Obesity Update 2020

PHARMACOTHERAPY

The Changing Landscape of Obesity Treatment

Royal Alexandra HOSPITAL FOUNDATION
CASES
Centre for Advancement of Surgical Education & Simulation

Faculty/Presenter Disclosure

- Faculty: Dr. Shahebina Walji, MD, CCFP

- Relationships with commercial interests:
  - Grants/Research Support: Nil
  - Speakers Bureau/Honoraria: Novo Nordisk, Bausch Health, Takaeda
  - Consulting Fees: Novo Nordisk, Bausch Health, Takaeda
  - Other: Nestle

Disclosure of Commercial Support

- Potential for conflict(s) of interest:
  - Dr. Shahebina Walji has received payment/funding from companies exhibiting in this program AND/OR companies whose product(s) are being discussed in this program.
  - The exhibitors did not provide content for Obesity Update 2020 nor did they have any editorial input or involvement with the selection of Dr. Walji as a speaker.
  - The Royal Alexandra Hospital Foundation and/or Centre for Advancement of Surgical Education & Simulation (CASES) has not developed /licensed / distributed/ benefited from the sale of any product that is discussed in this program

Learning Objectives

At the conclusion of this session, participants will be able to:

- Formulate a rationale for the role of obesity pharmacotherapy in multi-modal weight management
- Appropriately select individuals for whom weight loss medications are indicated.
- Discuss obesity pharmacotherapy with patients
- Compare and contrast the mode of action, safety and efficacy of available anti-obesity medications
- Select anti-obesity pharmacotherapies based on the specific properties of different agents
- Employ strategies to manage common side effects of pharmacotherapy

Polling Question

In general, what are your thoughts around the use of pharmacotherapy in the management of obesity?

A. I don't use them. They are either ineffective or there are too many safety concerns.

B. I am not familiar with anti-obesity medications or how to prescribe them.

C. I hesitate to prescribe them because I think patients should be able to manage their weight by changing their lifestyle.

D. I am comfortable discussing and prescribing anti-obesity medications with my patients.

Overview of Obesity

- Obesity is a chronic disease
- Obesity is a pervasive condition with many comorbidities
- Modest weight reduction results in significant health improvement
- Clinical Practice Guidelines Overview
- Biology review

Obesity is a Chronic Disease

- Obesity declared a chronic disease by the CMA in 2015 because:[1]
  - Decreases life expectancy
  - Impairs normal functioning of body
  - Can be caused by genetic factors

- Also considered a chronic disease by other health organizations:
  - World Health Organization
  - World Obesity Federation
  - American Medical Association

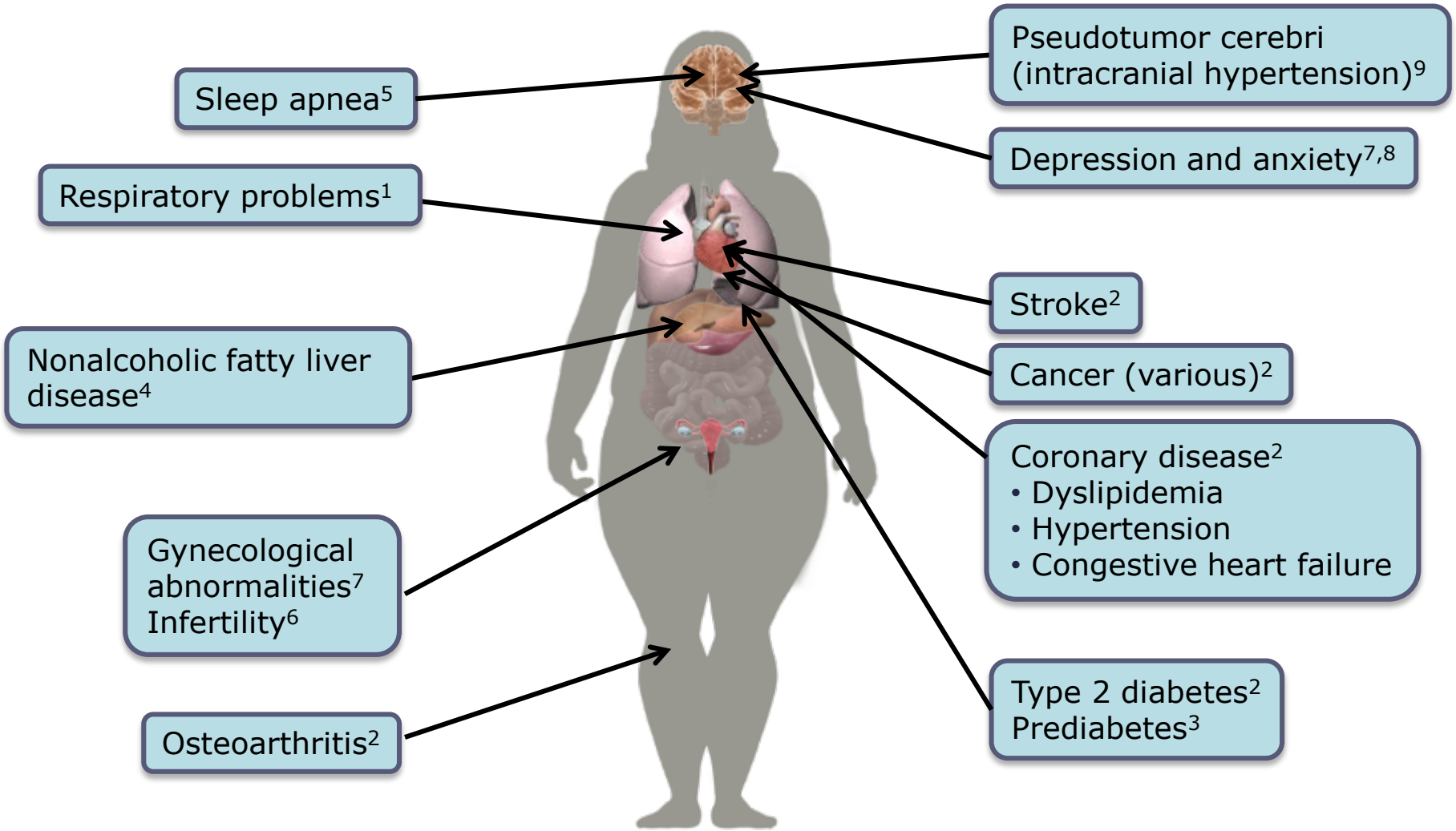
If obesity is a chronic disease then it follows we should:[2]

Manage the condition long-term

Offer a variety of interventions which could include:

- **Lifestyle** (similar to diabetes or dyslipidemia)
- **Medications** (similar to diabetes or hypertension)
- **Surgery** (similar to heart disease)

Obesity is Pervasive



1. Statistics Canada Health Reports. Vol. 17. No. 3. Catalogue no. 82-003-XIE. 2. Guh DP et al. BMC Public Health. 2009;9:88. 3. Shaikh S et al. Int J Diabetes Dev Countries. 2011;31:65–69. 4. Church TS et al. Gastroenterol. 2006;130:2023–2030. 5. Li C et al. Prev Med. 2010;51:18–23. 6. Esmaeilzadeh S et al. Arch Med Sci. 2013;9:499-505. 7. NIH. Obes Res. 1998;6(Suppl 2):51S–209S; 8. Zhao G et al. *Int J Obes (Lond).* 2009;33(2):257-66. 9. Daniel AB et al. *Am J Opthalmol* 2007;143:635-41.

Benefits of Modest Weight Reduction

Obesity Complication	Weight loss required for therapeutic benefit (%)
Diabetes (prevention)	3-10
Hypertension	5 to >15
Dyslipidemia	3 to >15
Hyperglycemia	3 to >15
Non-alcoholic fatty liver disease (NAFLD)	10
Sleep apnea	10
Osteoarthritis	5-10
Stress incontinence	5-10
Gastroesophageal reflex disease	5-10 in women; 10 in men
Polycystic ovary syndrome	5-15 (>10 optimal)

Canadian Guidelines for the Management of Obesity in Adults…

Treatment	BMI category (kg/m^2)				
	≥25	≥27	≥30	≥35	≥40
Behavioural modification Consists of nutrition, physical activity, and cognitive-behavioural therapy	With comorbidities	With comorbidities	✓	✓	✓
Pharmacotherapy Adjunct to behavioural modifications; consider if patient has not lost 0.5 kg per week by 3–6 months after behavioural changes		With comorbidities	✓	✓	✓
Bariatric surgery Consider if other weight loss attempts have failed. Requires lifelong medical monitoring				With comorbidities	✓

✓ Indicates a treatment recommendation for that BMI class. BMI, body mass index
Lau et al. CMAJ 2007;176(8 suppl):Online-1–117

Clinical Case: Meet Christa, age 32

Family:
- Divorced, with 2 young children

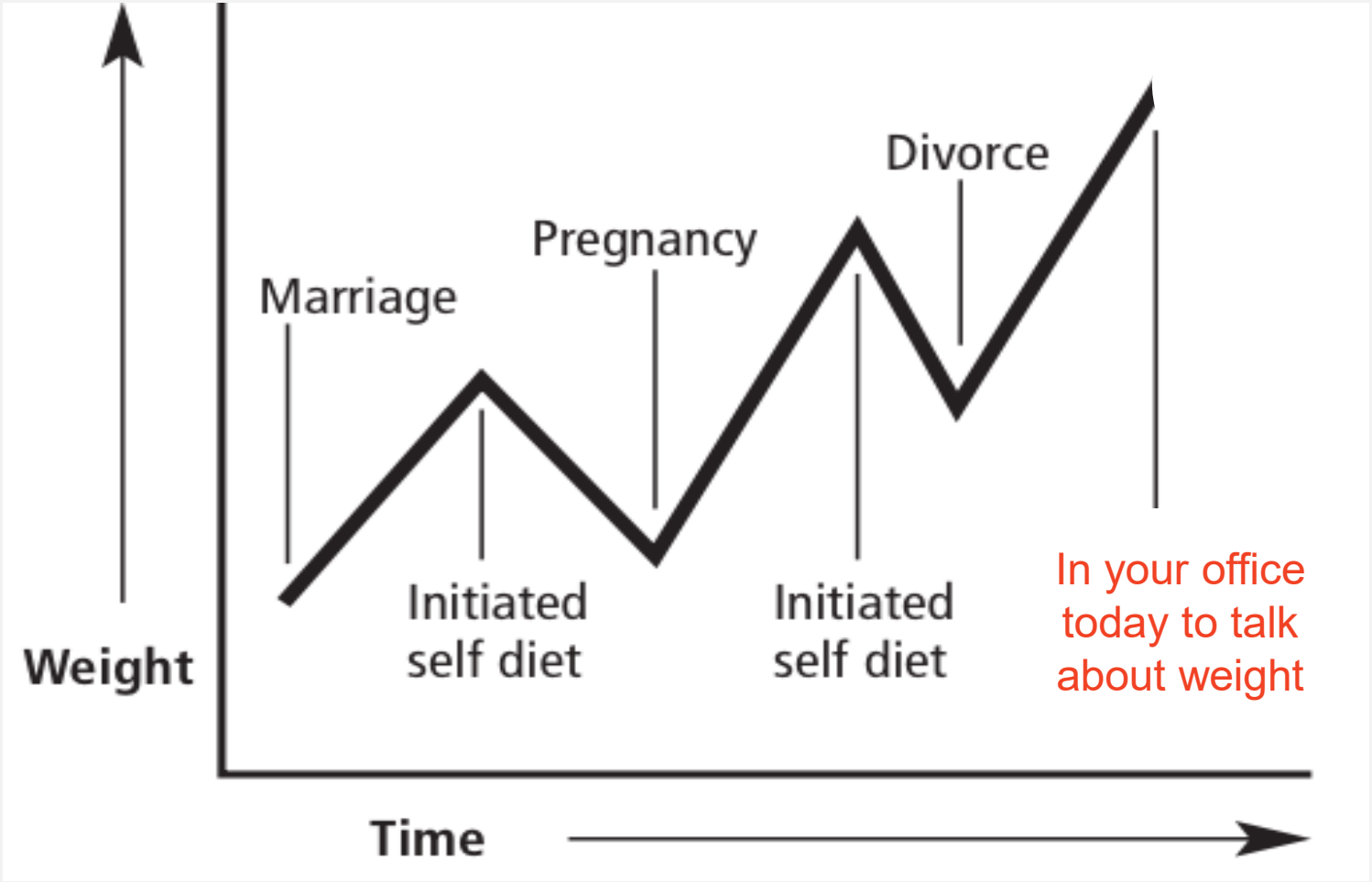
Job:
- Administrative assistant, full time

"I've struggled with my weight for a long time, and I am pretty sure it is affecting my health. I don't have enough energy to keep up with my kids, and I have been missing work because I have pain and I just feel unwell. I need some help with my weight."

Medical History:
- Mildly elevated liver enzymes

Height: 5'5"
Weight: 187 lb
BMI: 31.1

Clinical Case: Meet Christa, age 32



"I am so frustrated with my weight and myself."

Royal Alexandra HOSPITAL FOUNDATION
CASES Centre for Advancement of Surgical Education & Simulation

Polling Question

Which of the following statements is true?

When looking at averages, data has shown that:

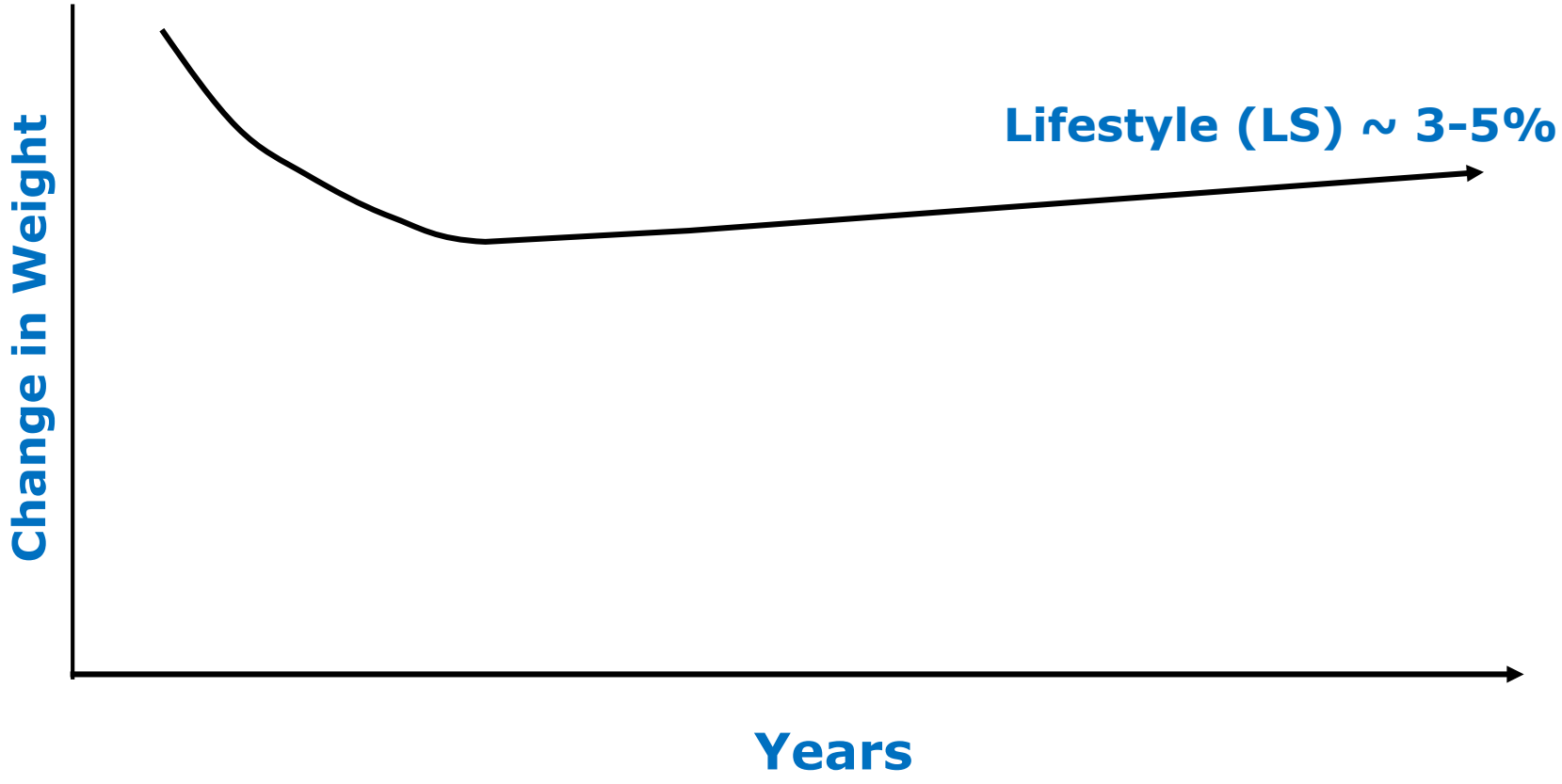
A. Improved diet is the most effective weight loss intervention long term.

B. Improved exercise level is the most effective weight loss intervention long term

C. Diet and exercise together is the most effective weight loss intervention long term

D. Diet and exercise produce modest amounts of weight loss long term.

Treatment Success



Review: What are the biological factors that mediate eating behavior?

Hypothalamic Hunger System[1,2]

- Drives eating based on body's energy/calorie needs for survival and function
- Primarily driven by 2 different neuron clusters within the **hypothalamus**
- Detection and integration of energy state information (neuronal and hormonal) from peripheral organs leads to hunger OR satiety
- Altered function in obesity
- **ENERGY HOMEOSTASIS**

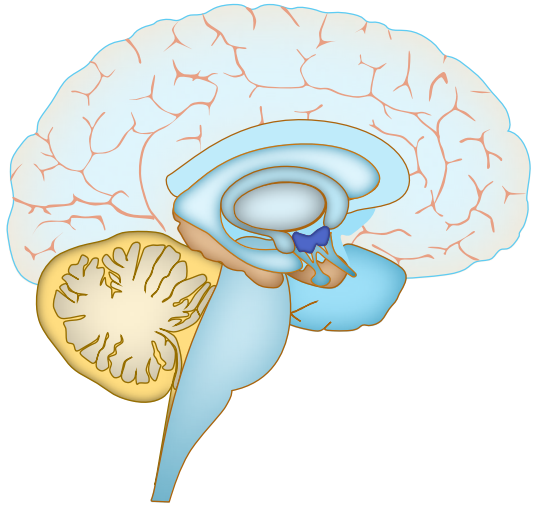


Figure adapteCNS = central nervous system; POMC = proopiomelanocortin.
d from Billes et al.,© 2014, with permission from Elsevier.

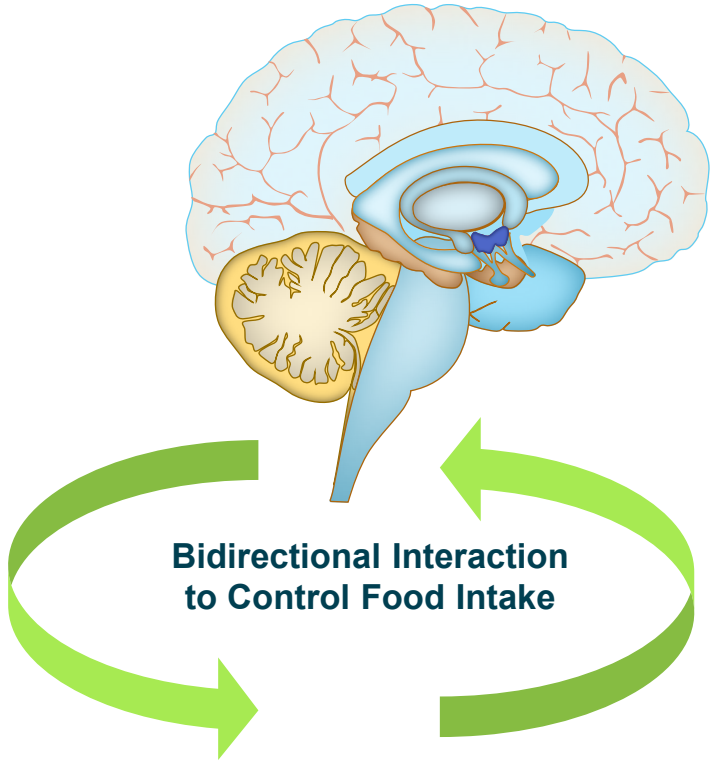
1. Billes SK et al. *Pharmacol Res*. 2014;84:1-11; 2. Yu JH et al. *Diabetes Metab J*. 2012;36:391-398; 3. Morton GJ et al. *Nature*. 2006;443(7109):289-295; 4. Volkow ND et al. *Obes Rev*. 2013;14:2-18.

HOMEOSTASIS in Action…

Review: What are the biological factors that mediate eating behavior?

Hypothalamic Hunger System[1,2]

- Drives eating based on body's energy/calorie needs for survival and function
- Primarily driven by 2 different neuron clusters within the **hypothalamus**
- Detection and integration of energy state information (neuronal and hormonal) from peripheral organs leads to hunger OR satiety
- Altered function in obesity
- **ENERGY HOMEOSTASIS**



Mesolimbic Reward System[3]

- Non-homeostatic drivers of eating
- Center of the brain that mediates pleasure, comfort, **motivation**, **reward**, and **desire** associated with eating
- **Dopamine** and **opioid** signaling known to play important roles

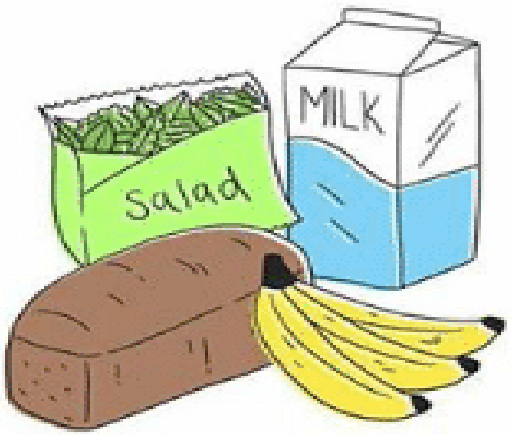
Mesolimbic Reward System can override the Hypothalamic Hunger System, increasing the consumption of highly palatable foods[4]

CNS = central nervous system; POMC = proopiomelanocortin.
Figure adapted from Billes et al.,© 2014, with permission from Elsevier.

1. Billes SK et al. *Pharmacol Res*. 2014;84:1-11;
2. Yu JH et al. *Diabetes Metab J*. 2012;36:391-398;
3. 3. Morton GJ et al. *Nature*. 2006;443(7109):289-295;
4. 4. Volkow ND et al. *Obes Rev*. 2013;14:2-18.

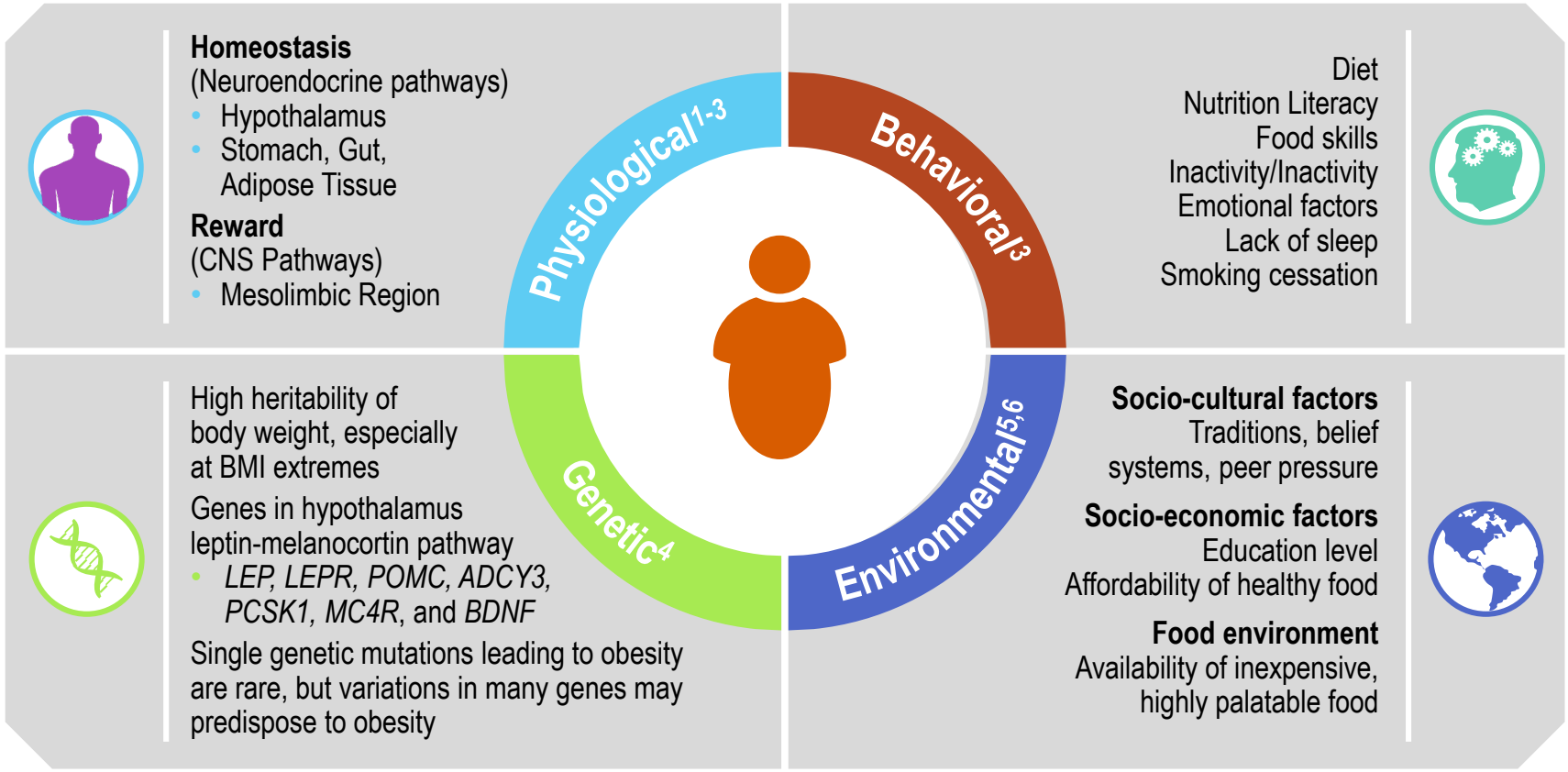
GROCERY SHOPPING

NORMAL DAY



Review:
Why do some people gain weight?

Other factors:
microbiome,
medications,
medical conditions,
mental health



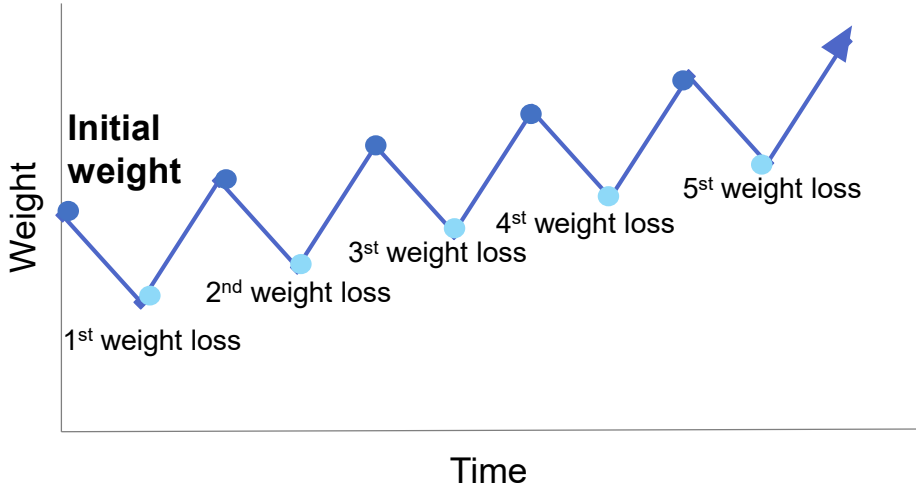
Body weight is determined by a complex interaction of modifiable and non-modifiable factors

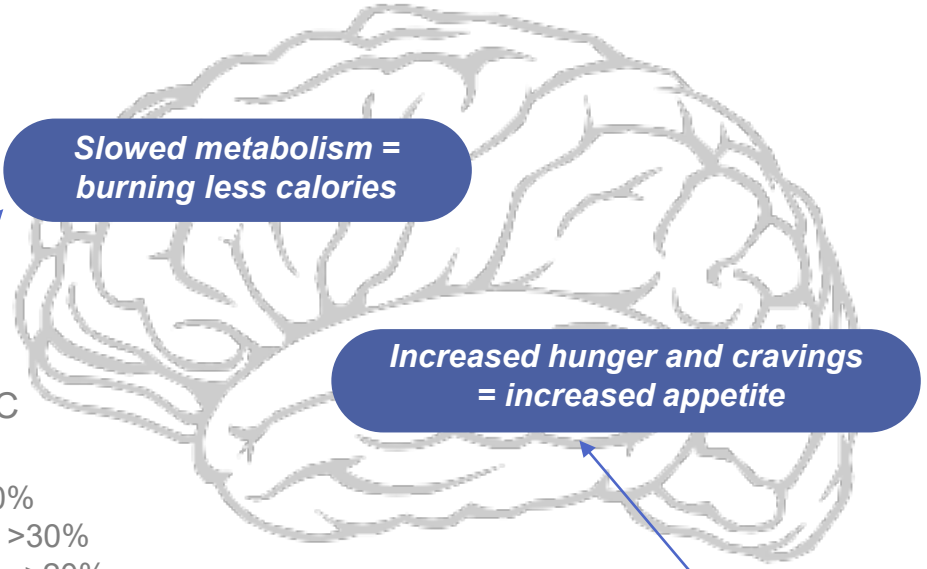
ADCY3 = adenylate cyclase 3; BDNF = brain-derived neurotrophic factor; BMI = body mass index; CNS = central nervous system; GLP-1 = glucagon-like peptide-1; LEP = leptin; LEPR = leptin receptor; MC4R = melanocortin receptor 4; POMC = proopiomelanocortin; PCSK1 = proprotein convertase subtilisin/kexin type 1.

1. Sharma AM, et al. *Obes Rev*. 2010;11:362-370; 2. Chesi A, et al. *Trends Endocrinol Metab*. 2015;26:711-721.

Review: Why do we weight cycle?

The body is designed to defend against weight loss





THERMOGENIC ADAPTATION

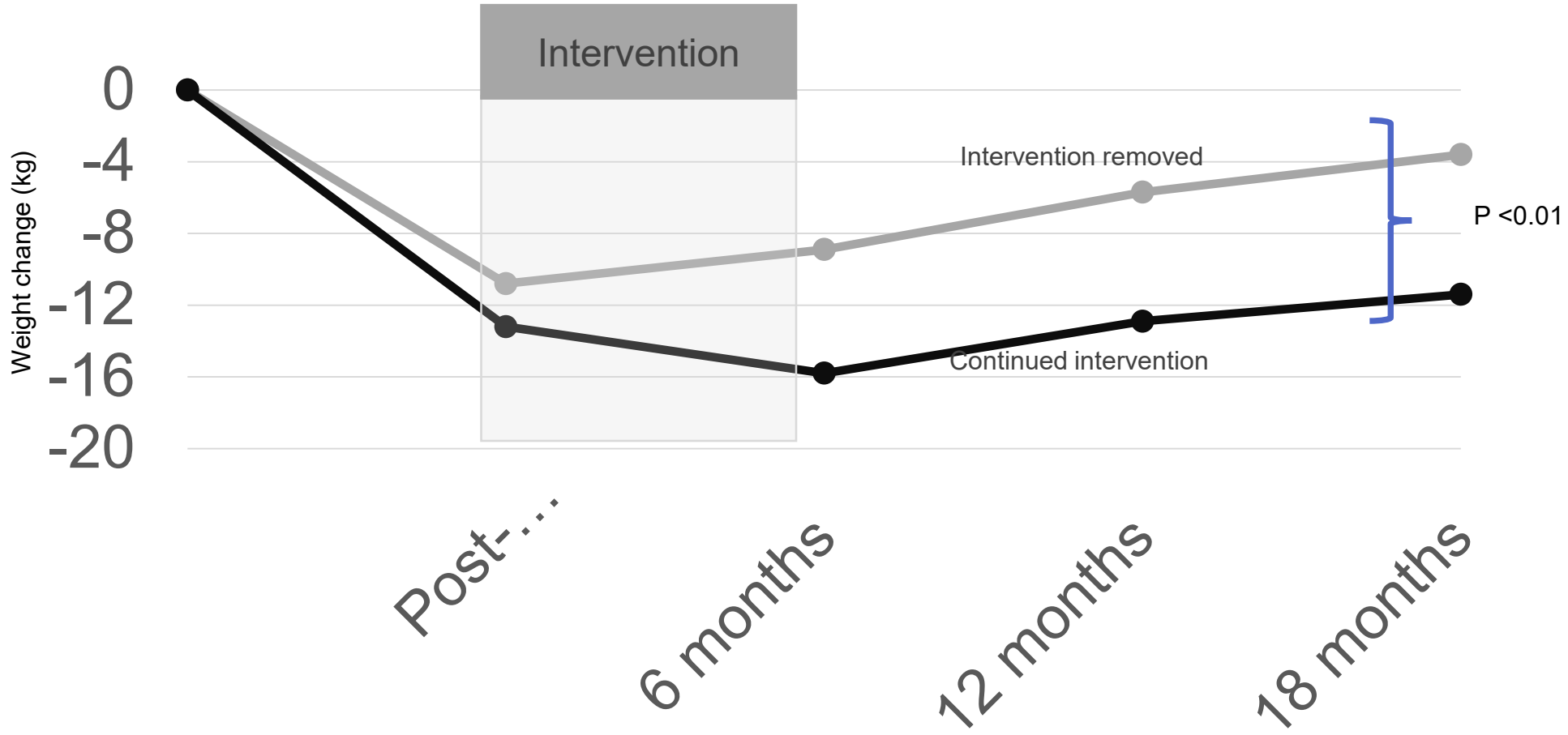
- 24-hour EE ↓ by >20%
- Non-resting EE ↓ by >30%
- Muscle efficiency ↑ by>20%

NEUROHORMONAL ADAPTATION

↓ Leptin
↓ GLP-1, ↓ CCK,
↓ PYY,
↑ Ghrelin

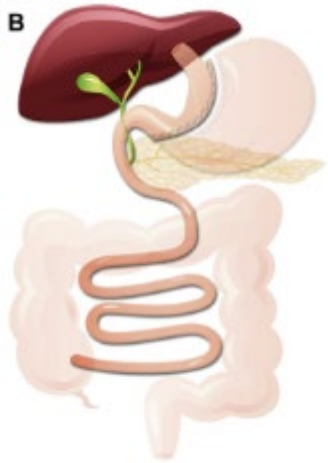
1. Sumithran P *et al*. *N Engl J Med*. 2011;365(17):1597-604.
2. Fothergill E *et al*. Obesity. 2016;24(8):1612-1619.
3. Behary P and Miras AD. *Exp Physoil*. 2014;99(9):1121-1127.

Long-term weight loss requires long term treatment maintenance



Perri MG, et al. J Consult Clin Psychol. 1988 Aug;56(4):529-34.

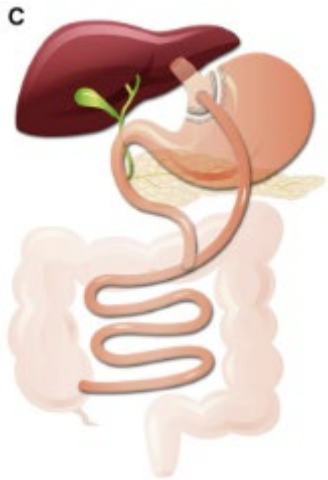
Is it possible to change physiology?



Vertical sleeve gastrectomy (restrictive)

Permanently removes most of the stomach, leaving a sleeve-shaped pouch; results in
↓ ghrelin (hunger hormone)

Weight loss: 25–30%



Roux-en-Y gastric bypass (restrictive & malabsorptive)

Creates a smaller stomach and bypasses part of the intestine; results in ↑ GLP-1 (satiety hormone)

Weight loss: 27–33%

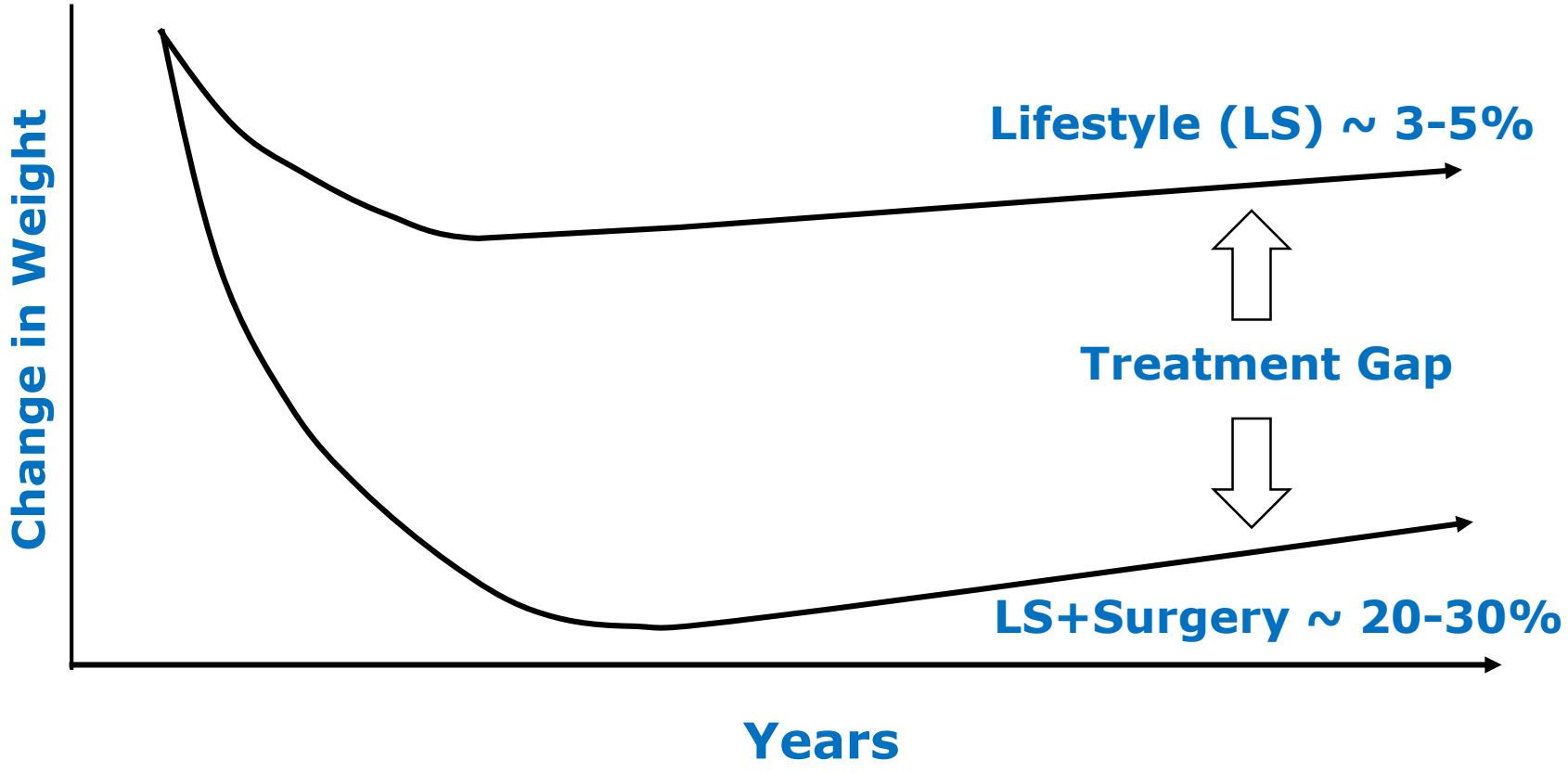
Bileopancreatic diversion (restrictive & malabsorptive)

Similar to Roux-en-Y.
A variant called a duodenal switch retains the pyloric valve

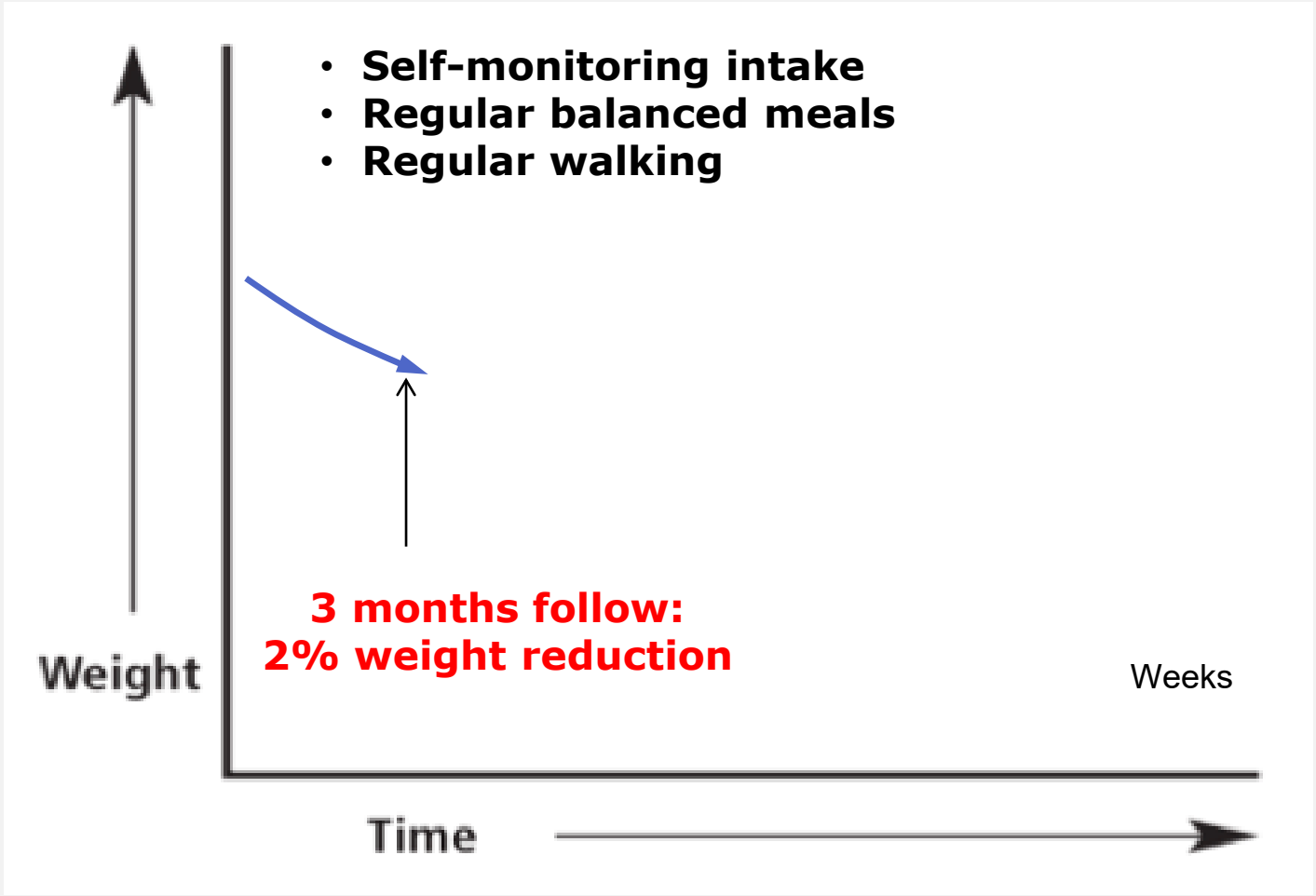
Weight loss: 34%

1. ASMBS. 2014. Available at: http://asmbs.org/patients/bariatric-surgery-procedures; 2. Patel SR, et al. *Surg Obes Relat Dis*. 2013; 9:482–4; 3. Vest AR, et al. *Circulation*. 2013; 127:945–59.

Typical Treatment Success…



Clinical Case: Christa's Progress



"I am doing the best I can, but this is so hard. Is there anything else that can help?"

Speaking with Patients about Anti-Obesity Medications

- Indications for Anti-Obesity Medications
- Orlistat
- Liraglutide
- Naltrexone/Bupropion
- Clinical scenarios…

Indications for Anti-Obesity Medications

BMI ≥27 kg/m^2 + risk factors

or

BMI ≥30 kg/m^2

As an adjunct to health behavior modification

Lau, et al. 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children. CMAJ. 2007;176(8 suppl):Online-1-117.

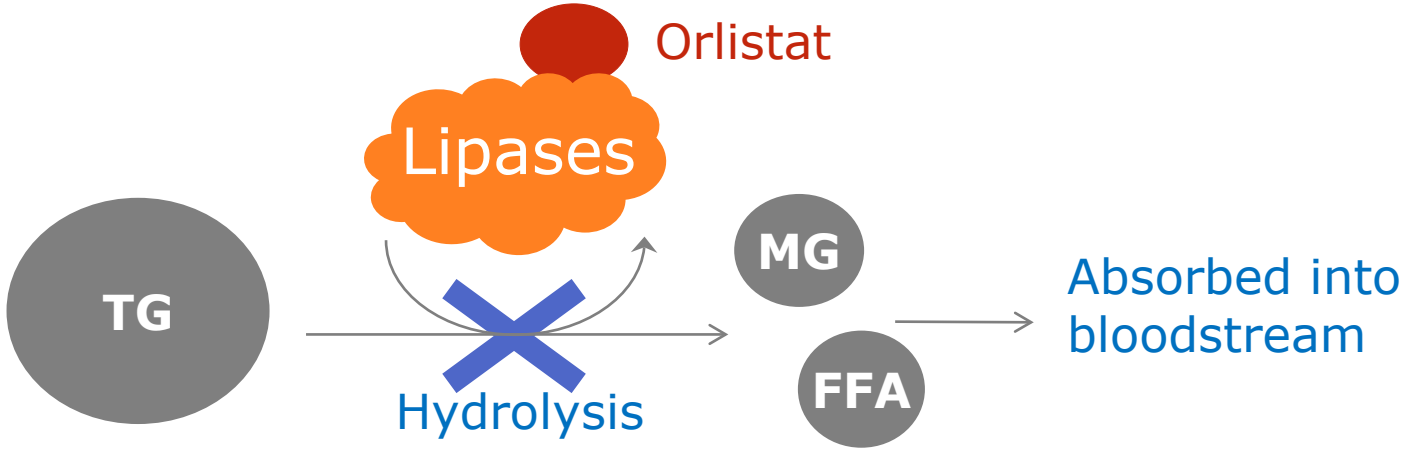
Approved Anti-Obesity Medications in Canada

Drug (trade name)	Health Canada Approval	Mechanism of Action	Major Safety Issues	Tolerability
Orlistat (Xenical®)[1]	1999	Gastrointestinal lipase inhibitor	Fat-soluble vitamin malabsorption	Fecal urgency, fecal incontinence, flatus with discharge, oily spotting
Liraglutide[2] (Saxenda®)	2015	GLP-1 receptor agonist	Gallstones, acute pancreatitis	Nausea, vomiting, diarrhea, constipation, dyspepsia, abdominal pain, headache, fatigue, hypoglycemia, increased lipase
Naltrexone hydrochloride/ Bupropion hydrochloride (CONTRAVE®)[3]	2018	Opioid receptor antagonist / aminoketone antidepressant	Use in controlled hypertension only	Nausea, vomiting, constipation, diarrhea, dizziness, dry mouth

1. Xenical® (product monograph), November 18, 2015, Hoffmann-La Roche Limited, Mississauga, ON;
2. Saxenda® (product monograph), July 12, 2017, Novo Nordisk Canada Inc, Mississauga, ON;
3. 3. CONTRAVE® [product monograph], February 12, 2018, Valeant Canada LP; Laval, QC.

Orlistat: Mechanism of Action

- Reversible inhibitor of pancreatic lipase
- Acts non-systemically in the lumen of the stomach and small intestine to inactivate lipases from hydrolyzing dietary fat
- Undigested triglycerides are not absorbed → resulting caloric deficit results in weight loss
  - At recommended dosage, inhibits dietary fat absorption by approximately 30%



FFA, free fatty acid; MG, monoglycerides; TG, triglycerides

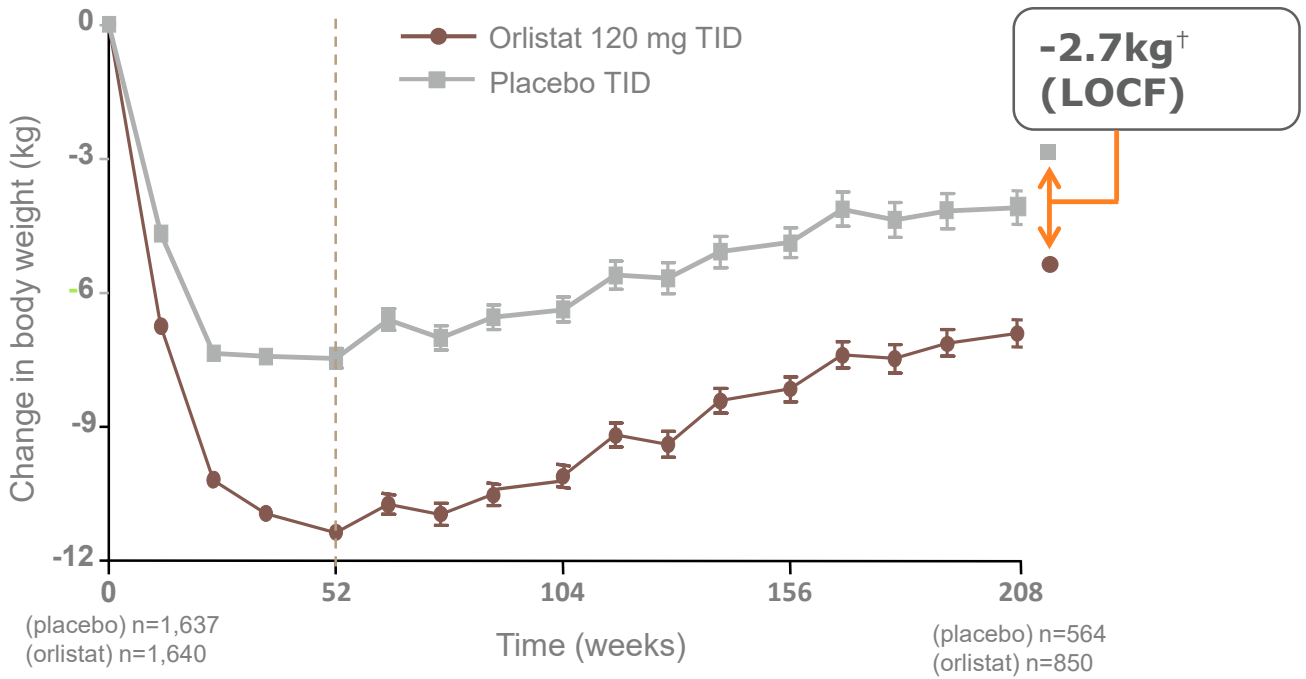
Xenical® (orlistat) Product Monograph. Hoffman-La Roche, Ltd. 2012.

Royal Alexandra HOSPITAL FOUNDATION

CASES Centre for Advancement of Surgical Education & Simulation

Weight reductions with pharmacotherapy: XENDOS trial

ORLISTAT 120 mg TID[1,2]



YEAR 1	YEAR 4
110.4–110.6 kg	110.4–110.6 kg
-11.4 kg	-6.9 kg
vs. 7.5 kg* (completers)	vs. -4.1 kg* (completers)
≥5% weight loss 73% vs. 45%*	≥5% weight loss 53% vs. 37%*
>10% weight loss 41% vs. 21%*	>10% weight loss 26% vs. 16%*

Relative risk reduction of developing type 2 diabetes: 45%

* $p<0.001$; † $p<0.001$ by LOCF analysis (last observation carried forward): IGT, impaired glucose tolerance; NNT, number needed to treat

1. Torgerson JS, et al. Diabetes Care. 2004;27:155-61; 2. Xenical® (orlistat) Product Monograph. Hoffman-La Roche, Ltd. 2012.

Orlistat: SAFETY AND TOLERABILITY

ADVERSE EVENT (AE)	ORLISTAT n = 1,913 (%)	PLACEBO n = 1,466 (%)
Oily spotting	26.6	1.3
Flatus with discharge	23.9	1.4
Fecal urgency	22.1	6.7
Fatty/oily stool	20.0	2.9
Oily evacuation	11.9	0.8
Increased defecation	10.8	4.1
Fecal incontinence	7.7	0.9

Xenical® (product monograph), September 27, 2017, Cheplapharm, Germany.

Clinical Considerations:
Orlistat

Dosage:

- 120 mg TID with food (during or up to 1 hour post meal)
- Should be on a nutritionally balanced, mildly hypocaloric diet that contains no more than 30% calories from fat
- Macronutrients should be distributed over meals/snacks

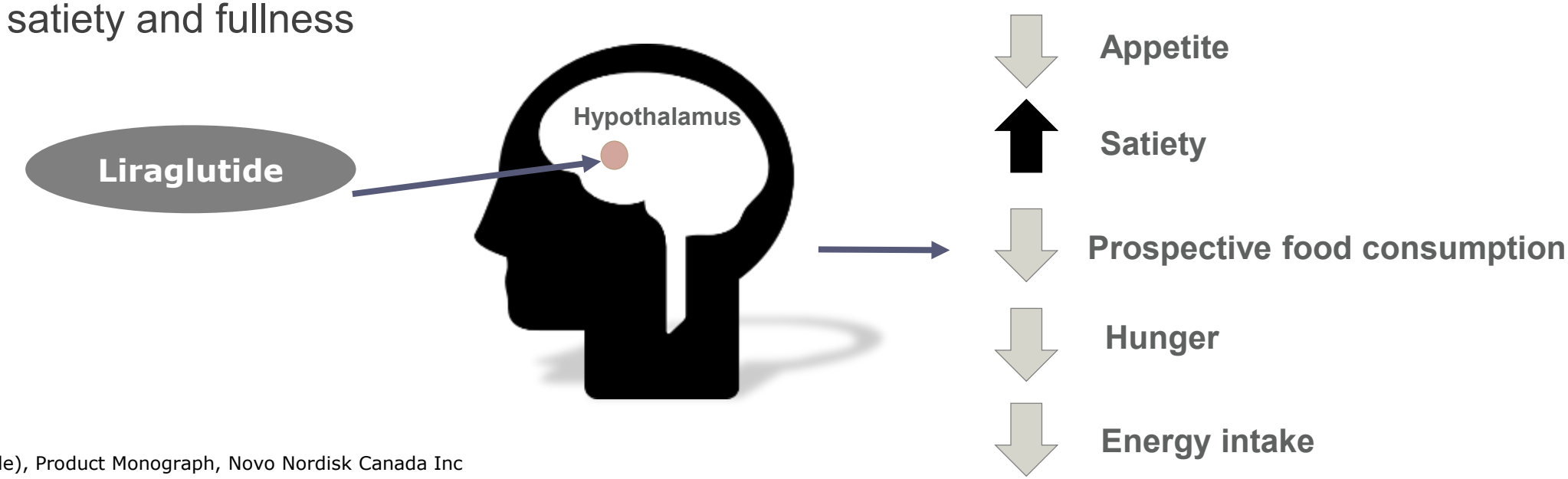
Contraindications:

- Chronic malabsorption syndrome
- Cholestasis
- Known hypersensitivity to orlistat or any components of the product

Xenical® (product monograph), September 27, 2017, Cheplapharm, Germany.

Liraglutide mechanism of action

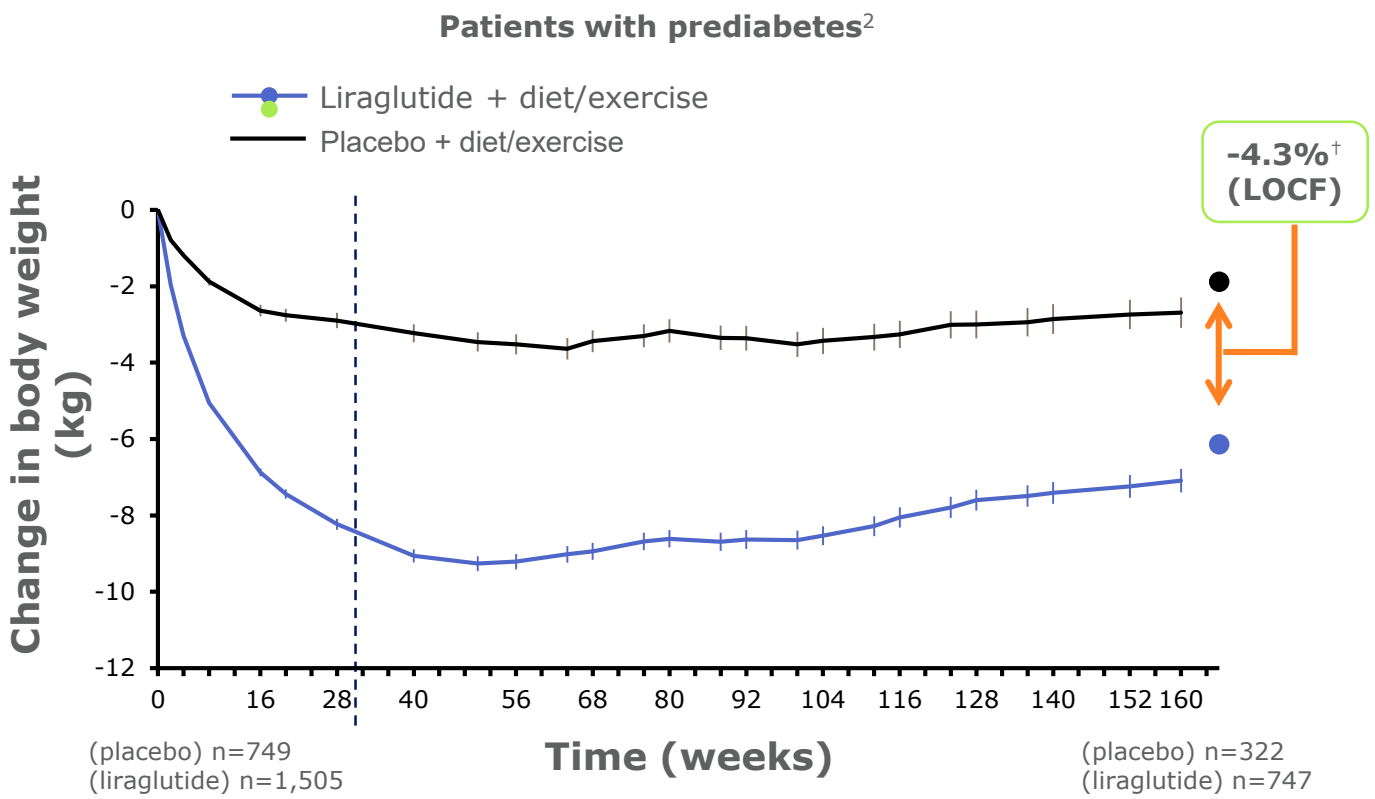
- Glucagon-like peptide-1 (GLP-1) is a physiologic regulator of appetite and food intake
  - GLP-1 receptors are present in several areas of the brain involved in appetite regulation
  - GLP-1 also exerts effects in other parts of the body, including the heart and GI tract
- Liraglutide is a human GLP-1 receptor agonist with 97% homology to endogenous human GLP-1
  - Liraglutide signal is highly localized—accesses the hypothalamus directly to mediate satiety and fullness



Saxenda® (liraglutide), Product Monograph, Novo Nordisk Canada Inc , July 2017; Secher A, et al. *J Clin Invest*. 2014;24(10):4473-88.

Weight reductions with pharmacotherapy: SCALE™ Obesity and Prediabetes trial

LIRAGLUTIDE 3 mg once daily



YEAR 1[1]	YEAR 3[2]
Patients with and without prediabetes (N=3,731)‡ 106.2 kg	Patients with prediabetes (N=2,254) 107.5–107.9 kg
-9.2% vs. -3.5%* (completers)	-7.1% vs. -2.7%§ (completers)
≥5% weight loss 63.2% vs. 27.1%*	≥5% weight loss 49.6% vs. 23.7%#
>10% weight loss 33.1% vs. 10.6%*	>10% weight loss 24.8% vs. 9.9%#

Relative risk reduction of developing type 2 diabetes: 79.3%

*p<0.001; † p<0.0001 by LOCF analysis (last observation carried forward); ‡ Weight loss was similar regardless of prediabetes status.[1] # p<0.0001; § p-value not available

1. Pi-Sunyer et al. *N Engl J Med*. 2015;373(1):11-22; 2. le Roux et al. *Lancet*. 2017. doi: 10.1016/S0140-6736(17)30069-7.

Liraglutide
SAFETY AND TOLERABILITY

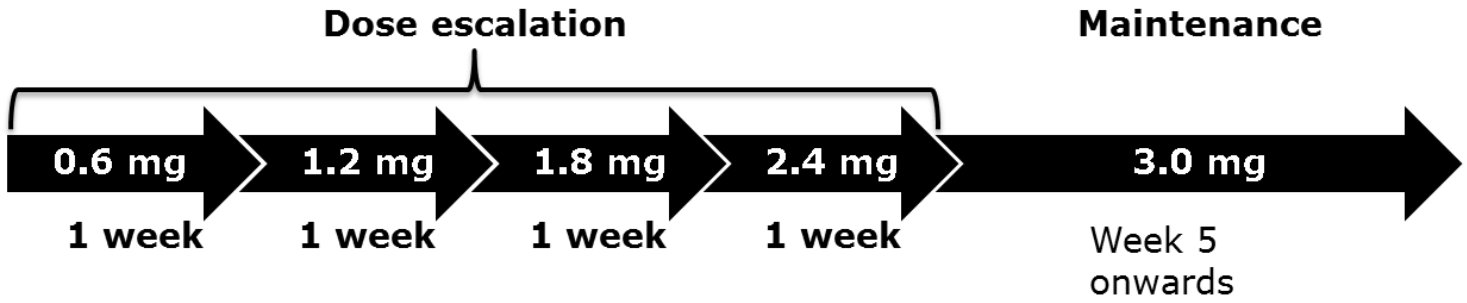
ADVERSE EVENT (AE)	LIRAGLUTIDE n = 3,384 (%)	PLACEBO n = 1,941 (%)
Nausea	39.3	13.8
Diarrhea	20.9	9.9
Constipation	19.4	8.5
Vomiting	15.7	3.9
Dyspepsia	9.6	2.7
Abdominal pain	5.4	3.1
Upper abdominal pain	5.1	2.7
Decreased appetite	10.0	2.3
Fatigue	7.5	4.6
Dizziness	6.9	5.0
Increased lipase	5.3	2.2

Saxenda® (product monograph), July 12, 2017, Novo Nordisk Canada Inc, Mississauga, ON.

Remember: Dose escalation protocol!

Clinical Considerations:
Liraglutide

Dosage:



- If difficulty with side effects, may slow down titration

Contraindications:

- Personal or family history of medullary thyroid carcinoma
- Multiple Endocrine Neoplasia syndrome type 2 (MEN 2)
- Hypersensitivity to liraglutide or any ingredient in the formulation
- Pregnancy or breast-feeding

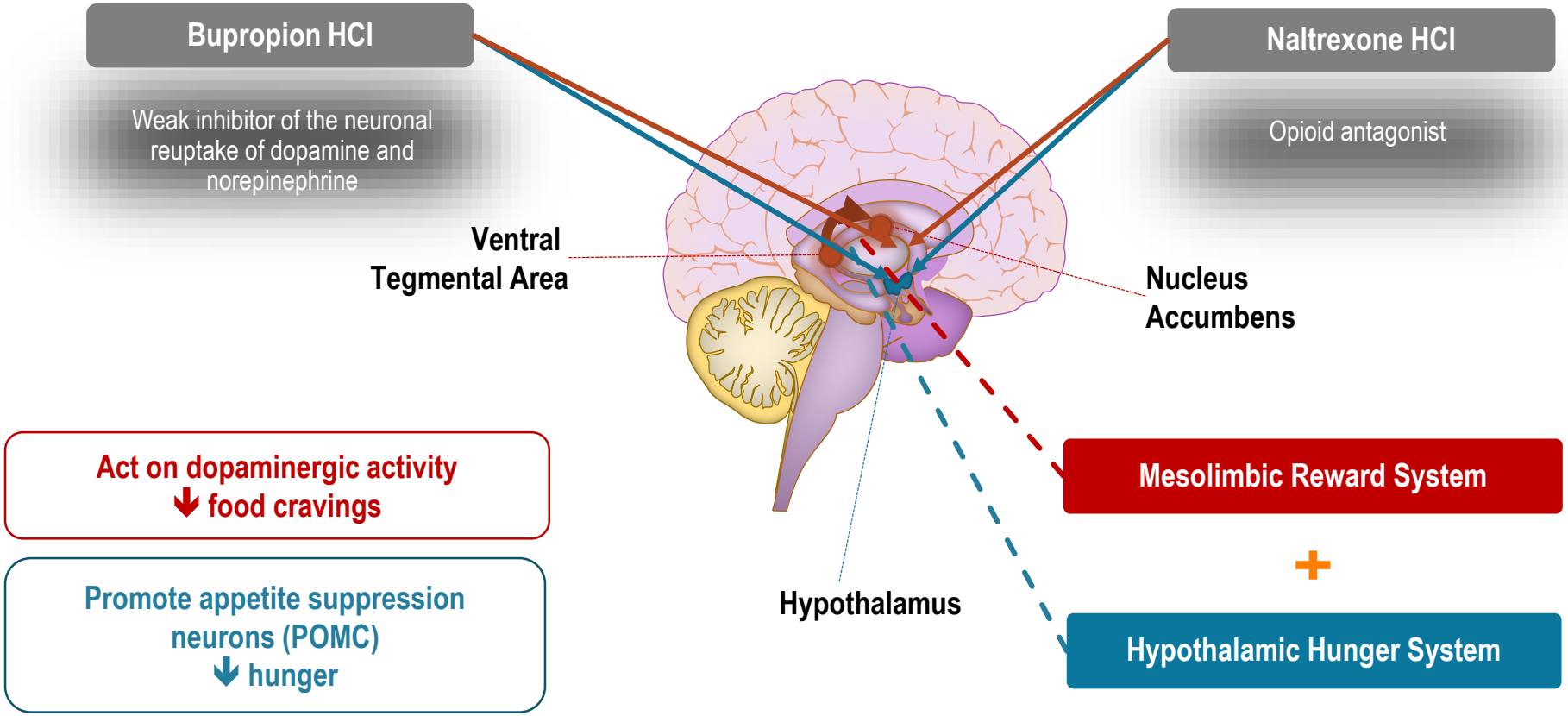
Saxenda® (product monograph), July 12, 2017, Novo Nordisk Canada Inc, Mississauga, ON.

Royal Alexandra HOSPITAL FOUNDATION

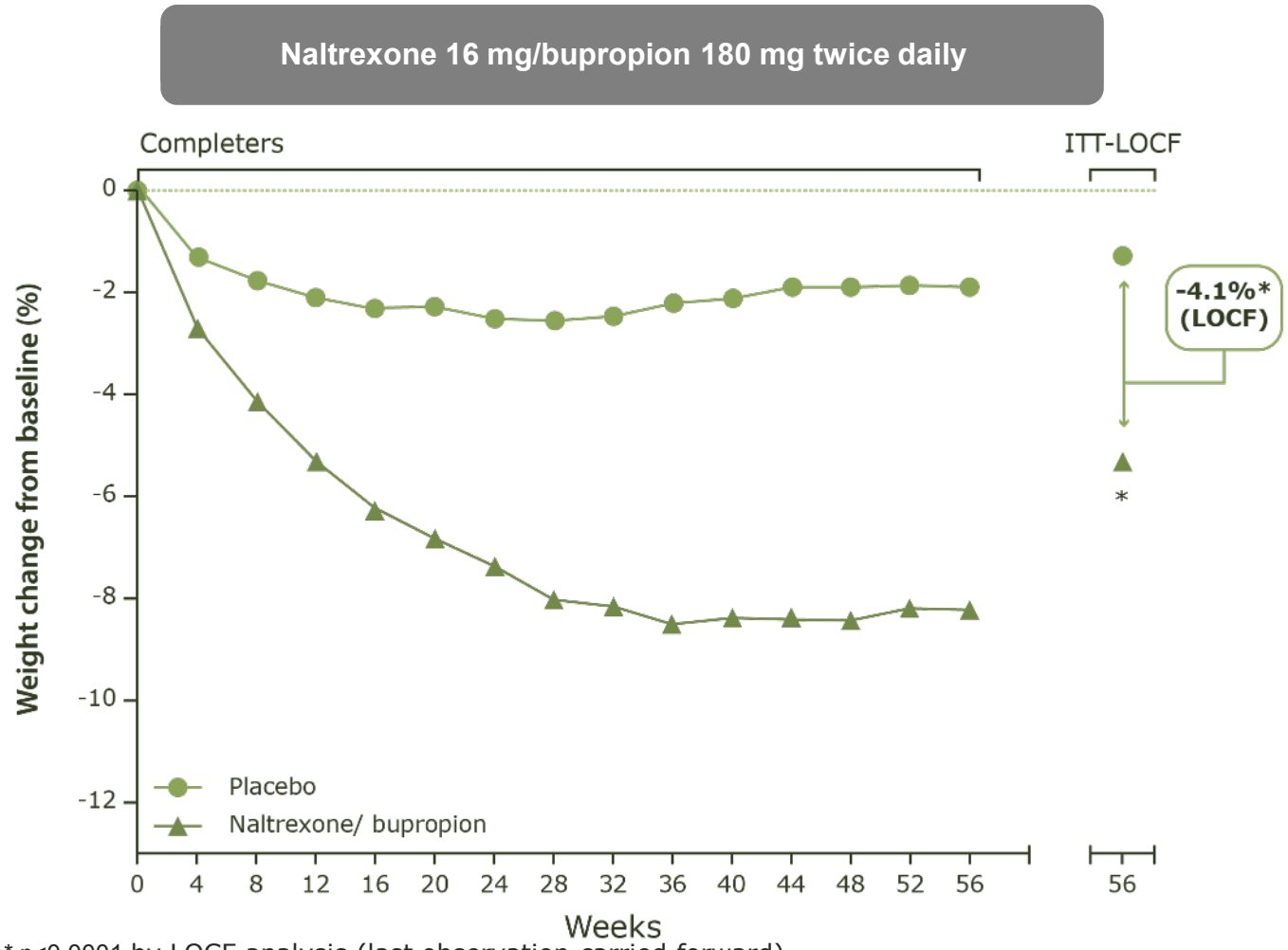
CASES Centre for Advancement of Surgical Education & Simulation

Naltrexone/Bupropion: MOA

Both components have effects on two separate areas of the brain involved in the regulation of food intake; the hypothalamus and the mesolimbic region



Weight reductions with pharmacotherapy: COR-I trial



At 56 weeks
N=538 99.7 kg
-8.1% vs. -1.8%* (completers)
≥5% weight loss 42% vs. 17%*
>10% weight loss 21% vs. 7%*

* $p<0.0001$ by LOCF analysis (last observation carried forward)

Contrave® (naltrexone/bupropion), Product Monograph, Valeant Canada, February 2018.

Royal Alexandra HOSPITAL FOUNDATION

CASES Centre for Advancement of Surgical Education & Simulation

Naltrexone/bupropion
SAFETY AND TOLERABILITY

POOLED ANALYSIS
- COR-I
- COR-II
- COR-BMOD
- COR-DM

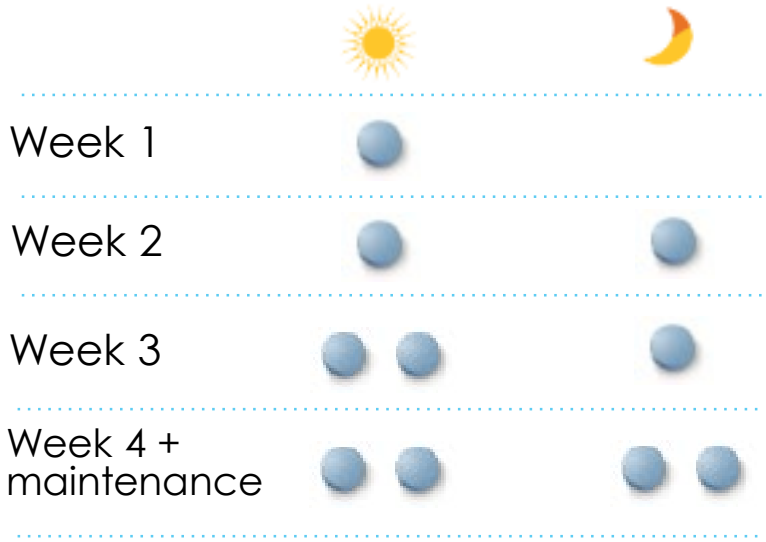
ADVERSE REACTION	CONTRAVE* n = 2,545 (%)	PLACEBO n = 1,515 (%)
Nausea	32.5	6.7
Constipation	19.2	7.2
Headache	17.6	10.4
Vomiting	10.7	2.9
Dizziness	9.9	3.4
Insomnia	9.2	5.9
Dry mouth	8.1	2.3
Diarrhea	7.1	5.2

BMOD = behavioural modification; DM = type 2 diabetes mellitus

*CONTRAVE® 32 mg/360 mg for up to 52 weeks (n=2,482) or a combination of naltrexone 32 mg and bupropion SR 400 mg/day (n=63) for up to 24 weeks CONTRAVE® (product monograph), February 12, 2018, Valeant Canada LP, Laval, QC.

Clinical Considerations: Naltrexone/Bupropion Dosing…

CONTRAVE dosing should be escalated over a 4-week period



Tablets should be taken by mouth in the morning and evening and should not be cut, chewed, or crushed.

The dose escalation protocol was designed with the intent to allow patients to acclimate to CONTRAVE and to minimize the risk of seizure as well as mitigate the onset of transient nausea.

In clinical trials, CONTRAVE was administered with meals; however, CONTRAVE should not be taken with a high-fat meal because of a resulting significant increase in bupropion and naltrexone systemic exposure.

CONTRAVE® (product monograph), February 12, 2018, Valeant Canada LP, Laval, QC.

Clinical Considerations
Naltrexone/Bupropion Contraindications…

NALTREXONE-RELATED	BUPROPION-RELATED
• Chronic opioid use	• Uncontrolled hypertension • Bupropion containing drugs • Seizures, bulimia, anorexia • Abrupt discontinuation of significant alcohol use • MAOI use • Thioridazine use • Tamoxifene use • Abrupt discontinuation of alcohol, benzodiazepines, or other sedatives and antiepileptic drugs
• Severe hepatic impairment • End-stage renal failure	• Severe hepatic impairment • End-stage renal failure
All weight management medications: Pregnancy	

MOAI = monoamine oxidase inhibitor

CONTRAVE® (product monograph), February 12, 2018, Valeant Canada LP, Laval, QC.

Polling Question

What would your next step be with Christa?

A. Explain the anti-obesity medications available, and prescribe one of them.

B. Encourage her to continue with health behaviour efforts for a few more months, then follow up to revisit anti-obesity medications.

C. Refer her to the allied health team to intensify her treatment.

D. A, B and C

E. Explain options A, B, C and D, and let the patient decide.

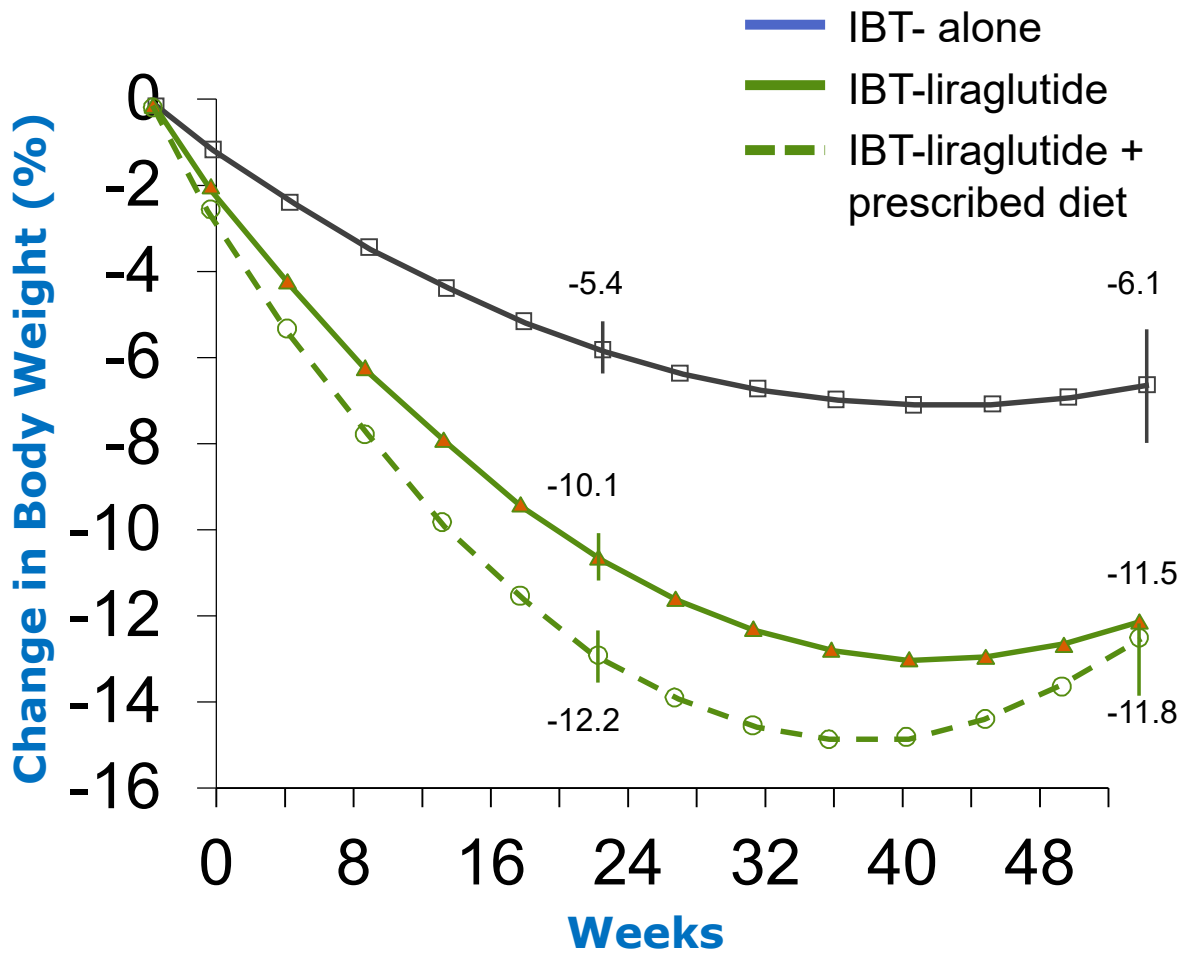
Clinical Case:

"If I do an intensive weight loss program, will medications help?"

Royal Alexandra HOSPITAL FOUNDATION

CASES
Centre for Advancement of Surgical Education & Simulation

Additive Benefits of Behaviour Change and Pharmacologic Intervention: Liraglutide



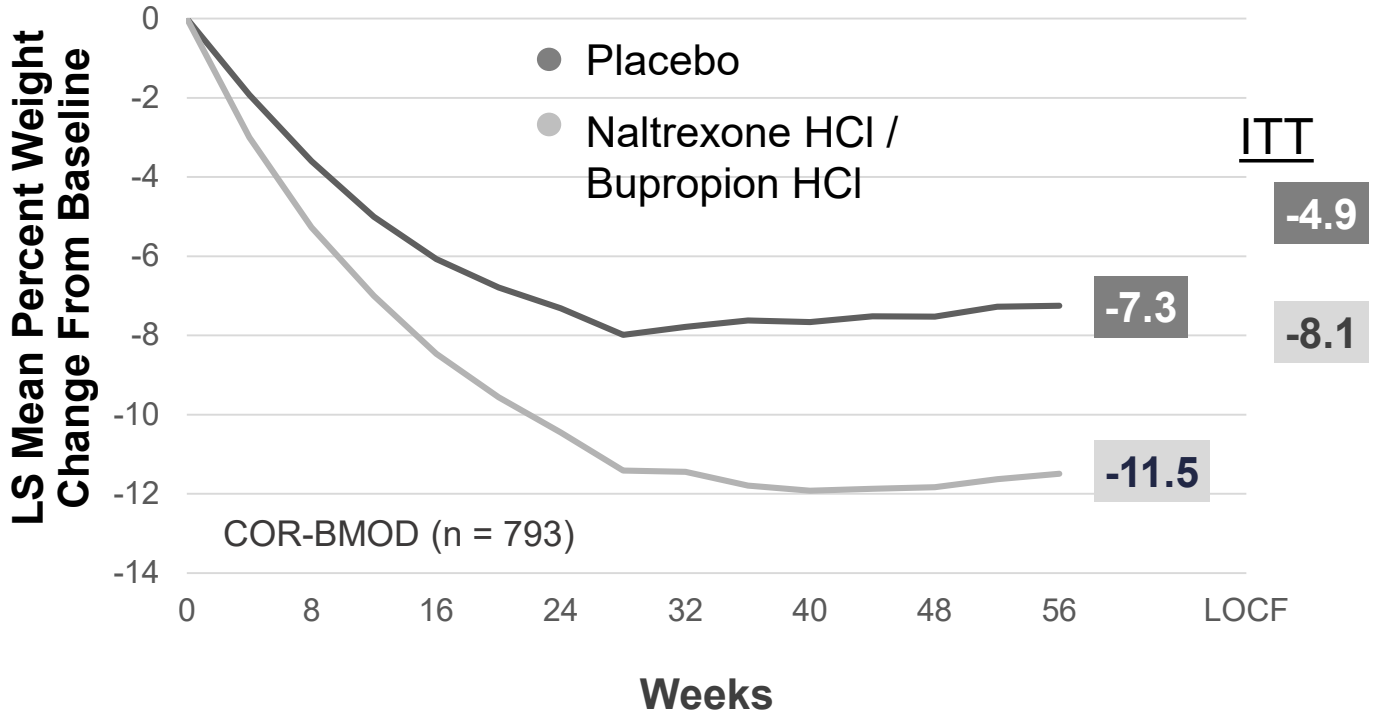
- 150 participants
- All received intensive behavioral therapy (IBT)
- Randomized 1:1:1 to receive no additional treatment, liraglutide, or liraglutide and a prescribed meal replacement diet (1000–1200 kcal/d)
- Mean weight loss was evident in all 3 groups, and significantly higher in both groups taking liraglutide relative to IBT-only ($P < 0.01$)

Wadden et al., Obesity. 2019; 27:75-86.

Royal Alexandra HOSPITAL FOUNDATION

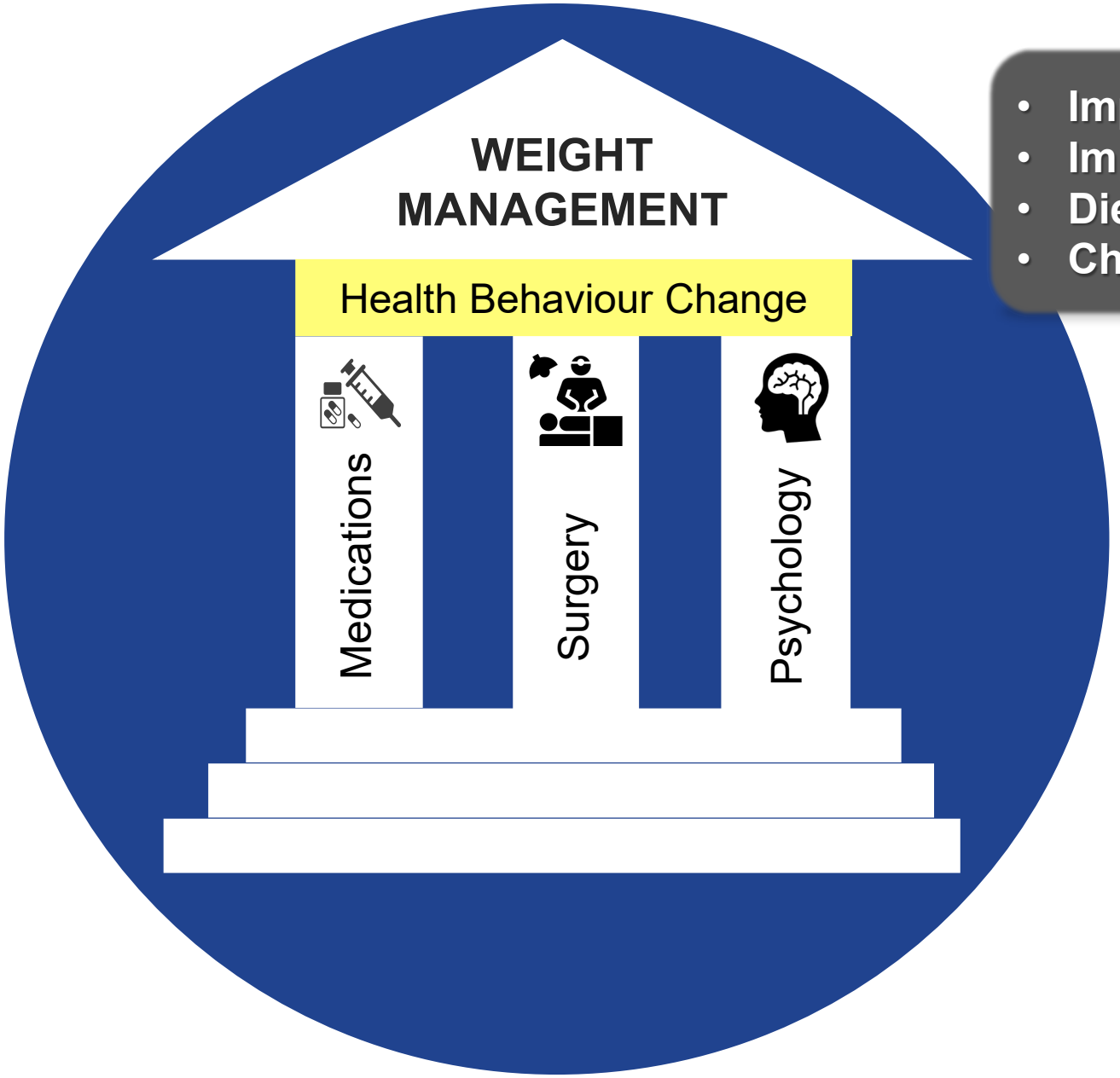
CASES Centre for Advancement of Surgical Education & Simulation

Additive Benefits of Behaviour Change and Pharmacologic Intervention: Naltrexone/ Bupropion



- 793 participants
- All received behavioural modification (BMOD) counselling
- Randomized 3:1 to receive naltrexone/ bupropion or placebo
- Mean weight loss was evident in both groups, and significantly higher in patients taking active treatment (P < 0.001)

Wadden TA, et al. Obesity (Silver Spring). 2011; 19(1): 110–120.



- Improved Health
- Improved Body Image
- Dietary changes
- Changes in activity

Adapted with permission from Dr. Sean Wharton, Co-Chair Canadian Clinical Practice Guidelines on the management of Obesity in Adults

Royal Alexandra HOSPITAL FOUNDATION

CASES Centre for Advancement of Surgical Education & Simulation

Clinical Case: Side Effects

She would like to try one of the newer anti-obesity medications.

You start at a lower dose, and educate her on how to titrate the medication up, and you ask her to follow up in 1 month.

She returns in 4 weeks for a follow up:

"I did well for the first 2 weeks. I noticed the effect of the medication and the side effects weren't so bad. But when I tried to increase the medication on week 3, I felt the side effects. I wasn't sure what to do, so I stopped the medication."

Polling Question

What would your next step be with Christa?

A. Discontinue the medication and prescribe something else

B. Restart the medication you originally prescribed and slow down the titration protocol.

Clinical Case

"How long should I stay on medication?"

Royal Alexandra HOSPITAL FOUNDATION

CASES
Centre for Advancement of Surgical Education & Simulation

Polling Question

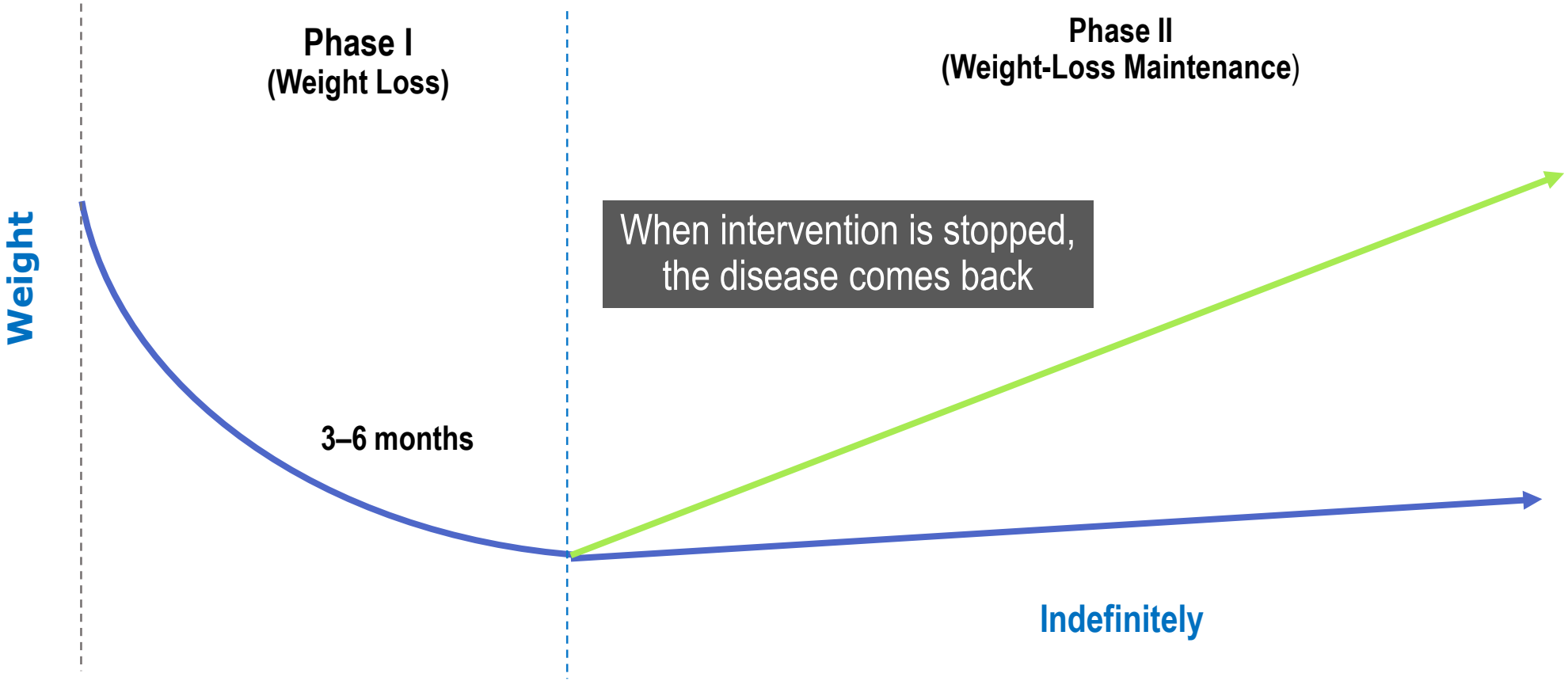
What would your response be?

A. She should stay on the medication until she reaches the target weight.

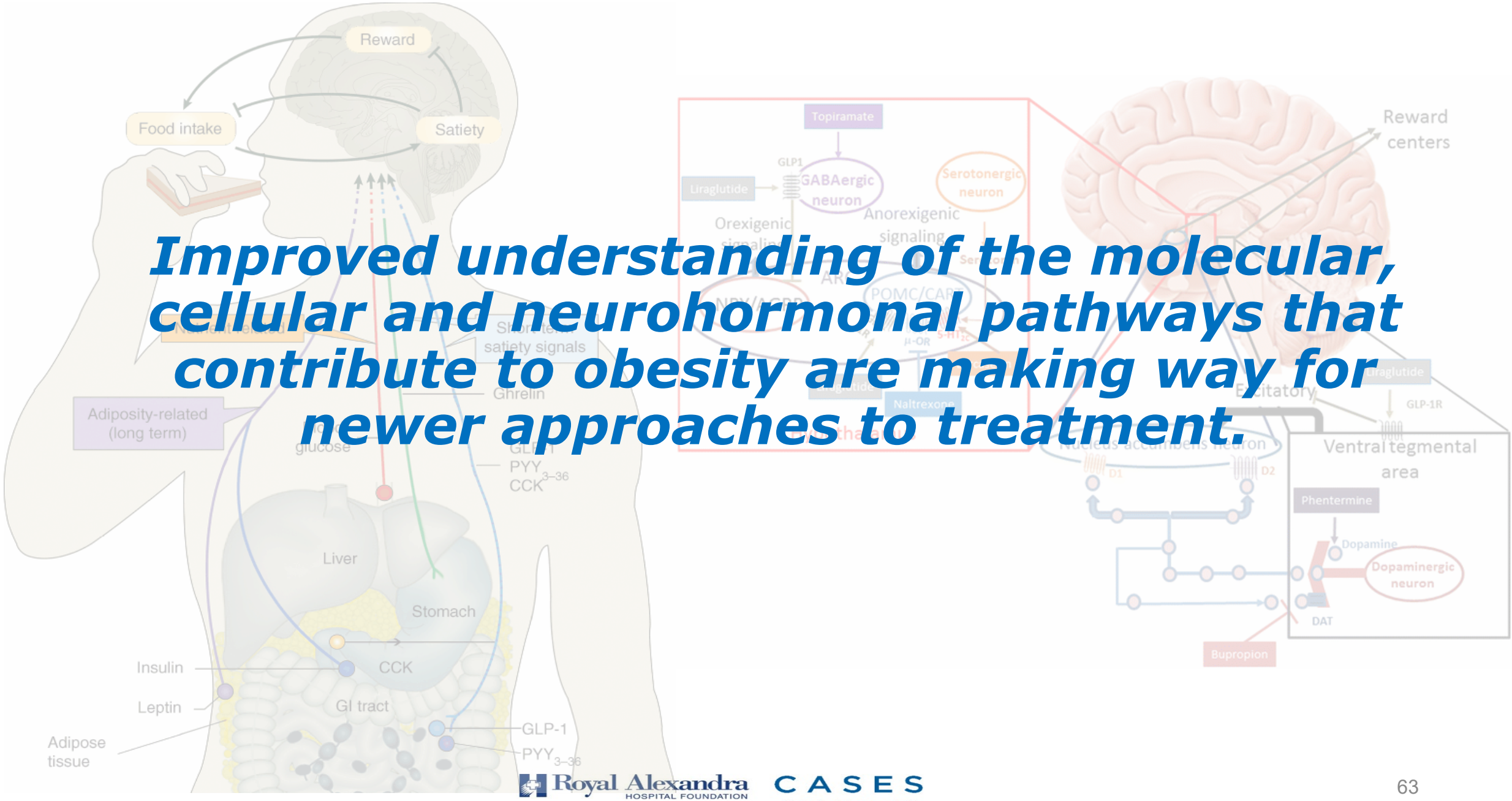
B. She can stay on the medication until it stops working.

C. Obesity is a chronic disease, and therefore needs to be treated long term, similar to diabetes and hypertension. If the medication is withdrawn, then she will be vulnerable to weight regain.

Obesity is a Chronic Disease.



Adapted from www.drsharma.ca and Ryan DH, et al. *Arch Intern Med* 2010;170(2):146



Improved understanding of the molecular, cellular and neurohormonal pathways that contribute to obesity are making way for newer approaches to treatment.

Royal Alexandra HOSPITAL FOUNDATION

CASES
Centre for Advancement of Surgical Education & Simulation

Summary…

- Obesity is a complex chronic disease.
- The brain plays a critical role in controlling hunger, cravings, and eating behaviour, as well as in regulating body weight.
- There are biological adaptive responses to weight loss that defend body weight and favour weight gain, making sustained weight loss very difficult with health behaviour alone.
- Multimodal intervention that is maintained long term is required for effective weight management. This can include behaviour therapy, pharmacotherapy and surgery.
- Newer approaches to obesity treatment are available in Canada.

QUESTIONS?