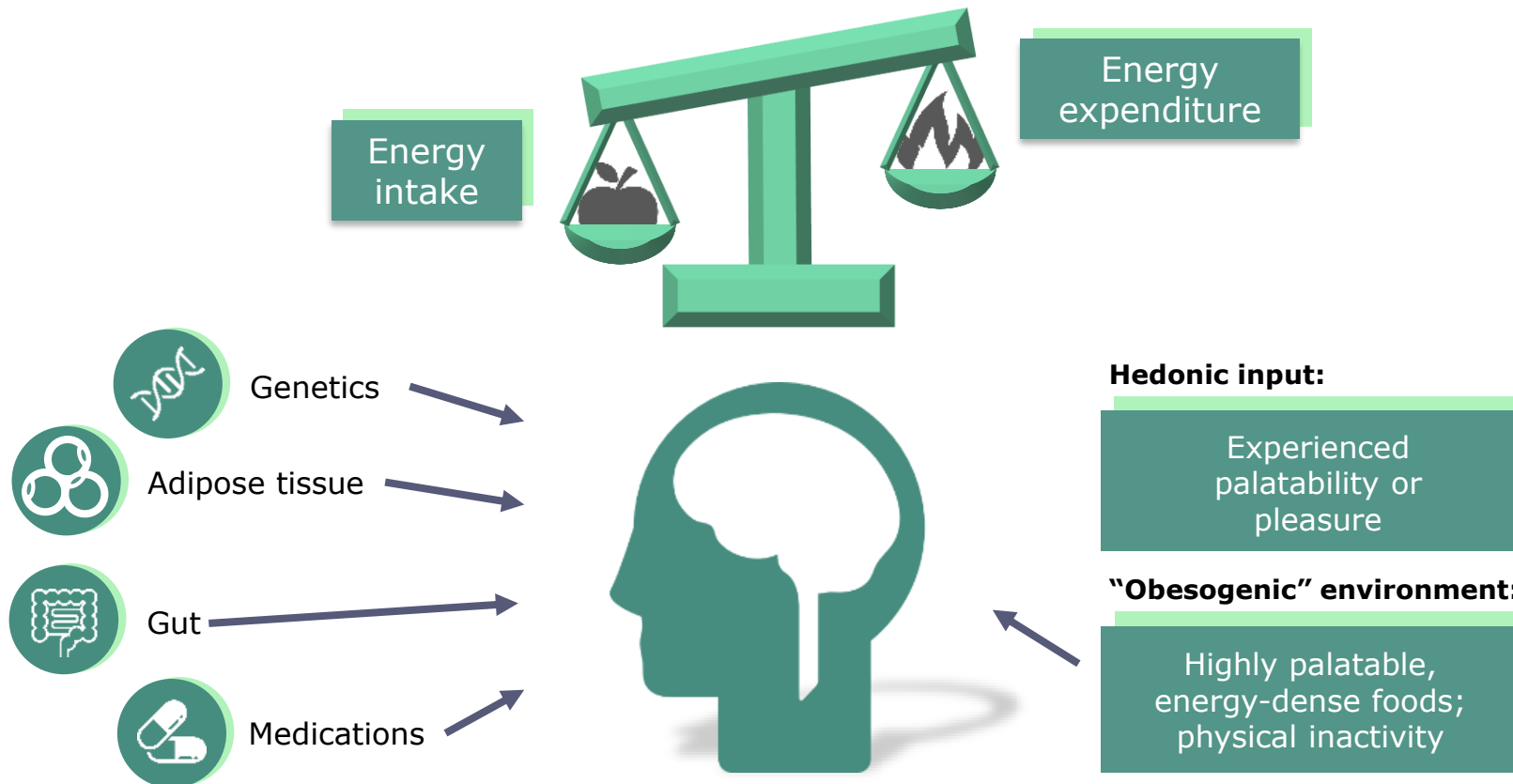
Your Best Weight?

The lowest weight you can achieve **and sustain** while living the healthiest lifestyle that you can truly enjoy.

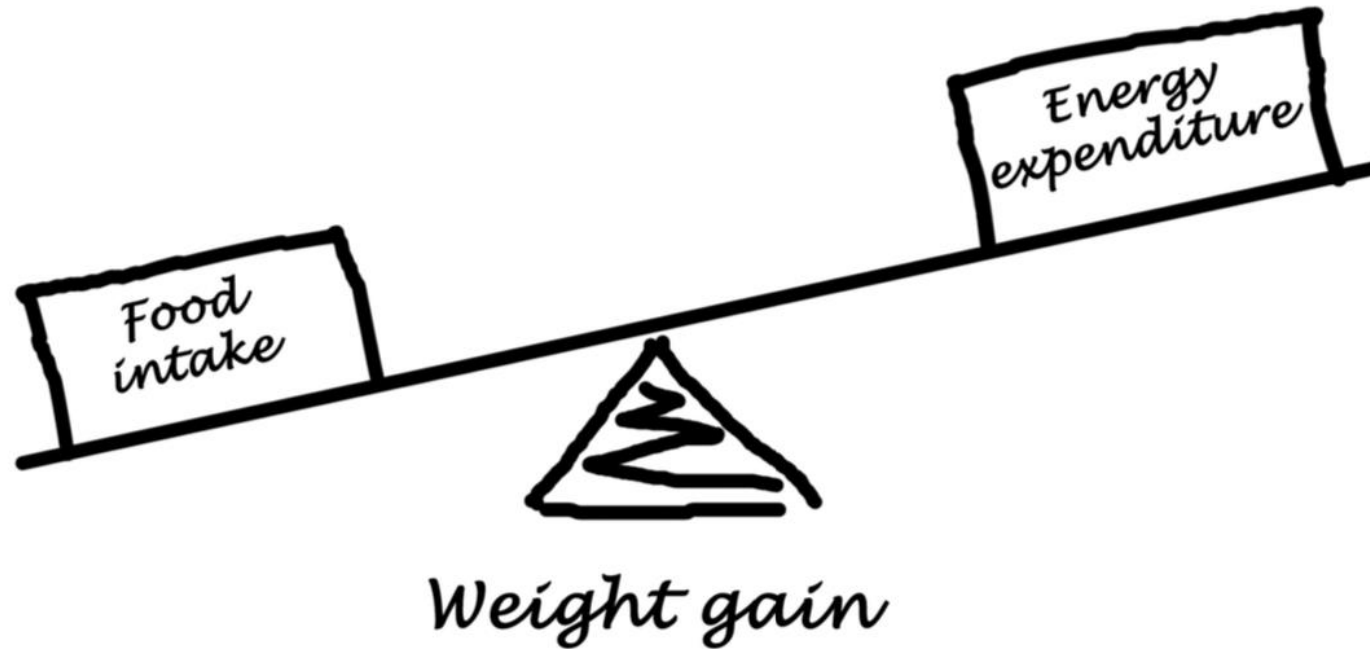




The pathophysiology of obesity is complex

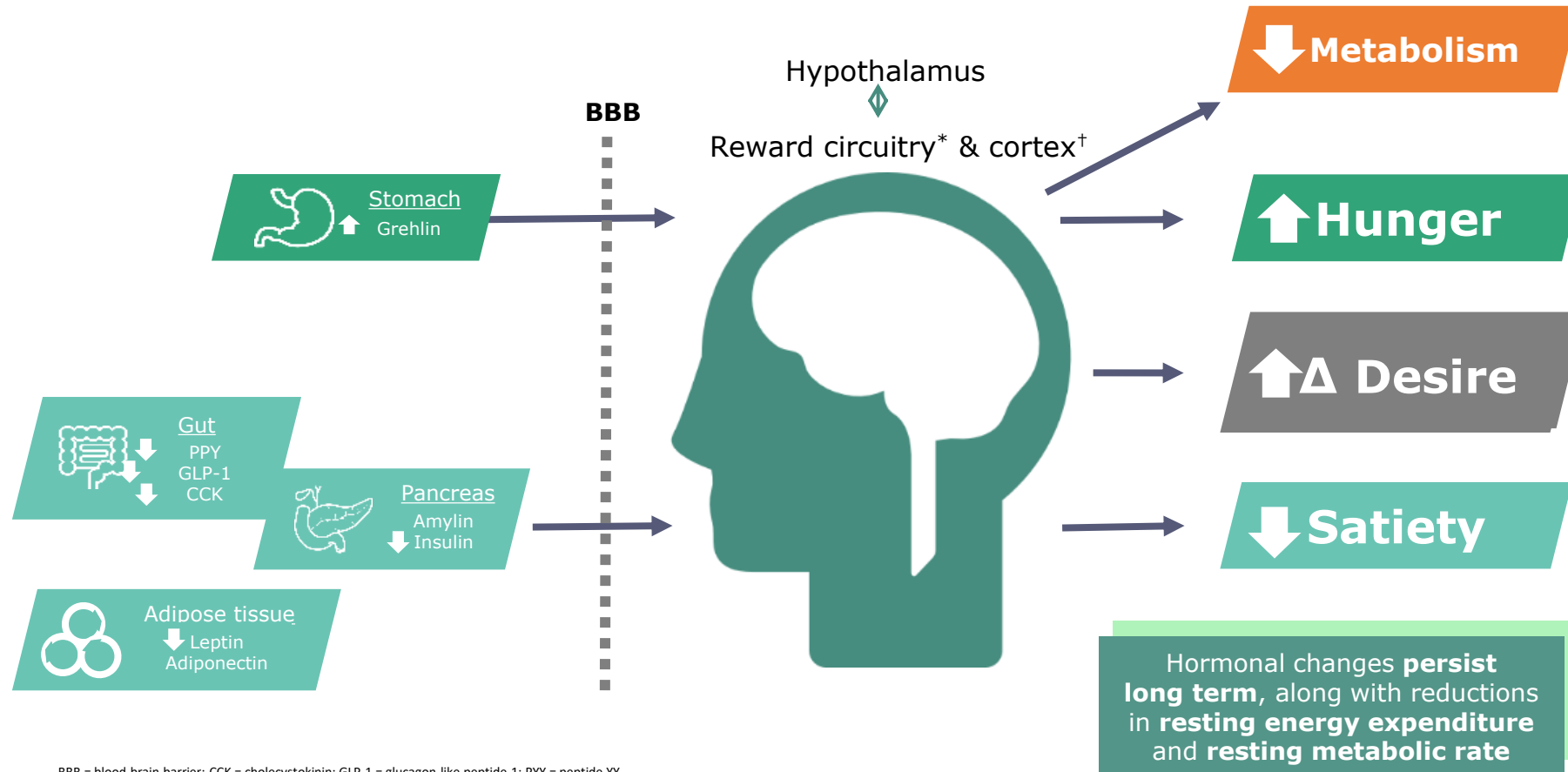


Body Adaptations to Weight Loss: “Obesity Protects Obesity”



- After weight loss, counter-regulatory hormones re-establish higher body weight.
- Reduction in energy expenditure caused by weight loss itself makes it hard to maintain weight loss.

The physiologic response to weight loss favours weight regain



BBB = blood-brain barrier; CCK = cholecystokinin; GLP-1 = glucagon-like peptide-1; PYY = peptide YY.
*the brain's reward circuitry, especially in the ventral tegmental area and nucleus accumbens. †especially the dorsolateral pre-frontal cortex.
Suzuki K et al. Exp Diabetes Res. 2012;2012:824305; Berthoud HR. Curr Opin Neurobiol. 2011;21(6):888-896. Schwartz A & Doucet E. Obes Rev. 2010;11:531-547.

Key Principles



Obesity is a Chronic Condition

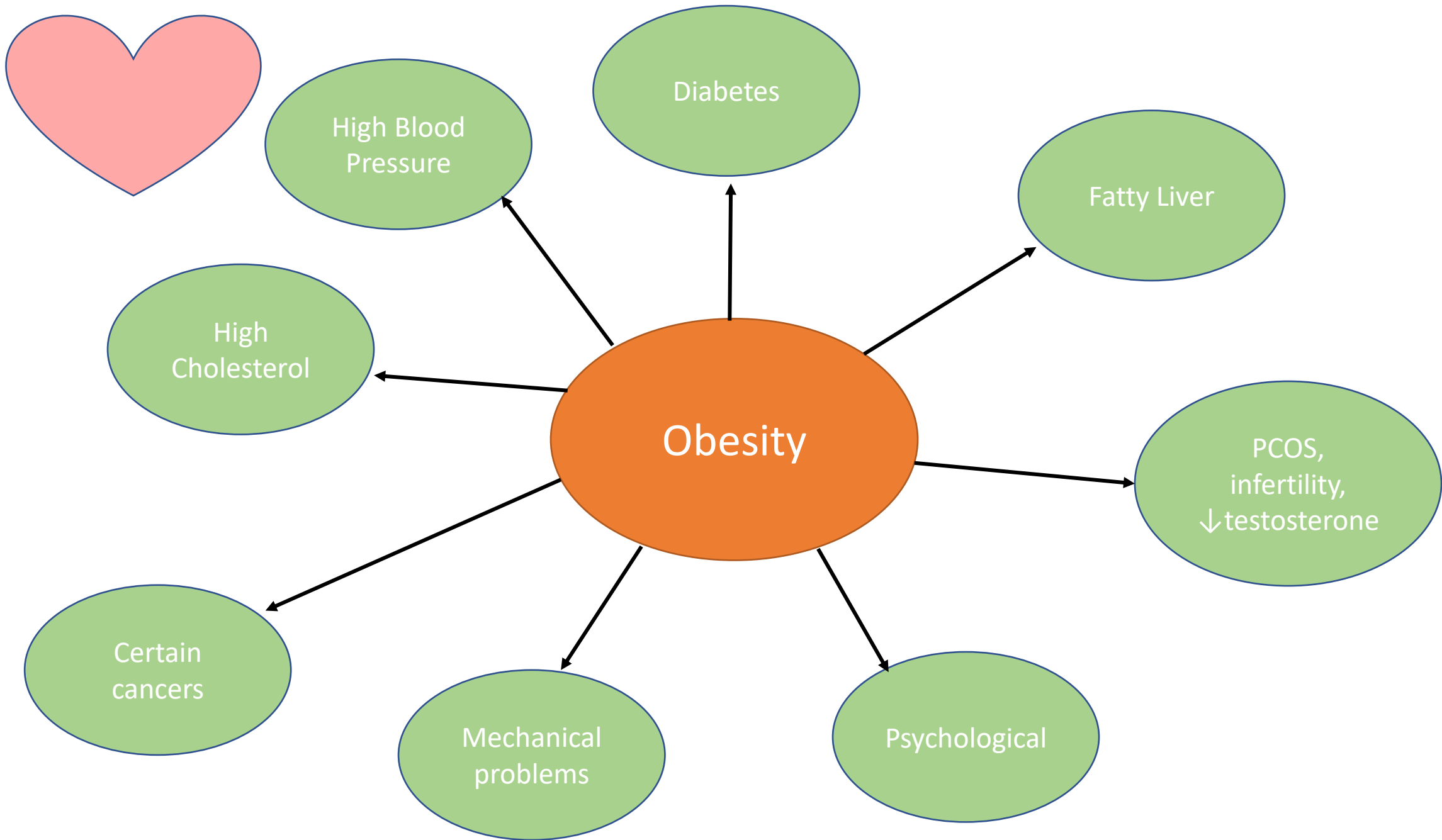
- Obesity is a chronic and often progressive condition not unlike diabetes or hypertension.
- Successful obesity management requires realistic and sustainable treatment strategies.
- Short-term “quick-fix” solutions focusing on maximizing weight loss are generally unsustainable and therefore associated with high rates of weight regain.

Key Principles

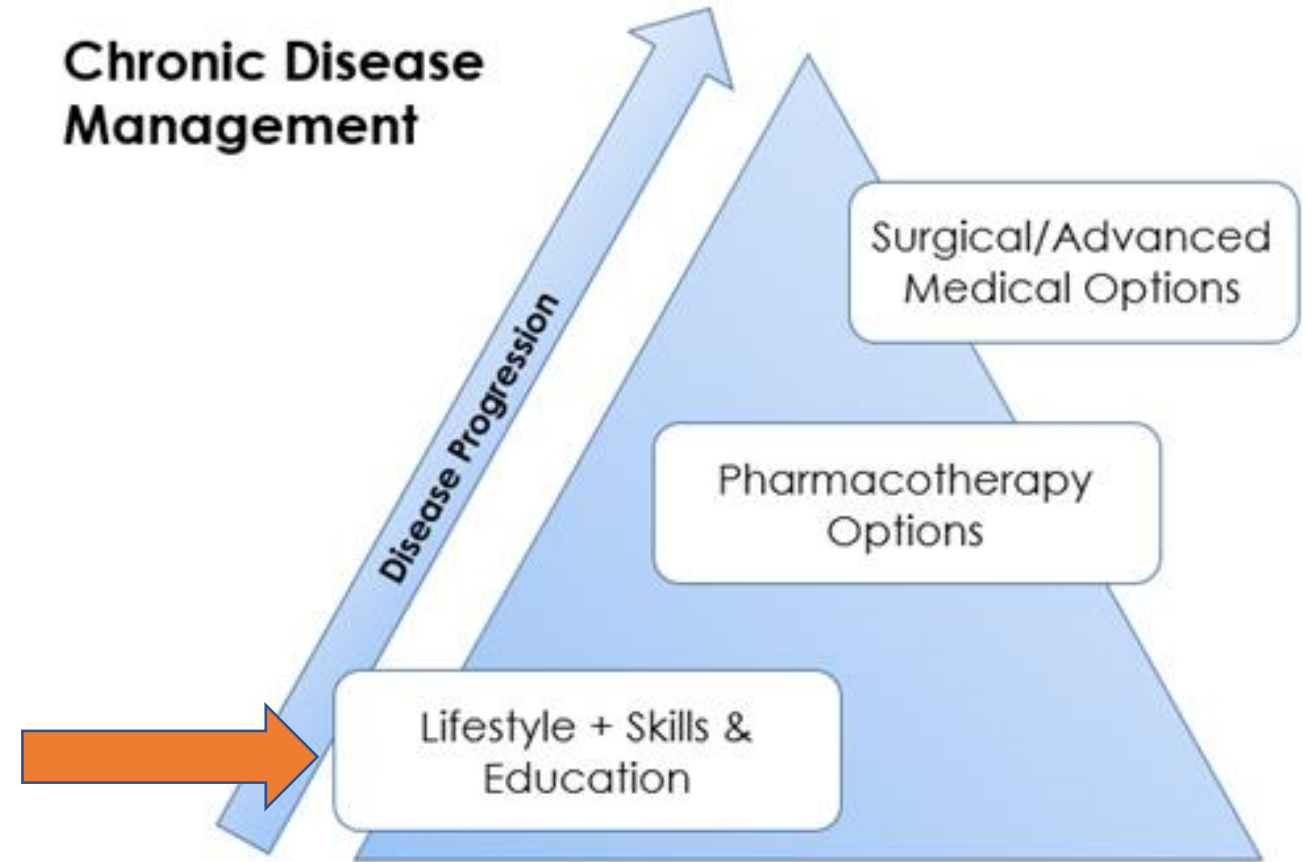


Obesity is a Chronic Condition

Obesity is a chronic, progressive and relapsing disorder requiring lifelong, and often comprehensive treatment.



Treatment is
Multifaceted

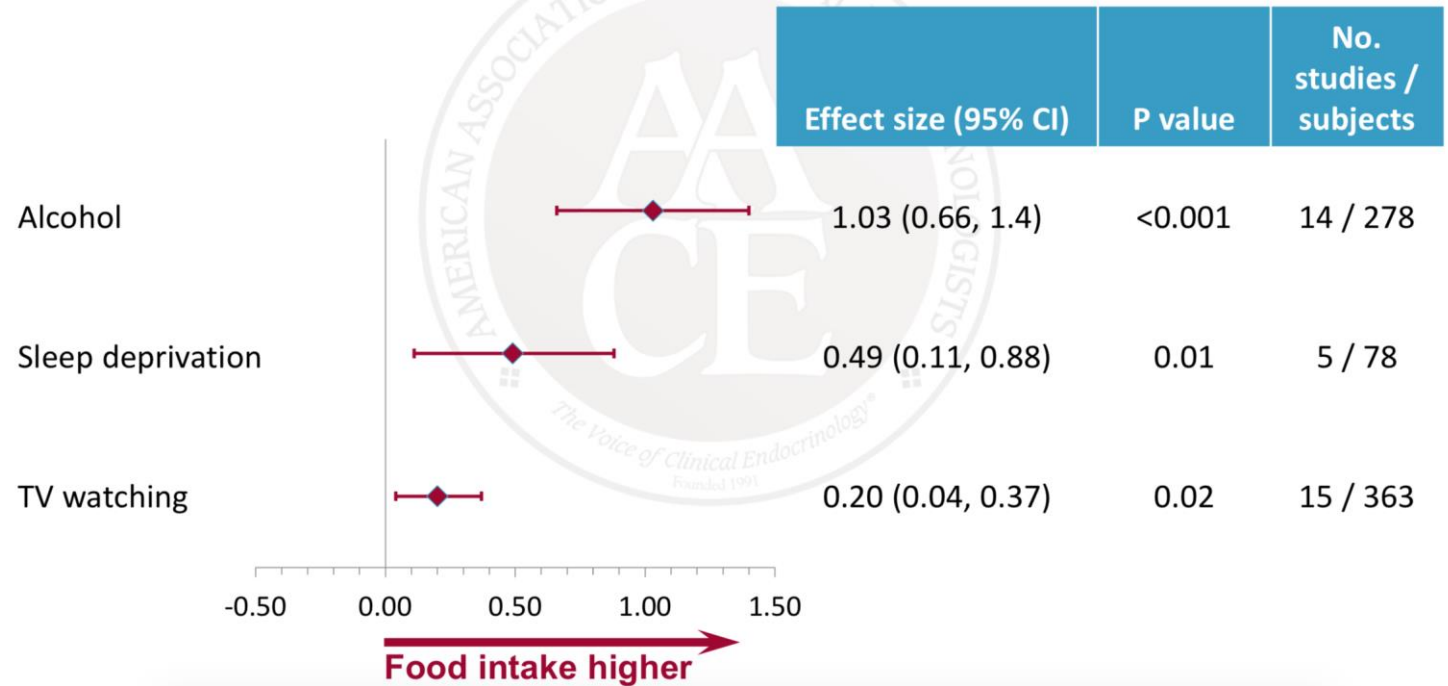


Lifestyle Change is Important

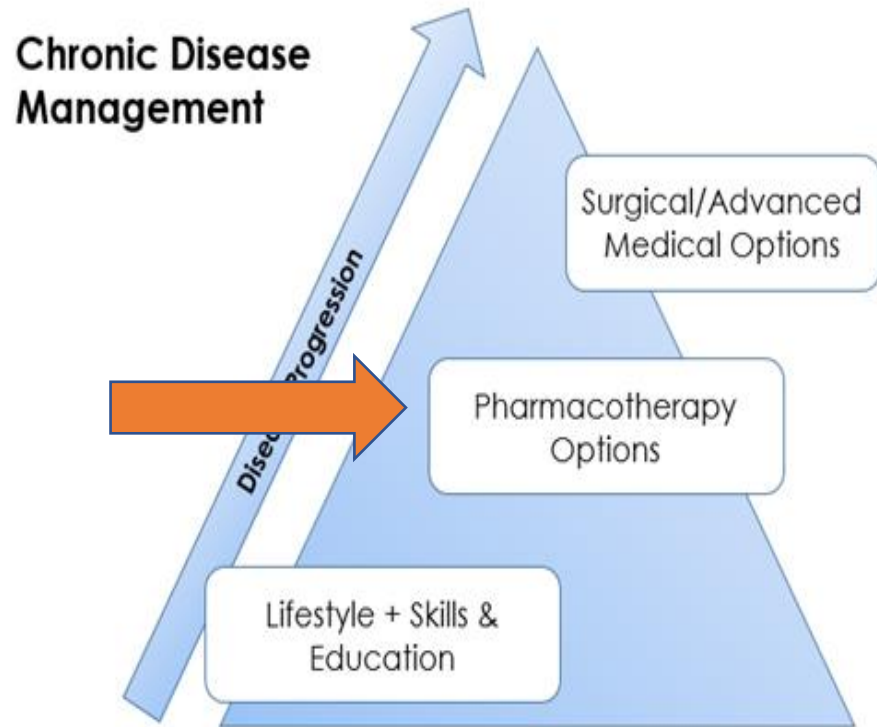
- **Improve metabolism**
 - Lower fasting glucose, prevent type 2 diabetes
 - Lower blood pressure
 - Improve cholesterol levels
- **Improve quality of life**
 - Less joint pain, better mobility
 - Improve reflux, sleep apnea
- **Increased life expectancy**
 - Lower incidence of certain cancers

Behavioural
Changes are
Key

Lifestyle Effects Meta-analysis



When to Add Medication



- Weight gain or regain on lifestyle therapy alone
- Insufficient improvement of complications on lifestyle therapy alone
- Severe/significant weight-related complications



ADVISE



ANTI-OBESITY MEDICATIONS,

in conjunction with behavioural interventions, can help patients achieve and sustain 5-10% weight loss. Discontinuation of medications generally results in weight regain.

Medications

- **Orlistat (Xenical)**
 - Lipase inhibitor
 - Three times a day before meals
 - WL: 4% at 1 year, 2.6% at 4 years
 - Contraindications:
 - malabsorption, pregnancy, oxalate kidney stones
 - Interacts with some meds
 - Common side effects:

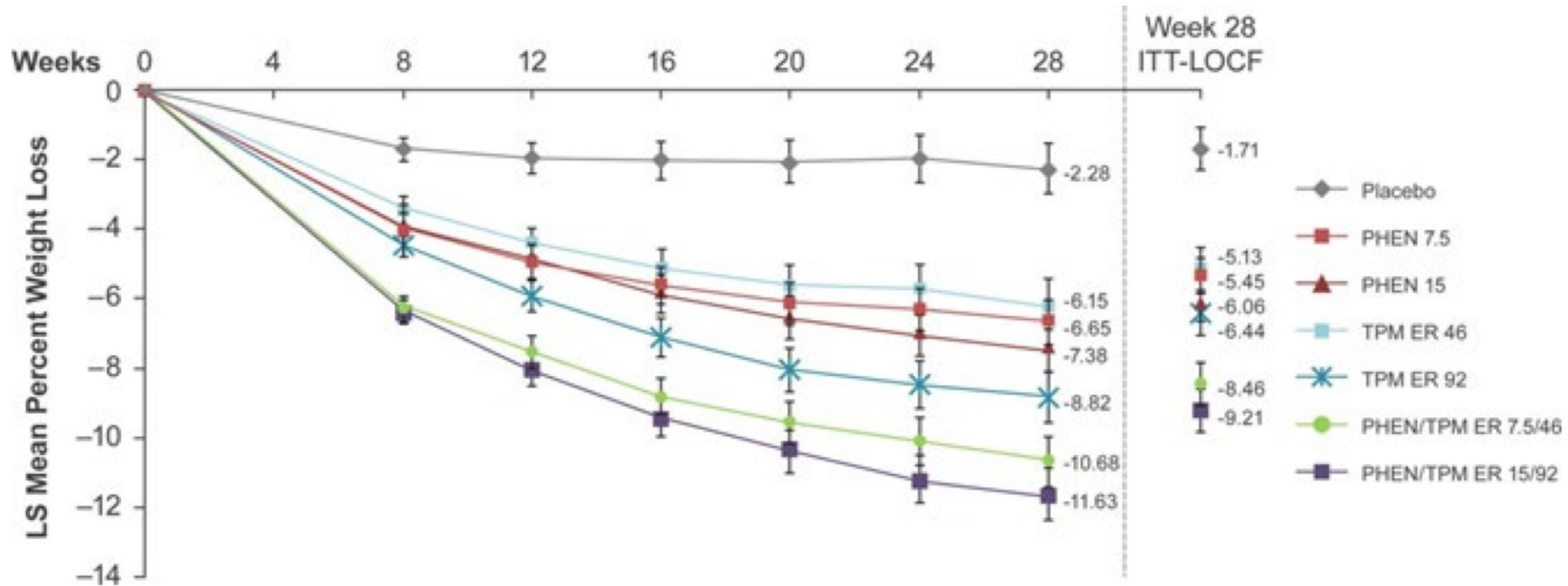


(Not available in Canada yet)



- **Phentermine/topiramate (Qsymia)**

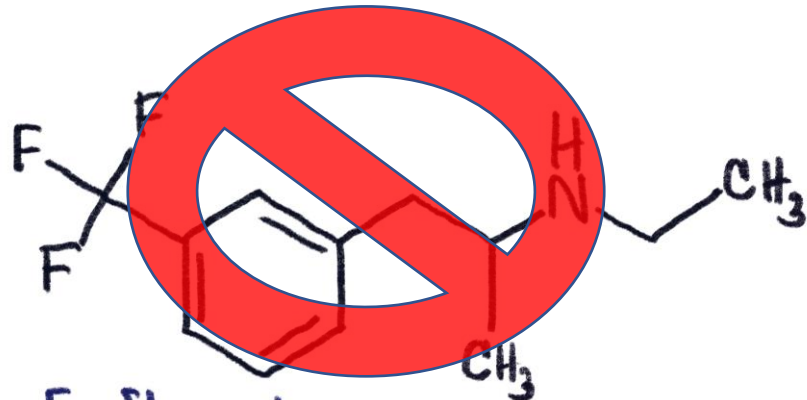
- Acts on neurotransmitters - norepinephrine and GABA
 - Decreased appetite and increased satiety throughout the day
- Once a day, dose increases gradually – stop after 12 weeks
- WL: 6.6-9.3% at 1 year; 7.5-8.7% at 2 years - dependent on dose
- Contraindications:
 - Pregnancy/breastfeeding, glaucoma, hyperthyroidism, cardiovascular disease, seizure disorder
- Common side effects:
 - Decreased sense of taste, dry mouth, dizziness, insomnia, numbness
 - Monitor for depression, anxiety, heart arrhythmias, electrolyte imbalances



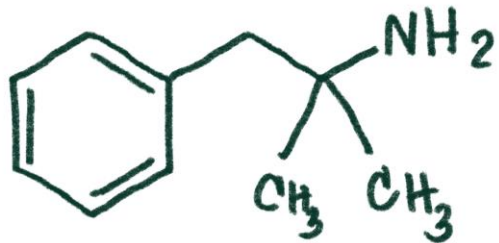
[Aronne, et al. Obesity \(Silver Spring\). 2013 Nov;21\(11\):2163-71](#)

Wait a minute....

- Phentermine as in Fen-Phen?



Fenfluramine



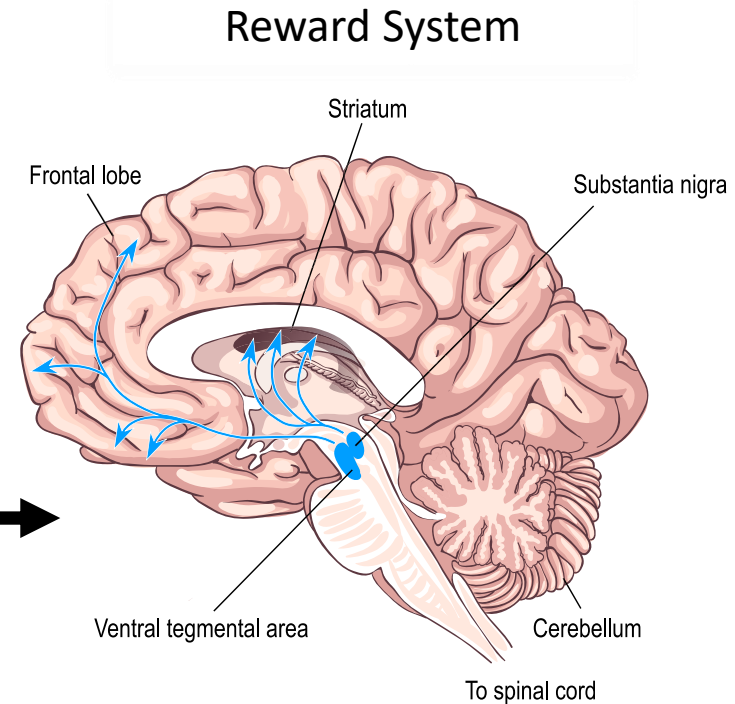
Phentermine

"Fen-Phen"

- Fen-Phen banned in 1997
- Fenfluramine (5-HT_{2B}) → heart valve disease and pulmonary hypertension.
- Phentermine → acts as an appetite suppressant and stimulant. Prescribed for 12 weeks at a time maximum.

- **Naltrexone/Bupropion (Contrave)**

- Naltrexone – opioid receptor blocker
- Bupropion – acts on neurotransmitters (dopamine and norepinephrine)



- **Naltrexone/Bupropion (Contrave)**

- Twice a day, dose increases gradually

- WL: 4.2-5.2% 1 year

- Contraindications:

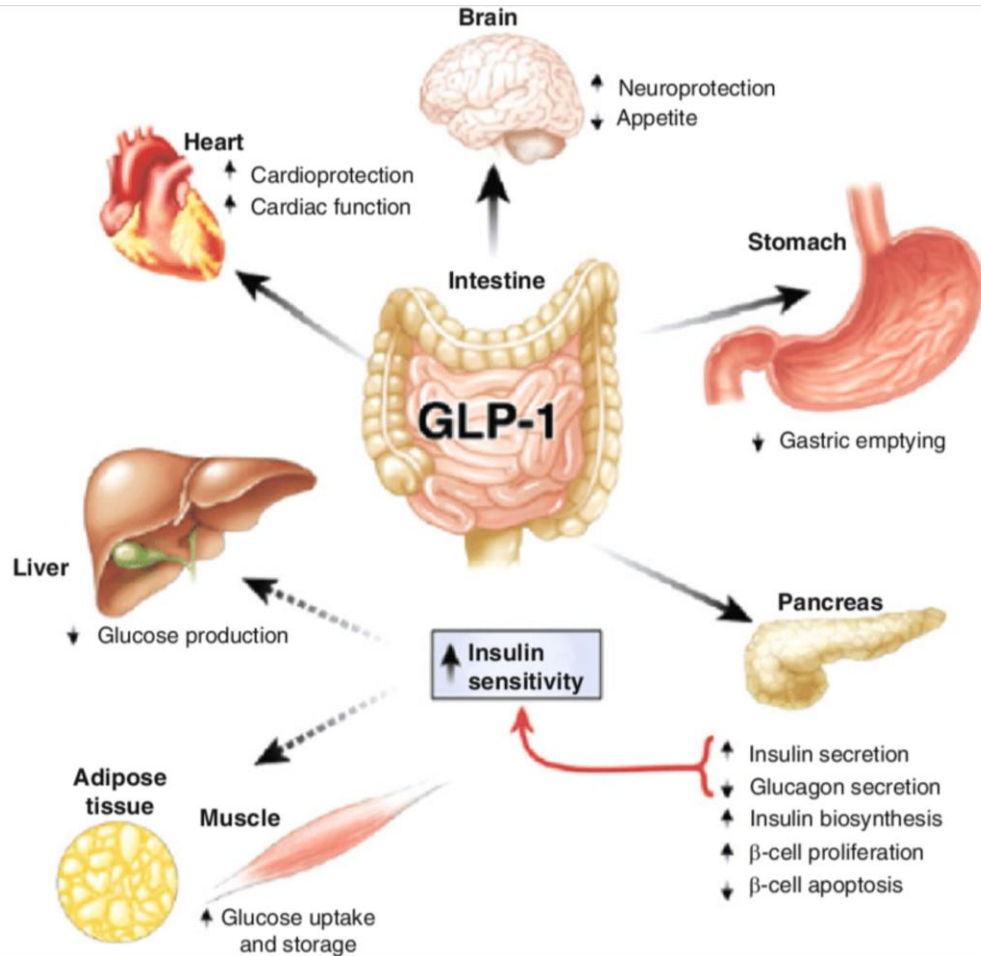
- Pregnancy, high blood pressure, anorexia, bulimia, severe depression, alcohol or drug withdrawal, chronic opioid use, seizure disorder

- Monitor for heart arrhythmias, seizures, migraines, depression, anxiety

- Side effects:

- Nausea, headache, dizziness, constipation

- Glucagon-like peptide receptor agonists (GLP-1 RA)
 ↑ effect of GLP-1



Exendin 4(exenatide)



- Naturally occurring 39AA GLP-1R agonist from salivary venom of Gila monster
- 53% homology with GLP-1
- Resistant to DPP-IV

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EcoR I 50
gaatt cAC GGG GAG GGA ACG TTT ACC AGT GAC TTG TCA AAA CAG ATG GAA
Exendin 4 H G E G T F T S D L S K Q M E
GAG GAG GCA GTG CGG TTA TTT ATT GAA TGG CTC AAA AAC BamH I 95
E E A V R L F I E W L K N G gga tcc

```


GLP1-RA

- WL: 5.6% 1 year
- Contraindications:
 - Pregnancy/breastfeeding
 - Pancreatitis
 - acute gallbladder disease
 - Personal or family history of medullary thyroid cancer or MEN2 genetic mutation
- Side effects:
 - Nausea, vomiting, bloating, constipation, diarrhea, headache
 - Low blood sugar*



- **Liraglutide**

- 1. Saxenda**

- Once daily injection, dose gradually increased
- 0.6 mg to 3 mg

- 2. Victoza**

- Once daily injection
- 0.6 mg to 1.8 mg

- **Semaglutide**

- 1. Ozempic:**

- Once weekly injection, dose gradually increased from 0.25 mg up to 1 mg
- Upcoming approval for for weight loss in Canada (up to 2 mg)

- 2. Rybelsus**

- ORAL once a day
- 3mg to 14 mg

- 3. Wegovy (in Canada Fall 2022)**

- Once weekly injection gradually increased from 0.25 mg up to 2.4 mg

The NEW ENGLAND JOURNAL of MEDICINE

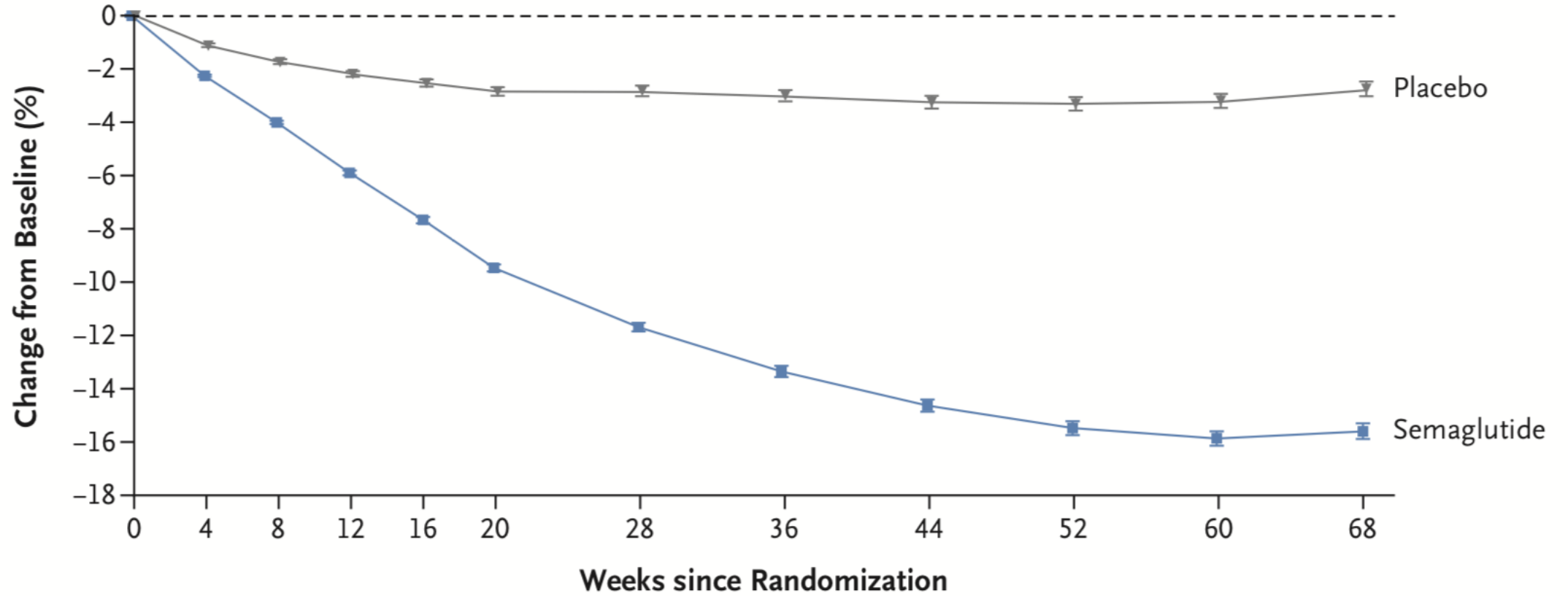
ORIGINAL ARTICLE

Once-Weekly Semaglutide in Adults with Overweight or Obesity

John P.H. Wilding, D.M., Rachel L. Batterham, M.B., B.S., Ph.D.,
Salvatore Calanna, Ph.D., Melanie Davies, M.D., Luc F. Van Gaal, M.D., Ph.D.,
Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Barbara M. McGowan, M.D., Ph.D.,
Julio Rosenstock, M.D., Marie T.D. Tran, M.D., Ph.D., Thomas A. Wadden, Ph.D.,
Sean Wharton, M.D., Pharm.D., Koutaro Yokote, M.D., Ph.D., Niels Zeuthen, M.Sc.,
and Robert F. Kushner, M.D., for the STEP 1 Study Group*

- 1961 adults with BMI ≥ 30 or BMI ≥ 27 + weight-related comorbidity
- All had lifestyle modification (calorie deficit 500 kcal) + encouraged to exercise 150 min/week
- Randomized to receive Ozempic up to 2.4 mg vs placebo
- Monitored for 68 weeks

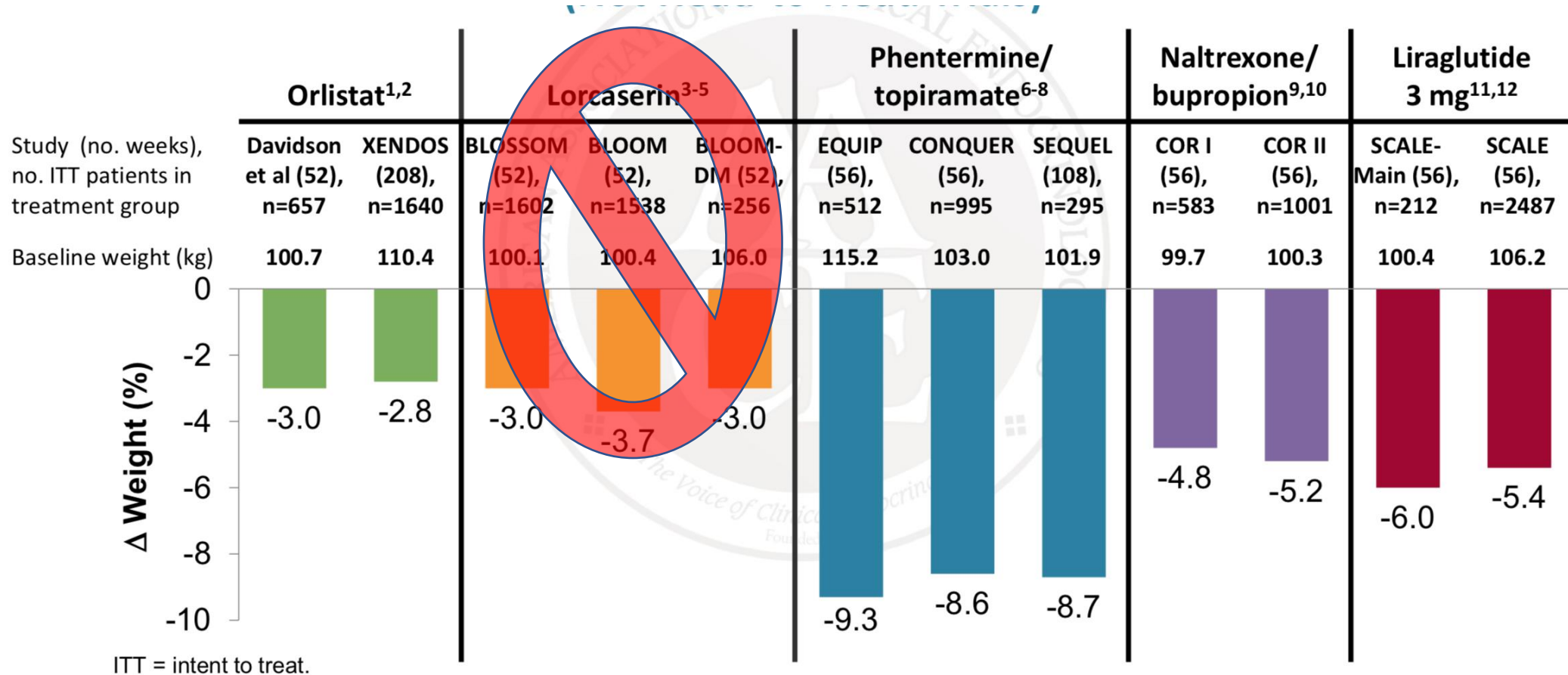
A Body Weight Change from Baseline by Week, Observed In-Trial Data



No. at Risk

Placebo	655	649	641	619	615	603	592	571	554	549	540	577
Semaglutide	1306	1290	1281	1262	1252	1248	1232	1228	1207	1203	1190	1212

Placebo-Subtracted Changes from Baseline, Highest Approved Dose (Not Head-to-Head Trials)

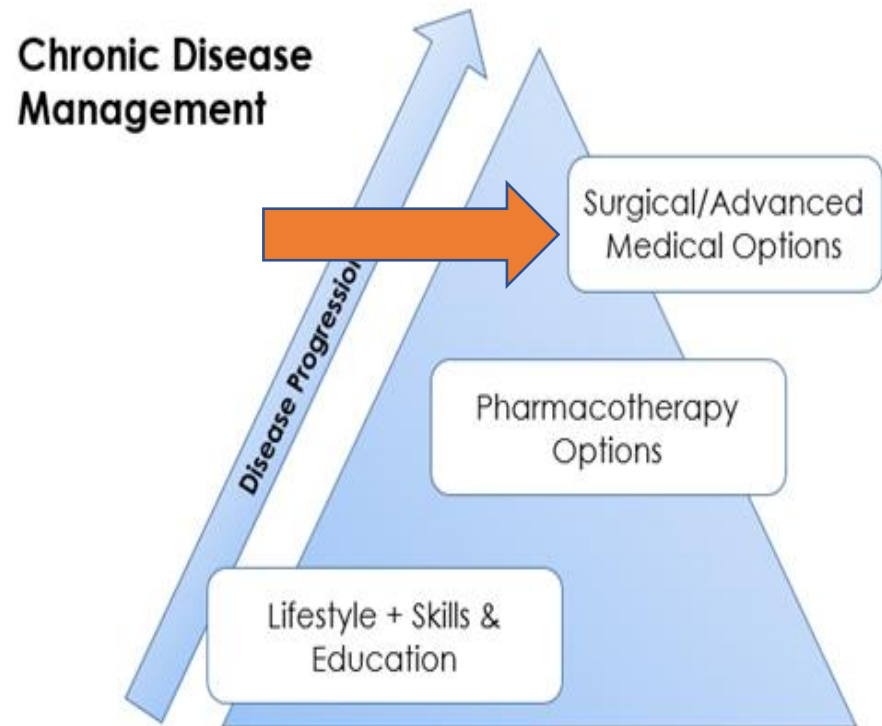


1. Davidson MH, et al. *JAMA*. 1999;281:235-242. 2. Torgerson JS, et al. *Diabetes Care*. 2004;27:155-161. 3. Fidler MC, et al. *J Clin Endocrinol Metab*. 2011;96:3067-3077. 4. Smith SR, et al. *N Engl J Med*. 2010;363:245-256. 5. O'Neil PM, et al. *Obesity*. 2012;20:1426-1436. 6. Allison DB, et al. *Obesity (Silver Spring)*. 2012;20:330-342. 7. Gadde KM, et al. *Lancet*. 2011;377:1341-1352. 8. Garvey WT, et al. *Am J Clin Nutr*. 2012;95(2):297-308. 9. Greenway FL, et al. *Lancet*. 2010;376:595-605. 10. Apovian CM, et al. *Obesity (Silver Spring)*. 2013;21:935-943. 11. Wadden TA, et al. *Int J Obes (Lond)*. 2013;37:1443-1451. 12. Pi-Sunyer X, et al. *N Engl J Med*. 2015;373:11-22.

Summary - Medications

- In combination with lifestyle changes, not on their own
- None should be used in pregnancy/breastfeeding
- 2 main drugs used in Canada:
 - Contrave
 - May help with cravings, impulsive eating behaviours
 - \$250/mo (after 20% manufacturer discount), unless covered by third party drug plan
 - GLP-1 RA
 - May help if you have increased hunger, trouble feeling full, diabetes or pre-diabetes
 - Saxenda: \$450/month unless covered by third party drug plan
 - Ozempic: can be covered by pharmacare for diabetes in some cases; otherwise \$180-230/month

Bariatric Surgery



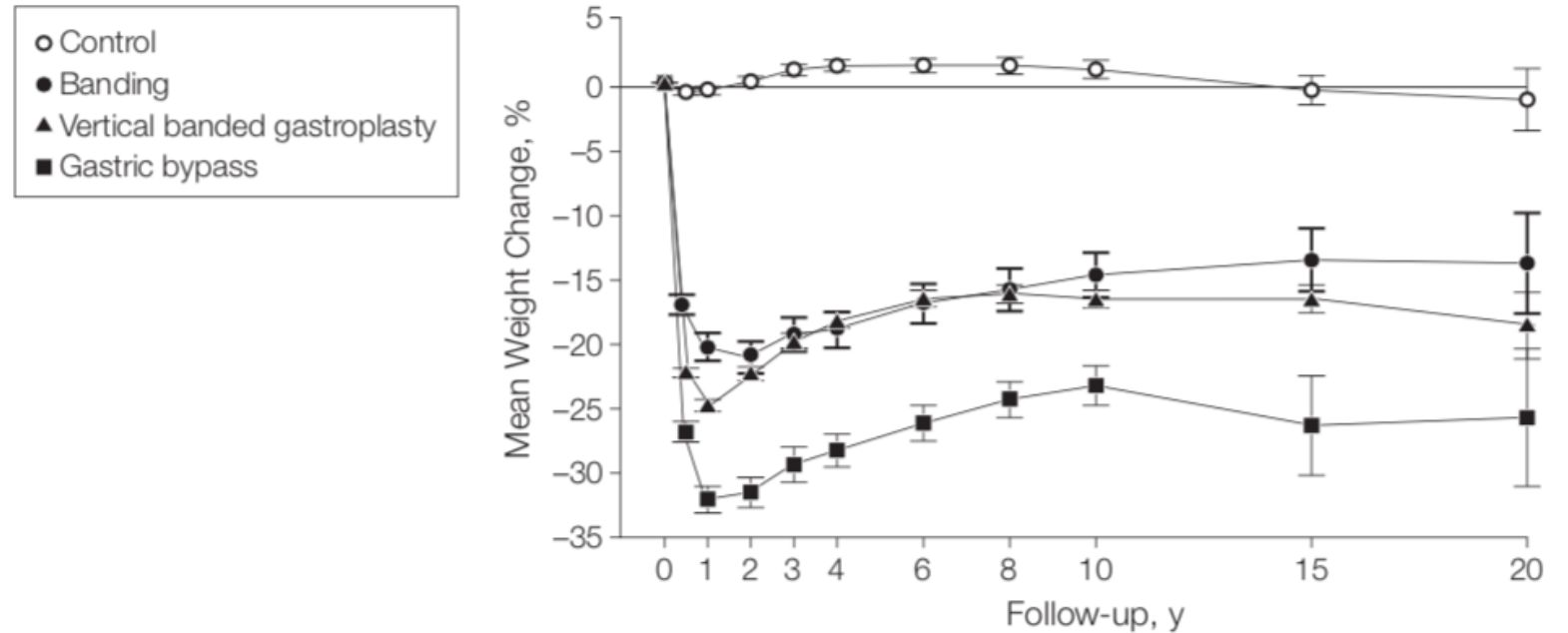
ADVISE



BARIATRIC SURGERY should be considered for all patients requiring more than 15% sustainable weight loss. Modern laparoscopic bariatric surgery is both safe and effective, and substantially reduces morbidity and mortality. All surgical patients require multidisciplinary presurgical assessment and long-term medical, nutritional, and psychosocial support.

Effective for
weight loss

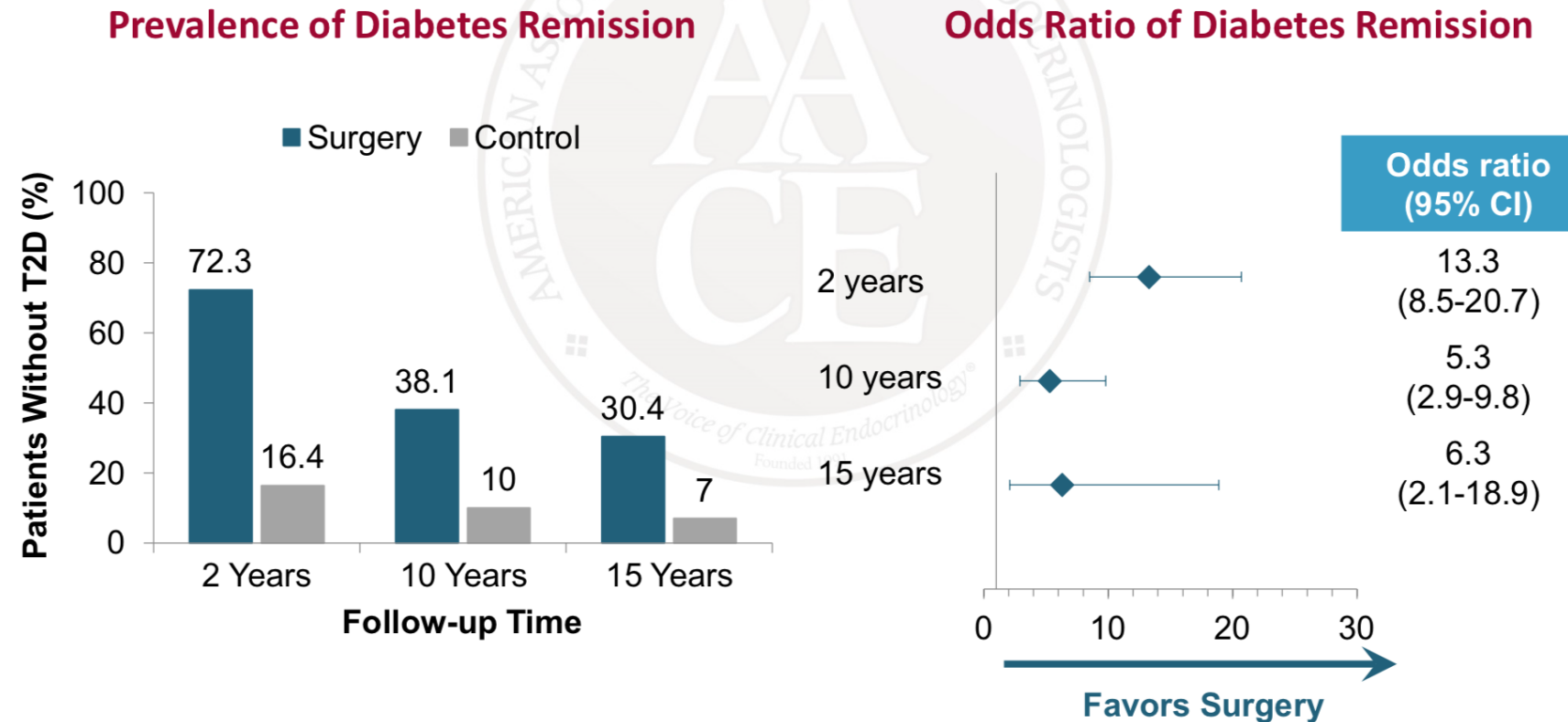
Figure 1. Mean Weight Change Percentages From Baseline for Controls and the 3 Surgery Groups Over 20 Years in the Swedish Obese Subjects Study



No. of patients	0	1	2	3	4	6	8	10	15	20
Control	2037	1490	1242	1267	556	176				
Banding	376	333	284	284	150	50				
Vertical banded gastroplasty	1369	1086	987	1007	489	82				
Gastric bypass	265	209	184	180	37	13				

But that's not all...

Swedish Obese Subjects Study (N=603 Patients with T2D at Baseline)

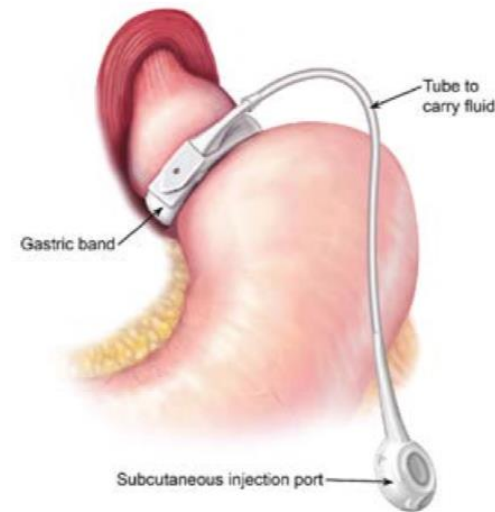


T2D = type 2 diabetes.

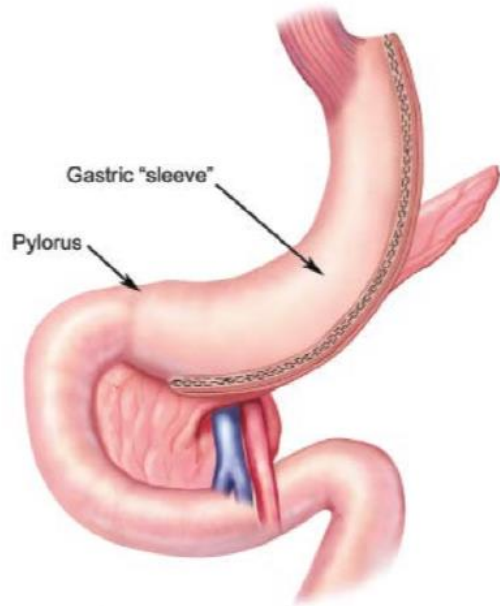
Sjostrom L, et al. *JAMA*. 2014;311:2297-2304.

Types of surgery

- Adjustable band creates small stomach pouch (15-45 mL)
- Restrict food intake and increase satiety
- Requires greater adherence to lifestyle to maintain weight loss
- We NEVER refer ANYONE for an adjustable laparoscopic band



**Laparoscopic Adjustable
Gastric Band (LAGB)**



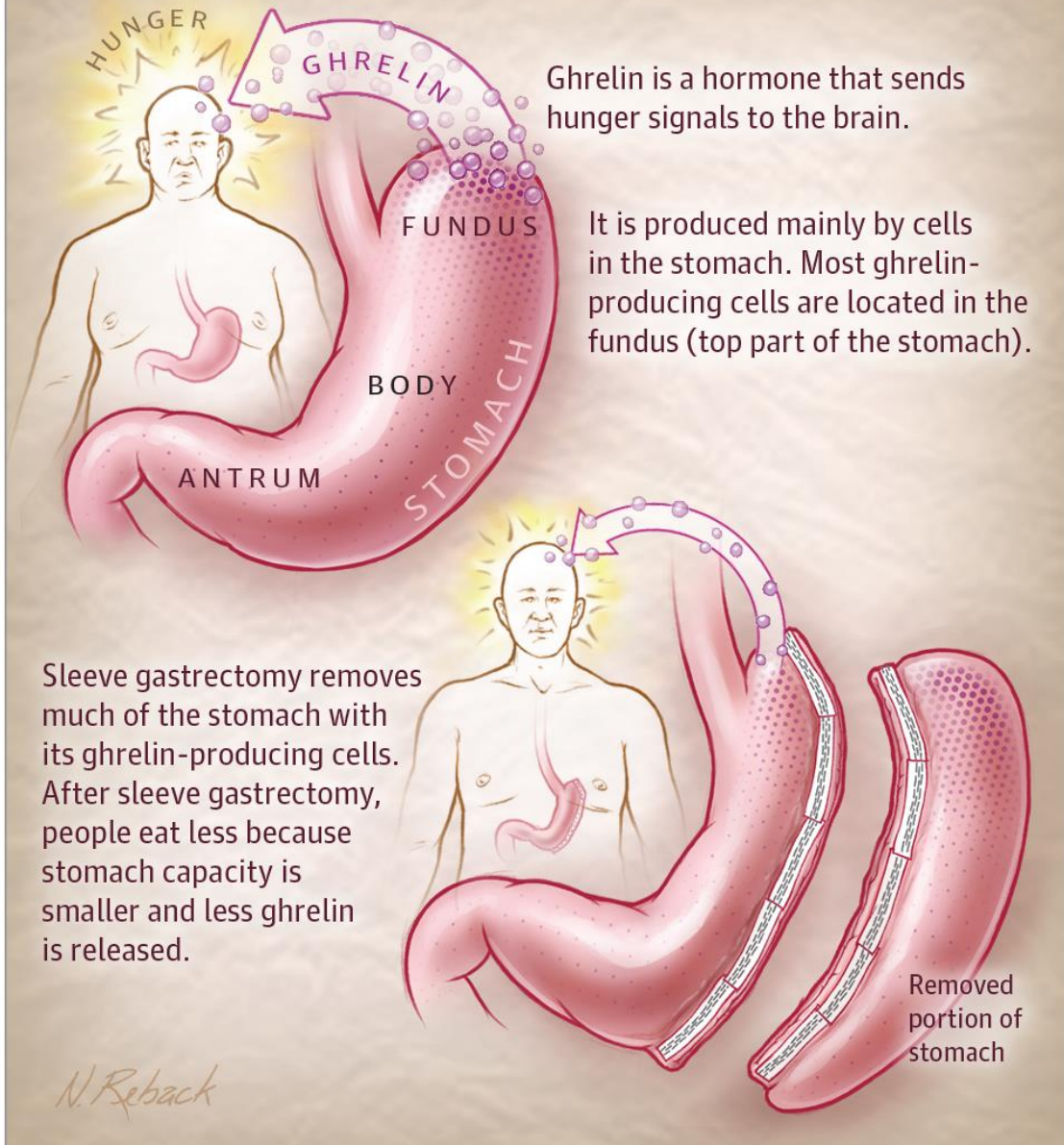
Laparoscopic Sleeve Gastrectomy (LSG)

- Remove portion of stomach, leaving a narrow tube

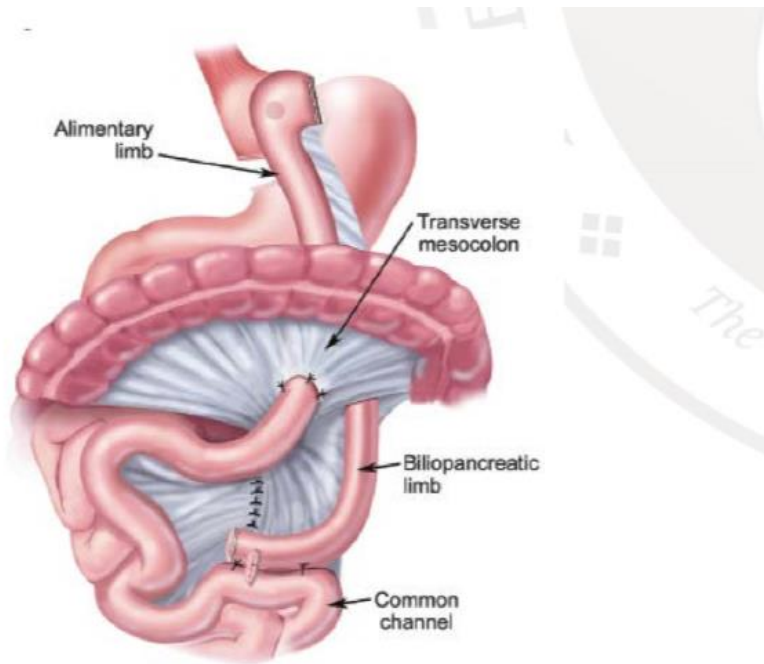


- Limits food intake
- Modulates hormones
 - \uparrow GLP-1 and PYY
 - \downarrow Ghrelin

Hunger Signaling and Sleeve Gastrectomy

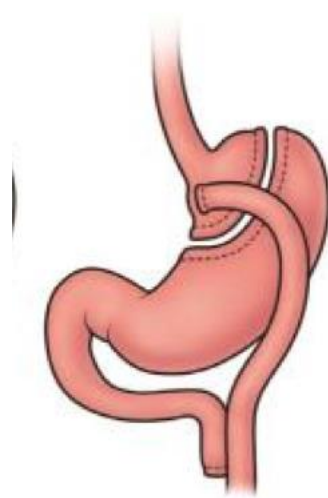


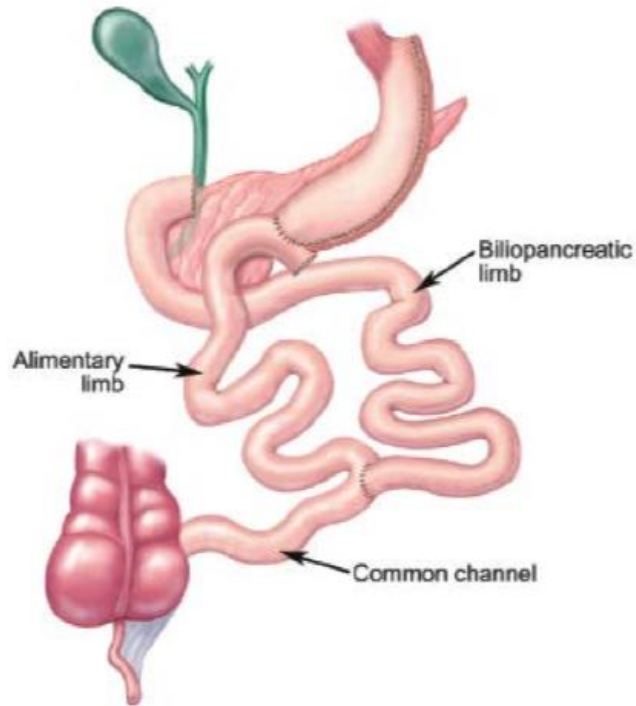
- Mechanical and hormonal effects



Roux-en-Y Gastric Bypass (RYGB)

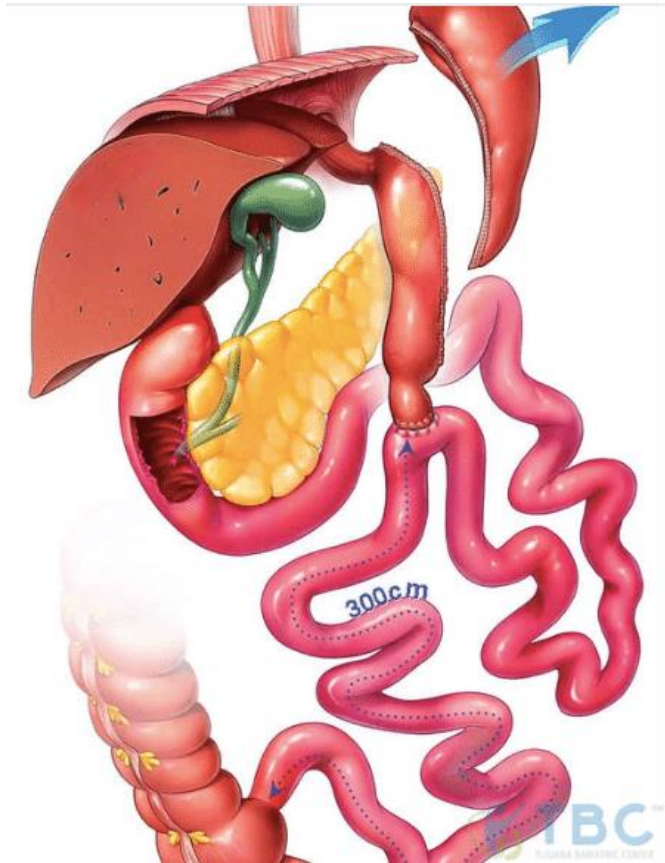
- Create small stomach pouch (30mL), small intestine bypasses the rest of the stomach
- Limits food intake
- Causes nutrient malabsorption
- Modulates hormones
 - ↑ GLP-1 and PYY
 - ↓ Ghrelin





Biliopancreatic Diversion with Duodenal Switch (BPD-DS)

- Sleeve gastrectomy + bypass of most of the small intestine (all but 100-150 cm)
- Benefits of sleeve gastrectomy +
 - Limits absorption and digestion in the small intestine
 - Extensive nutrient and calorie malabsorption



- Similar to biliopancreatic diversion with duodenal switch except done with only 1 “anastomosis” or joining point of the bowel
- Sleeve gastrectomy + the small intestine is detached just below the stomach and then reattached to a loop of small intestine about 3 meters from the colon

Single Anastomosis Duodeno-ileostomy with Sleeve Gastrectomy (SADI-S)

BPD-DS vs SADI-S

BPD/DS

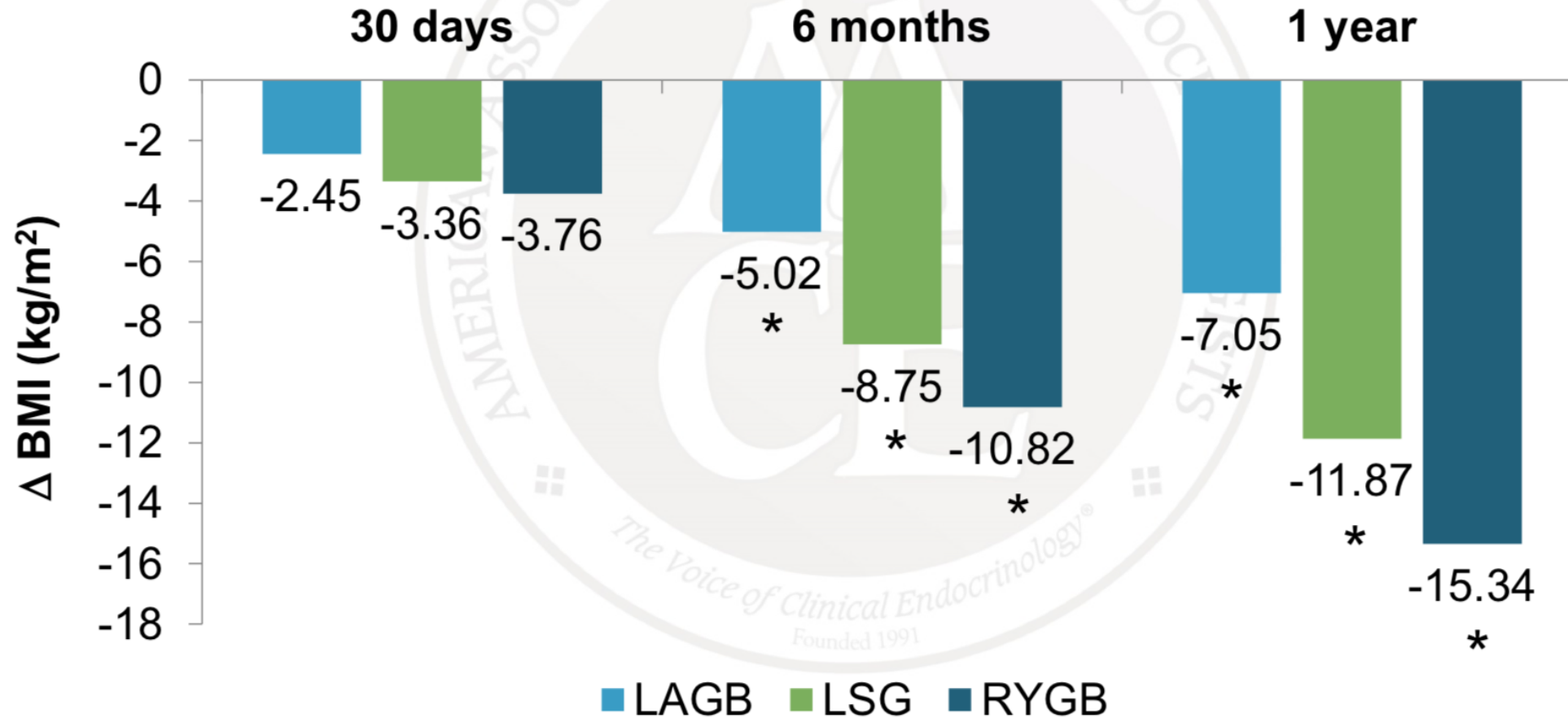
- The most effective surgery for weight loss, diabetes, metabolic syndrome resolution
- **Best option for BMI>55** and for patients with severe metabolic disease (i.e., insulin dependent diabetes)
- Most commonly done in 2 stages

SADI-S

- Less issues with gas/frequent BM/body odor, internal hernia, nutritional deficiency and chronic abdominal pain
- Can often be done in one stage
- Not ideal for BMI >55
- Fewer long-term complications
- Less data on long-term effectiveness

ACS Bariatric Surgery Center Network Prospective Observational Study

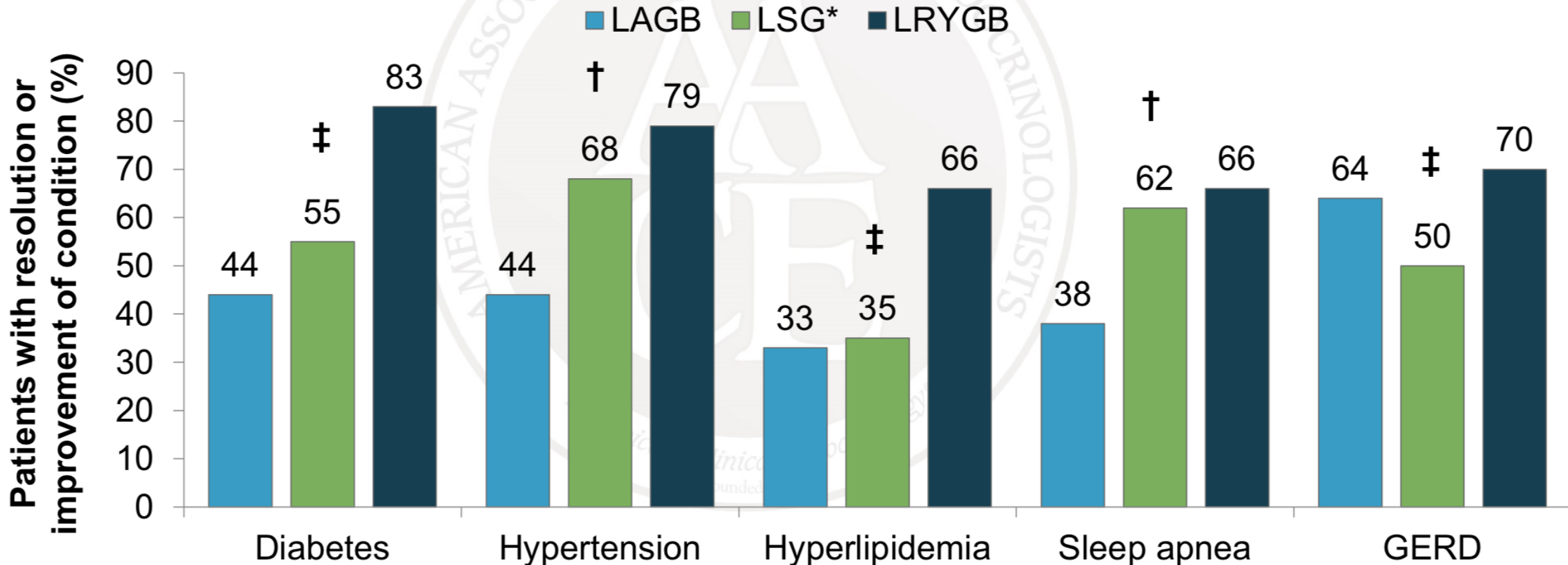
(N=28,616)



ACS = American College of Surgeons; BL = baseline; BMI = body mass index; LAGB = laparoscopic adjustable gastric band; LSG = laparoscopic sleeve gastrectomy; RYGB = Roux-en-Y gastric bypass.

Hutter MM, et al. *Ann Surg.* 2011;254:410-420.

ACS Bariatric Surgery Center Network Prospective Observational Study (N=28,616)



ACS = American College of Surgeons; BMI = body mass index; GERD = gastroesophageal reflux disease; LAGB = laparoscopic adjustable gastric band; LSG = laparoscopic sleeve gastrectomy; LRYGB = laparoscopic Roux-en-Y gastric bypass.

Hutter MM, et al. *Ann Surg.* 2011;254:410-420.

Criteria for Bariatric Surgery

Factor	Criteria
Weight (adults)	BMI ≥ 40 kg/m ² with no comorbidities BMI ≥ 35 kg/m ² with ≥ 1 severe obesity-associated comorbidity BMI 30-34.9 kg/m ² with diabetes or metabolic syndrome
Weight loss history	Failure of previous nonsurgical attempts at weight reduction, including nonprofessional programs (eg, Weight Watchers)
Commitment	Expectation that patient will adhere to postoperative care <ul style="list-style-type: none">▪ Follow-up visits with healthcare team▪ Recommended medical management, including use of dietary supplements▪ Instructions regarding any recommended procedures or tests
Exclusion	<ul style="list-style-type: none">▪ BMI < 30 kg/m²; there is insufficient evidence to recommend bariatric surgery for control of glucose, lipids, or CV risk reduction independent of BMI▪ Reversible endocrine or other disorders that can cause obesity▪ Current drug or alcohol abuse▪ Uncontrolled, severe psychiatric illness▪ Lack of comprehension of risks, benefits, expected outcomes, alternatives, and required lifestyle changes▪ Inability to tolerate general anesthesia due to cardiopulmonary illness

ASMBS = American Society for Metabolic & Bariatric Surgery; BMI = body mass index; CV = cardiovascular; TOS = The Obesity Society.

Mechanick JI, et al. *Endocr Pract.* 2008;14(suppl 1):1-83. Mechanick JI, et al. *Endocr Pract.* 2013;19:337-372.



Medical Clearance for Bariatric Surgery

- ✓ Assess for cardiovascular disease
- ✓ Optimize diabetes management, goal A1C <8.5
- ✓ Screen for GI or liver problems
- ✓ Screen for OSA, CPAP compliance
- ✓ Smoking cessation at least 6 months prior to referral to Richmond Program
- ✓ Avoid pregnancy for 12 months pre- and 18 months postoperatively; switch to non-oral contraceptive like IUD
- ✓ Extensive nutritional evaluation

Metabolic Complications of Bariatric Surgery


Complication	Clinical Features	Management
Iron deficiency	Anemia	Ferrous fumarate, sulfate, or gluconate Up to 150-300 mg elemental iron daily Add vitamin C and folic acid
Osteoporosis	Fractures	DXA, calcium, vitamin D, and consider bisphosphonates
Oxalosis	Kidney stones	Low oxalate diet Potassium citrate Probiotics
Secondary hyperparathyroidism	Vitamin D deficiency Negative calcium balance Osteoporosis	DXA Serum intact PTH level 25-Hydroxyvitamin D levels Calcium and vitamin D supplements

Complication	Clinical Features	Management
Acid-base disorder	Metabolic acidosis, ketosis	Bicarbonate orally or intravenously; adjust acetate content in PN
	Metabolic alkalosis	Salt and volume loading (enteral or parenteral)
Bacterial overgrowth (primarily with BPD-DS)	Abdominal distention Pseudo-obstruction Nocturnal diarrhea Proctitis Acute arthralgia	Antibiotics (metronidazole) Probiotics
Fat-soluble vitamin deficiency	Vitamin A—night vision Vitamin D—osteomalacia Vitamin E—rash, neurologic Vitamin K—coagulopathy	Vitamin A, 5,000-10,000 U/d Vitamin D, 400-50,000 U/d Vitamin E, 400 U/d Vitamin K, 1 mg/d ADEK, 2 tablets twice a day (http://www.scandipharm.com)
Thiamine deficiency (vitamin B ₁)	Wernicke-Korsakoff encephalopathy Peripheral neuropathy Beriberi	Thiamine intravenously followed by large-dose thiamine orally
Vitamin B ₁₂ deficiency	Anemia Neuropathy	Parenteral vitamin B ₁₂ Methylmalonic acid

Expedited Bariatric Surgical Program

- We work with a patient until they are considered an appropriate surgical candidate, and then we arrange a referral to the Richmond Metabolic and Bariatric Surgery Program (RMBS)
- Expedited means you waive the 2.5 year waitlist to get into RMBS, and may require less visits with the Richmond Program health care team.
- We NEVER refer ANYONE for an adjustable laparoscopic band

The Expedited Bariatric Surgical Patient

- Meets the BMI criteria for bariatric surgery (>40 or greater than 35 with significant obesity related comorbidities)
 - Patient is aware of the risks and benefits and has made the decision to pursue surgery
 - Patient has made appropriate changes in their eating and activity habits
 - Patient has been compliant in attending medical appointments with physicians, including regular attendance for group medical visits
- 

If you are interested in pursuing weight loss medication or bariatric surgery



EMAIL YOUR
REQUEST TO:



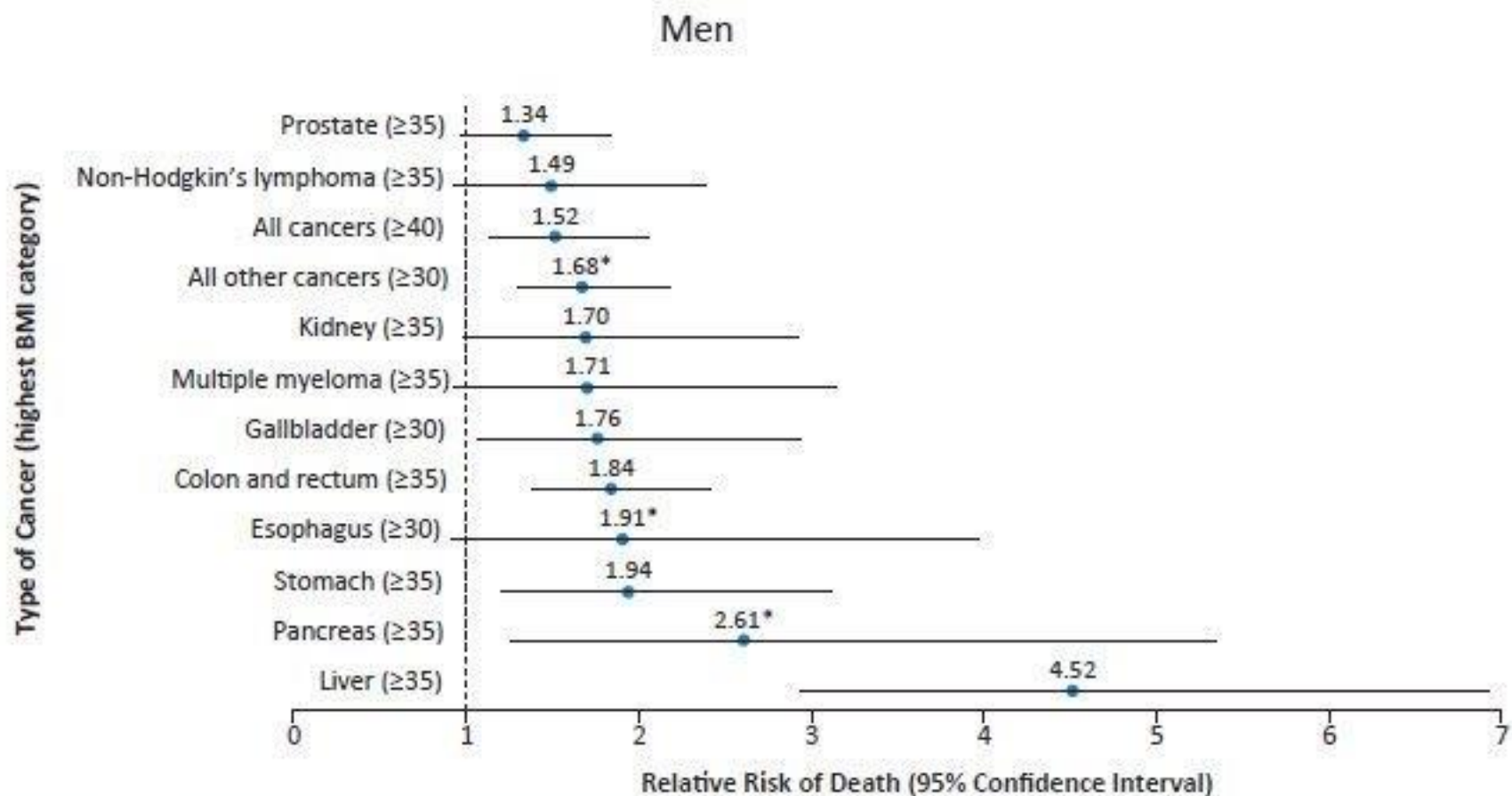
(FOR MEDS)

INFO@MEDWEIGHT.CA

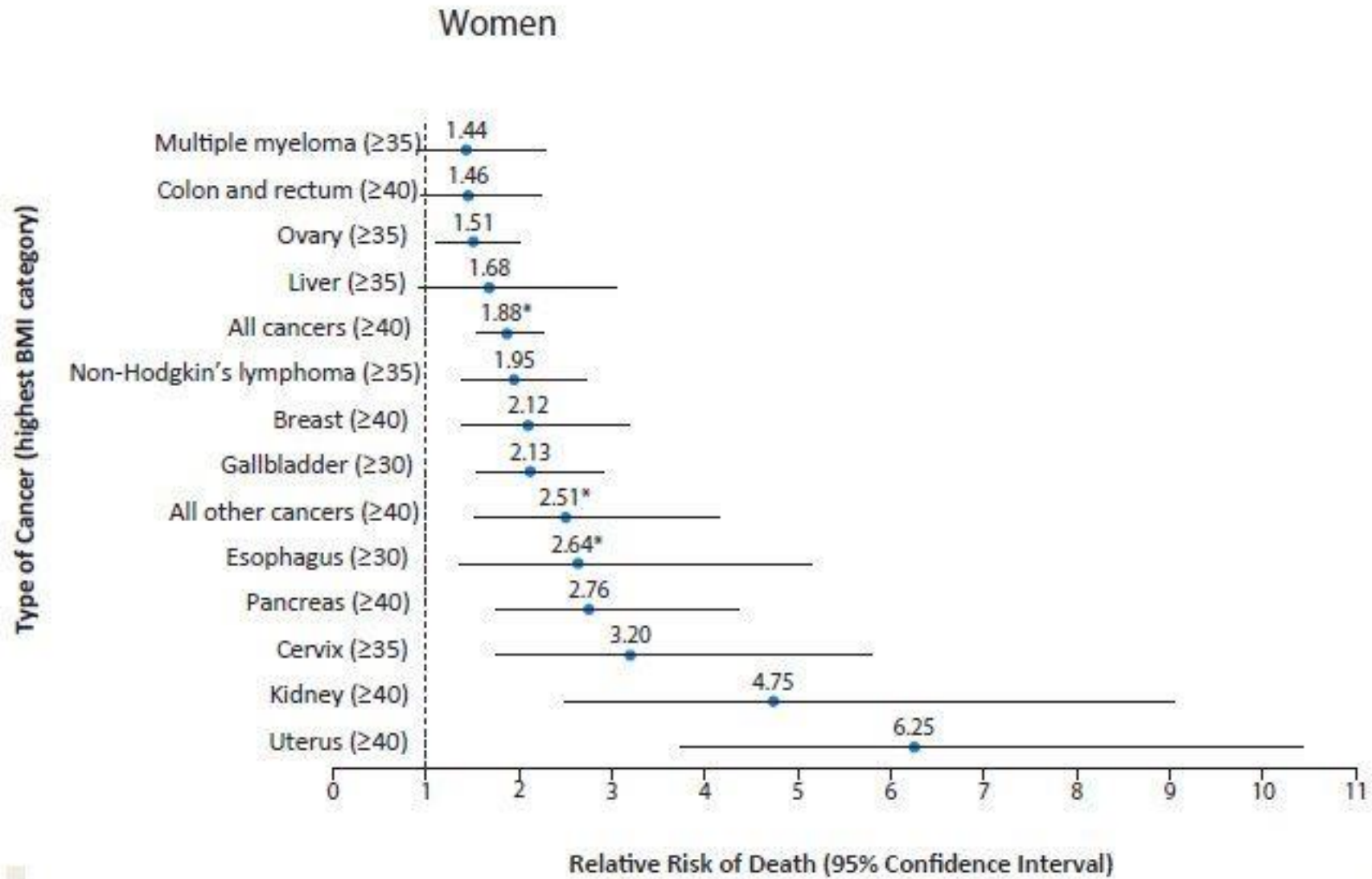
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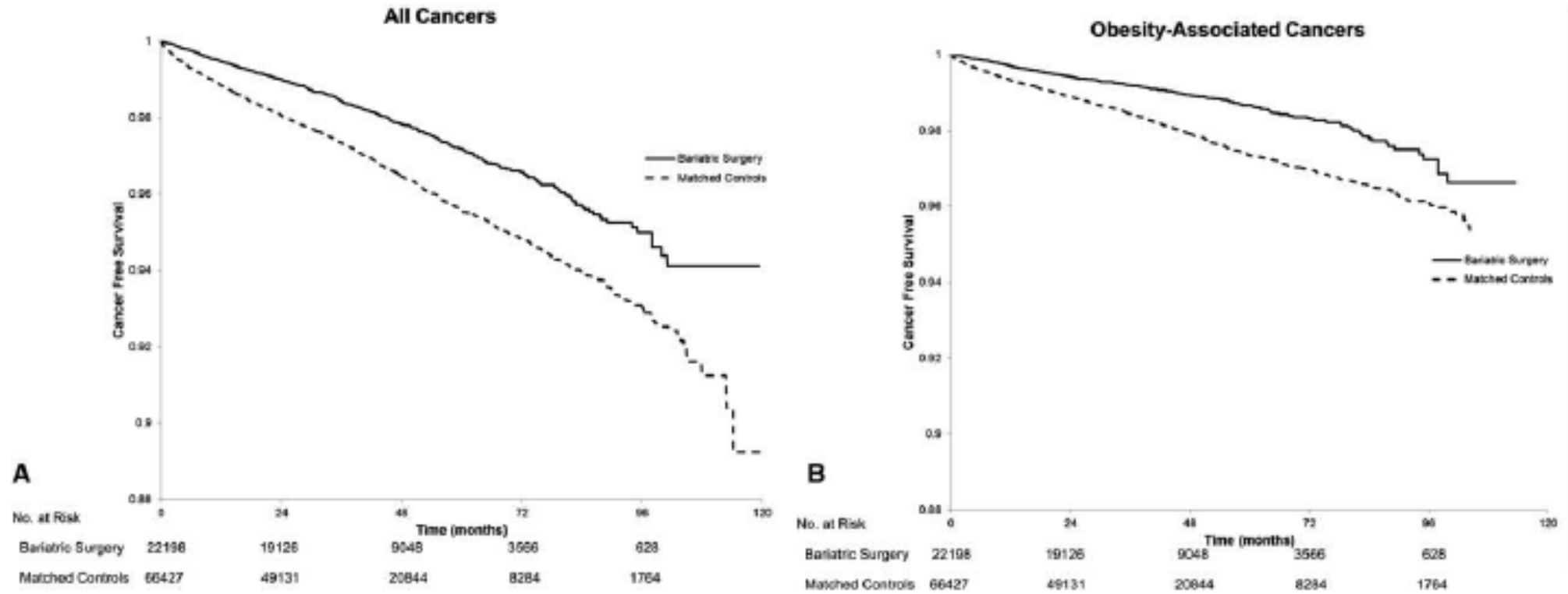
BARIATRIC@MEDWEIGHT.CA

Obesity and risk of cancer in MEN



Obesity and risk of cancer in WOMEN





22,198 people who had undergone weight loss surgery between 2005 and 2012

in as little 3.5 years, the risk of cancer in surgery group was 33% lower. The risk of breast, colon, endometrial, and pancreatic cancer had dropped by a whopping 45-55%.