Northern Ontario Women's Health Conference

Obesity Treatment: Know Better, Do Better

Dr. Sasha High FRCPC ABOM

Disclosure Slide

- **Relationships with commercial interests:**
  - **Speakers Bureau/Honoraria:** Novo Nordisk, Bausch Health, Takeda, Obesity Canada
  - **Consulting Fees:** Novo Nordisk, Bausch Health
  - **Other:** Founder of the High Metabolic Clinic and *Best Weight with Sasha High MD*

- **Potential for conflict(s) of interest:**
  - Sasha High has received payment from Novo Nordisk and Bausch Health whose product(s) are being discussed in this program

Learning Objectives

At the end of this presentation, participants will be able to:

1. Review and discuss the definition of obesity (including potential bias/stigma).

2. Review current evidence on obesity and relevant risk factors, specifically pertaining to women's health.

3. Discuss how to address and treat obesity in an empowering way.

Old Paradigm

Calories in

Calories out

Rx = Eat less, exercise more

Obesity is a brain-based disorder

Genetics and Epigenetics

Psychology

Hyperpalatable Food environment

Peripheral hormones

Medical conditions and medications

Age, ethnicity, sex Menopause

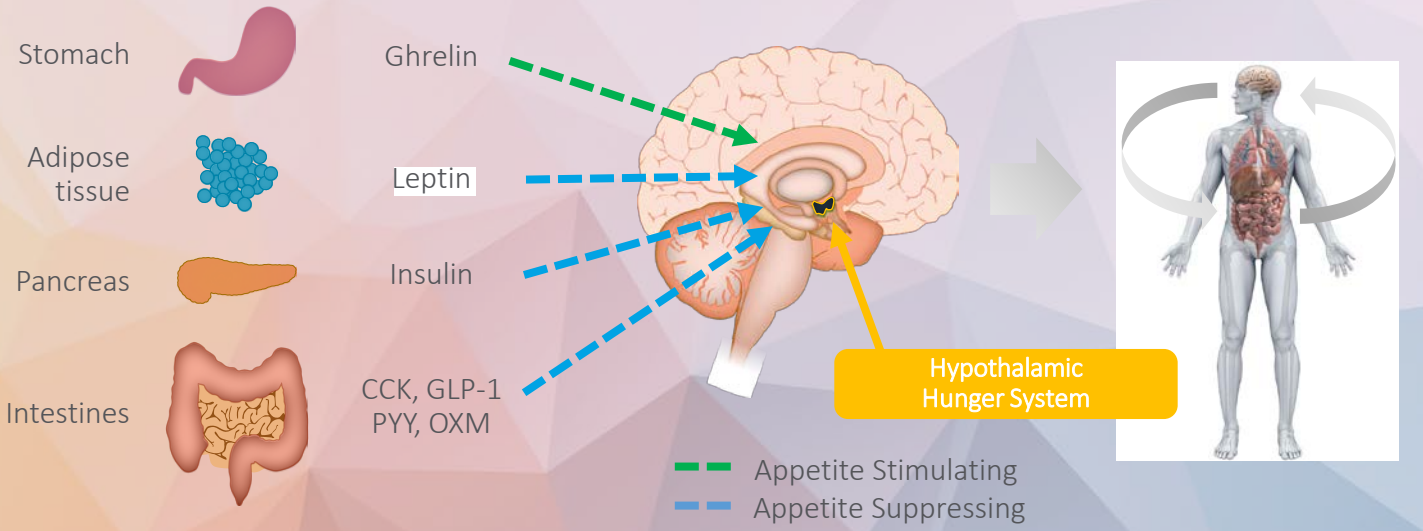
Sociocultural factors, Economics

Hypothalamus: Homeostatic eating – eating for hunger

Peripheral signals relay information about nutritional status

Signals are integrated in specific regions of the CNS

Control of food intake, Control of energy expenditure, Body weight homeostasis



CCK = cholecystokinin; CNS = central nervous system; GLP-1 = glucagon-like peptide 1; OXM = oxyntomodulin; PYY = peptide YY.

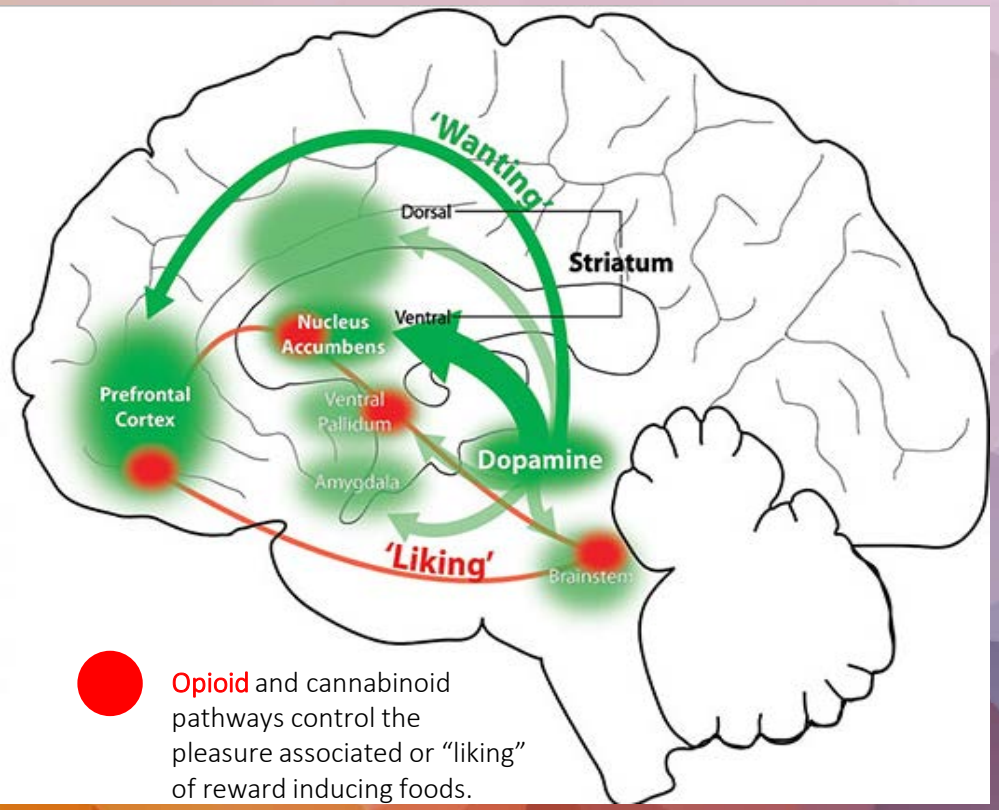
Mendieta-Zerón H et al. Gen Comp Endocrinol. 2008;155:481-495.

Homeostatic eating – eating for hunger

Yes, it's your hormones.
No, it's not your thyroid.

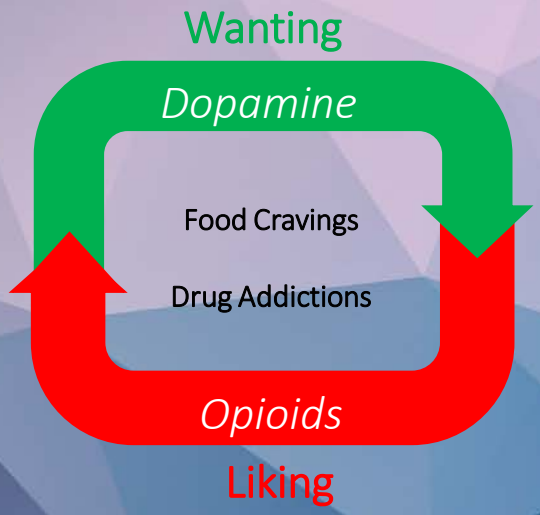
CCK = cholecystokinin; CNS = central nervous system; GLP-1 = glucagon-like peptide 1; OXM = oxyntomodulin; PYY = peptide YY.
Mendieta-Zerón H et al. Gen Comp Endocrinol. 2008;155:481-495.

Limbic system:
Hedonic eating – eating for pleasure



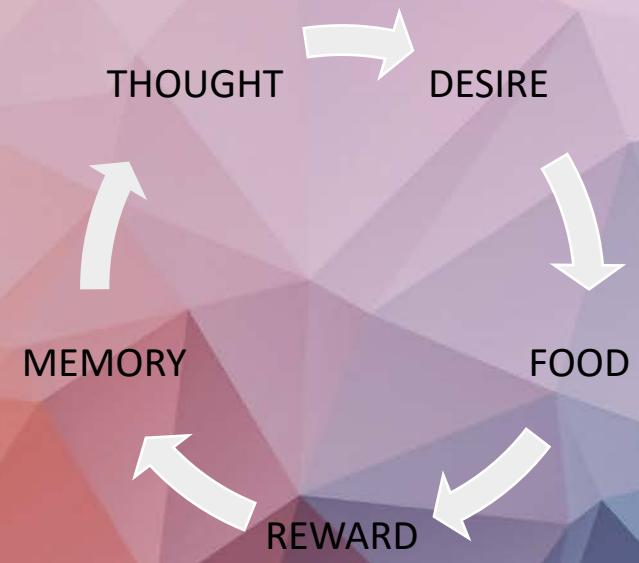
Opioid and cannabinoid pathways control the pleasure associated or "liking" of reward inducing foods.

Dopaminergic pathways control the motivation and drive or "wanting" to eat reward inducing foods.



Adapted from: Berridge KC (2018) Evolving Concepts of Emotion and Motivation. Front. Psychol. 9:1647

Natural cycle of reward learning: Learning is intensified by our reward



What happens with over-reward?

THOUGHT

OVER DESIRE

FOOD

OVER REWARD

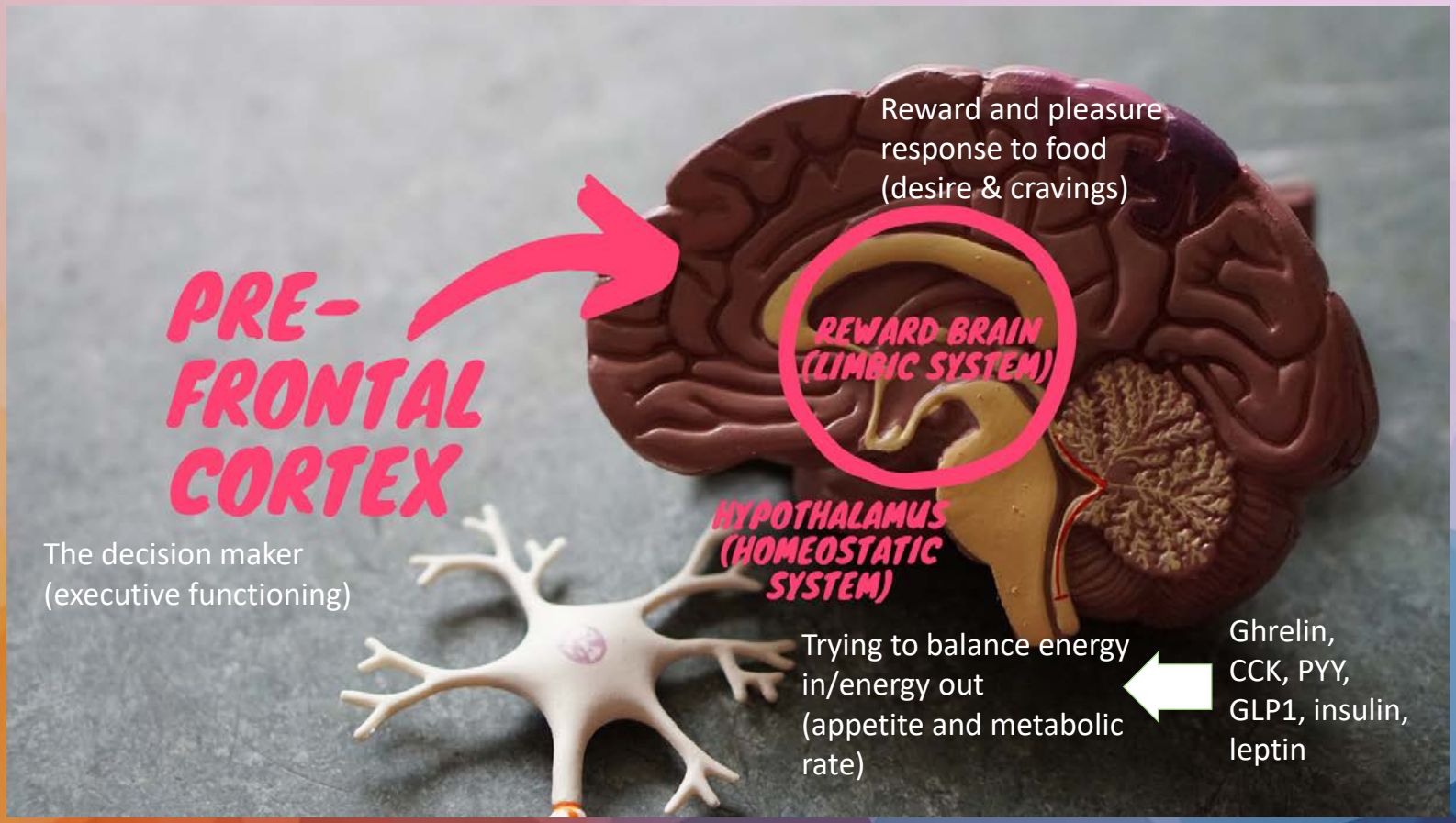
MEMORY

ASSOCIATIVE LEARNING

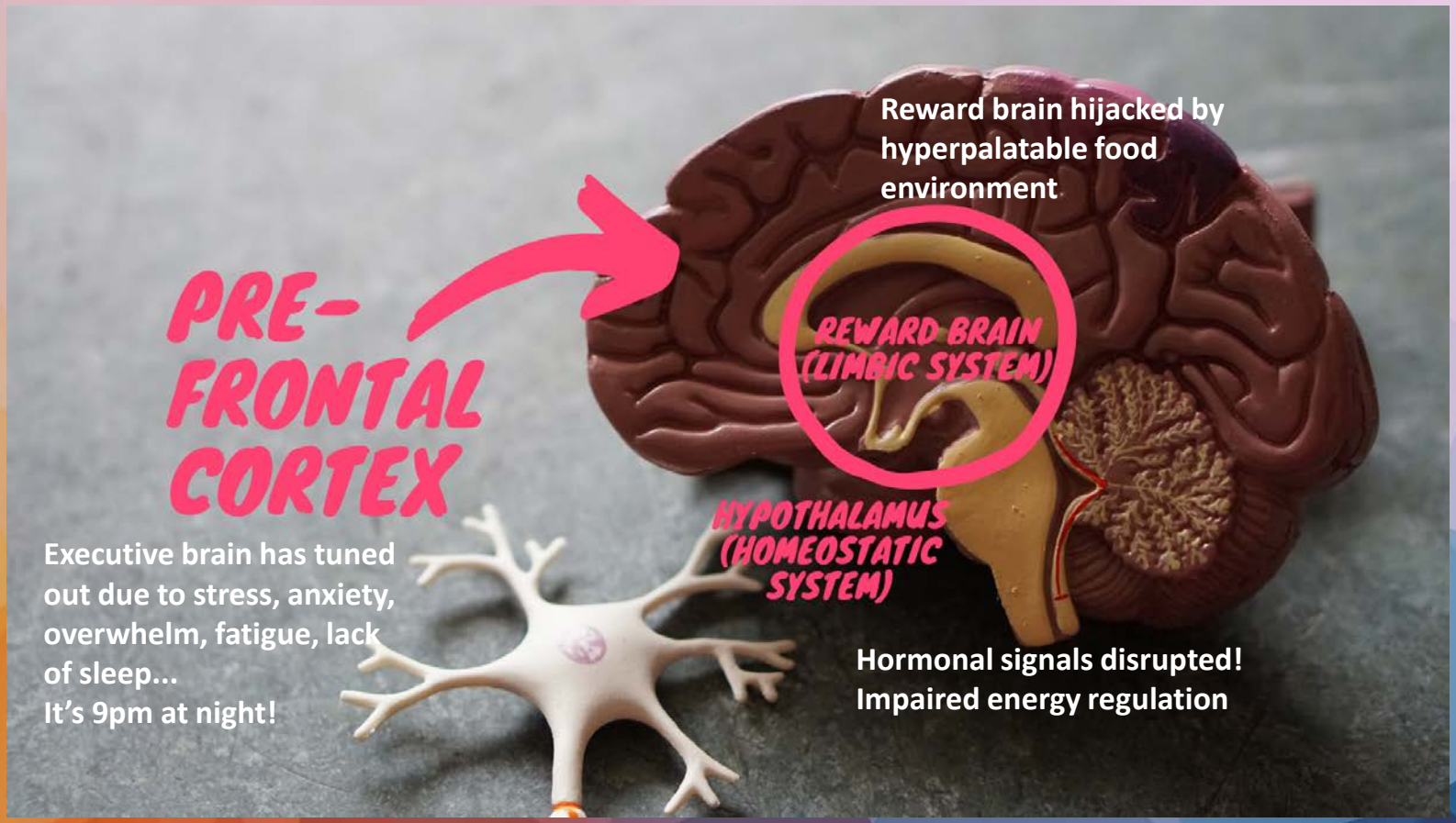
Evening
Dim lighting
Sitting in front of TV
Relaxing
Stress

Food is arguably the most powerful reinforcer of behaviour on the planet.

The Brain is the Energy and Appetite Regulation Center



The Brain is the Energy and Appetite Regulation Center

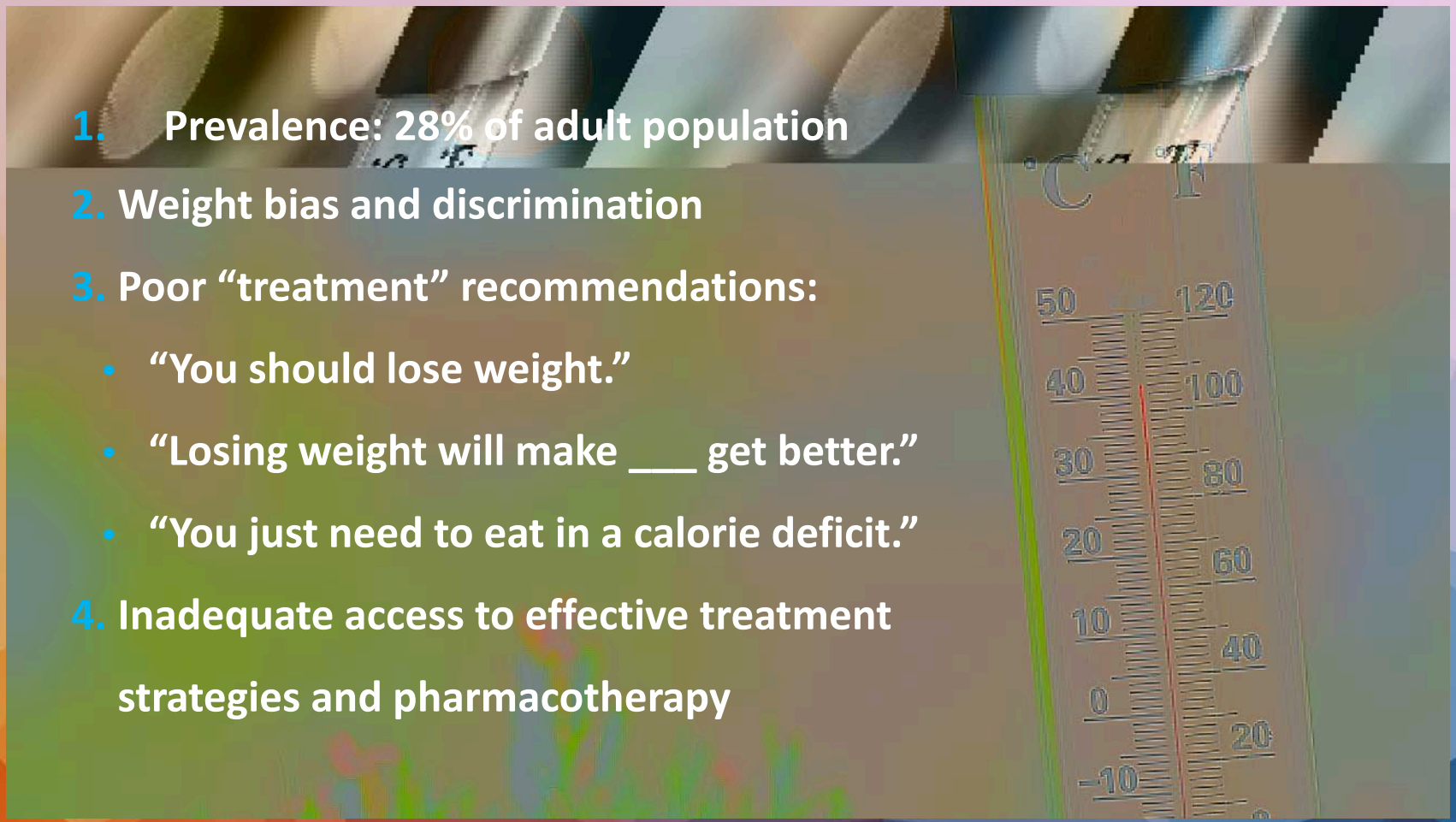


We are Biased Because We Weren't Taught the Pathobiology of Obesity

The common HCP recommendation for obesity:

Eat less and exercise more

Climate of Obesity in Canada



1. Prevalence: 28% of adult population
2. Weight bias and discrimination
3. Poor "treatment" recommendations:
   - "You should lose weight."
   - "Losing weight will make ___ get better."
   - "You just need to eat in a calorie deficit."
4. Inadequate access to effective treatment strategies and pharmacotherapy

Many Women with Obesity Have Self-bias

- 52% of people with obesity have negative weight-biased beliefs about themselves
- People tend to believe that they:
  - Deserve negative attitudes and treatment they receive
- People with weight bias will commonly used statements such as:
  - "I am less attractive than most other people because of my weight,"
  - "I feel anxious about being overweight because of what people might think of me."

Kirk SFL, Ramos Salas X, Alberga A, Russell-Mayhew S. Canadian Adult Obesity Clinical Practice Guideline: Reducing Weight Bias in Obesity Management, Practice & Policy. Published online August 4, 2020. Accessed August 4, 2020. http://obesitycanada.ca/wp-content/uploads/2020/08/1-Reducing-Weight-Bias-v5_FINAL.pdf

Discrimination further isolates.
Stigma disempowers.

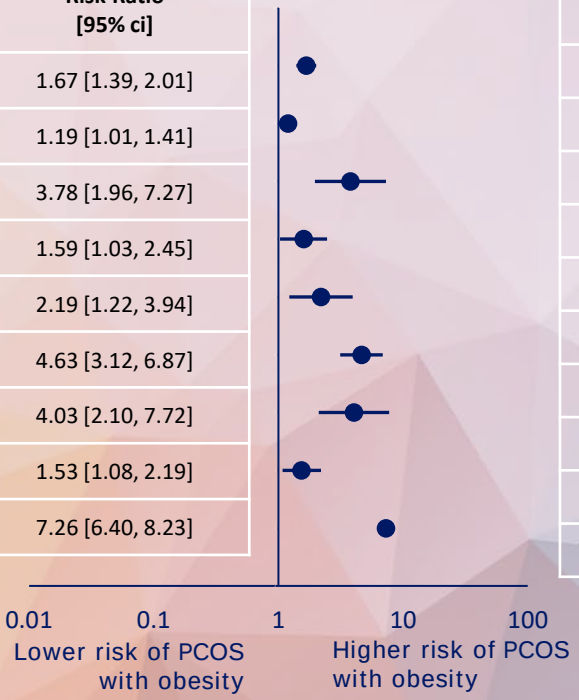
We need to have better conversations.

What is Obesity?

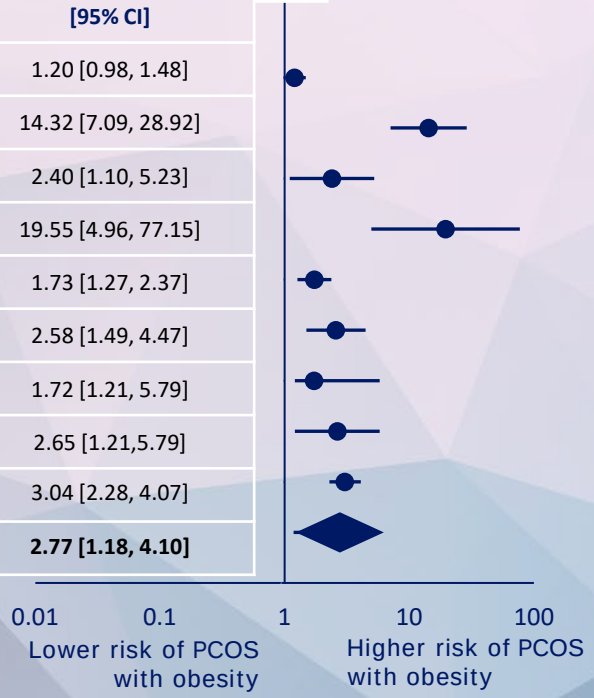
Obesity is a chronic, progressive and relapsing disease, characterized by the presence of abnormal or excess adiposity that impairs health (physical, mental or metabolic) and social well-being.

Higher risk of PCOS in women with obesity

Study or Subgroup	Risk Ratio [95% ci]
Al-Ojaimi 2006	1.67 [1.39, 2.01]
Azziz 2004	1.19 [1.01, 1.41]
Beydoun 2009	3.78 [1.96, 7.27]
Carmina 2006	1.59 [1.03, 2.45]
Chhabra 2010	2.19 [1.22, 3.94]
Dokras 2005	4.63 [3.12, 6.87]
Echiburu 2008	4.03 [2.10, 7.72]
Glueck 2003	1.53 [1.08, 2.19]
Glueck 2005	7.26 [6.40, 8.23]



Study or Subgroup	Risk Ratio [95% CI]
Glueck 2005a	1.20 [0.98, 1.48]
Glueck 2006	14.32 [7.09, 28.92]
Glueck 2008	2.40 [1.10, 5.23]
Hahn 2007	19.55 [4.96, 77.15]
Liou 2009	1.73 [1.27, 2.37]
Patel 2008	2.58 [1.49, 4.47]
Shroff 2007	1.72 [1.21, 5.79]
Vrbikova 2007	2.65 [1.21,5.79]
Wang 2009	3.04 [2.28, 4.07]
Total	**2.77 [1.18, 4.10]**



Total event, PCOS: 1964, control: 798; Meta-analysis of the prevalence of obesity (BMI ≥30 kg/m^2) in women with and without PCOS

BMI, body mass index; PCOS, polycystic ovary syndrome

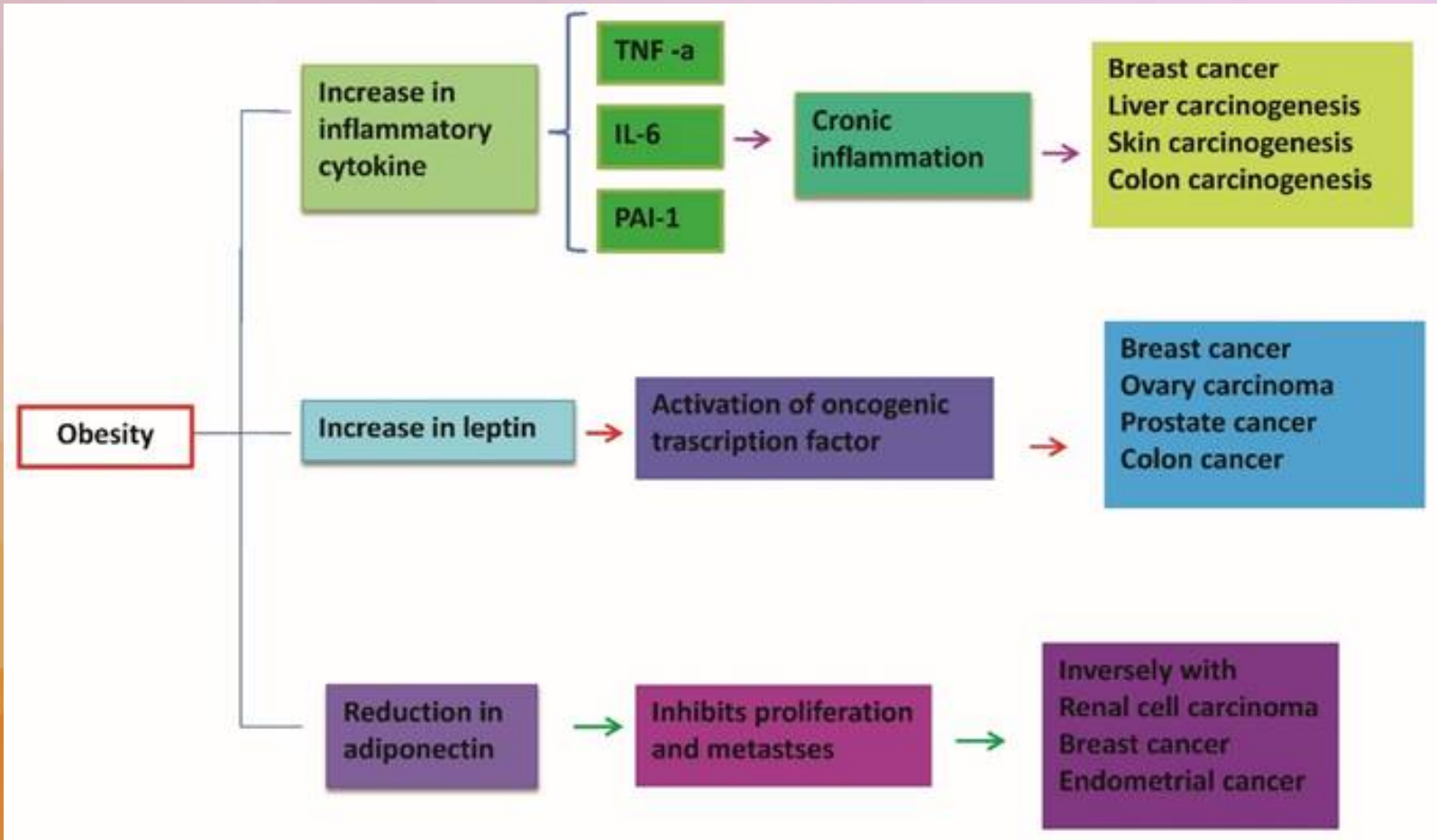
Adapted from: Lim et al. *Hum Reprod Update* 2012; 18(6): 618-637

Higher rates of infertility in women with obesity

- Risk of infertility increased approx. 78% in women with obesity[1]
- Most common cause of infertility is PCOS

1. Ramlau-Hansen CH, Thulstrup AM, Nohr EA, et al. Subfecundity in overweight and obese couples. Hum Reprod 2007;22:1634–7
2. Moran LJ, Norman RJ, Teede HJ. Metabolic risk in PCOS. Trends Endocrinol Metab 2015;26:136–43.
3. Baillargeon J-P,Nestler JE. Polycystic ovary syndrome: A syndrome of ovarian hypersensitivity to insulin? J Clin Endocrinol Metab 2006;91:22–4.
4. van der Steeg JW, Steures P, Eijkemans MJC, et al. Obesity affects spontaneous pregnancy chances in subfertile, ovulatory women. Hum Reprod 2008;23: 324–8

Obesity and Cancer Risk



Divella, R et al. Obesity and Cancer. *J Cancer* 2016; 7(15):2346-2359.

4.7-Fold Increased risk of Endometrial Cancer

- Increased risk with weight gain and weight cycling.
- Early-life obesity was associated with a moderately increased risk of endometrial cancer later in life.
- Evidence for a protective effect of weight loss.

Shaw E., Farris M., McNeil J., Friedenreich C. (2016) Obesity and Endometrial Cancer. In: Pischon T., Nimptsch K. (eds) Obesity and Cancer. Recent Results in Cancer Research, vol 208. Springer, Cham

Obesity is associated with a number of mental health issues

~50-80%
PwO referred for bariatric surgery have mental health concerns

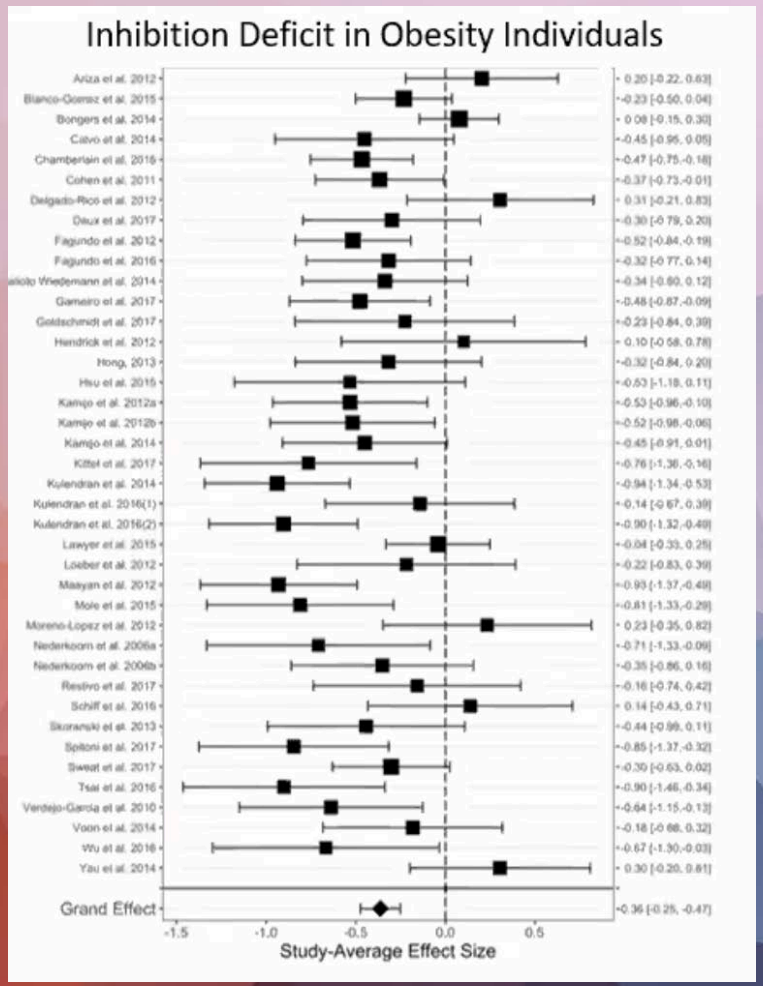
~50%
PwO have depression

~30%
PwO have anxiety

10-15%
adults with BMI >50 exhibiting intellectual disability

BMI, body mass index; PwO, persons with obesity.
1. Stahel P et al. *Diabetes* 2019;68:2235-46; 2. Boeka AG et al. *Arch Clin Neuropsychol* 2008;23:467-74; 3. Rutledge T. *Obes Surg* 2011;21:1570-1579; 4. Pitzul, KB et al. *Obes Surg 2014;*24:134-40; 5. Shakory S et al. *Appetite* 2015;91:69-74.

Obesity Associated with Executive Function Deficits



Yang Y, Shields GS, Guo C, Liu Y. Executive function performance in obesity and overweight individuals: A meta-analysis and review. Neurosci Biobehav Rev. 2018 Jan;84:225-244. doi: 10.1016/j.neubiorev.2017.11.020. Epub 2017 Dec 7. PMID: 29203421.

Emotional Eating

Adverse stress experiences

Poor appetite regulation, increased food intake, emotional eating, binge eating and sedentary behaviour

Weight gain and obesity

1. Allyson Diggins, et al, The association of perceived stress, contextualized stress, and emotional eating with body mass index in college-aged Black women, Eating Behaviors, Volume 19, 2015, Pages 188-192, ISSN 1471-0153, https://doi.org/10.1016/j.eatbeh.2015.09.006.

2. Irina Lazarevich, et al, Relationship among obesity, depression, and emotional eating in young adults, Appetite, Volume 107, 2016, Pages 639-644, ISSN 0195-6663, https://doi.org/10.1016/j.appet.2016.09.011.

3. Schulz, S., Laessle, R.G. Associations of negative affect and eating behaviour in obese women with and without binge eating disorder. *Eat Weight Disord* 15, e287–e293 (2010). https://doi.org/10.1007/BF03325311

It's different for women…

- Increased prevalence of emotional eating tendencies
- Great body dissatisfaction
- High risk times: menarche, pregnancy, menopause
- Less muscle mass
- Hormonal Medications: OCP, IUD
- Lifestyle intervention results in 16% more weight loss in men vs women
  - Men: decrease fat mass, decreased HR, improved MetS
  - Women: decrease in HDL, decrease in lean body mass

Christensen P et al. **Men and women respond differently to rapid weight loss: Metabolic outcomes of a multi-centre intervention study after a low-energy diet in 2500 overweight, individuals with pre-diabetes (PREVIEW).** Diabetes Obes Metab. 2018 Dec;20(12):2840-2851. doi: 10.1111/dom.13466. Epub 2018 Aug 7.

“Eat in a calorie deficit” isn’t so simple

Mood disorders, decreased executive functioning, trauma, stress response can affect **food choices, health behaviours, impulsive control, eating patterns**

+

Brain **defending against weight loss** hormonal dysregulation

=

Complex chronic progressive condition requiring multipronged approach

BMI, body mass index; PwO, persons with obesity.

1. Stahel P et al. *Diabetes* 2019;68:2235-46; 2. Boeka AG et al. *Arch Clin Neuropsychol* 2008;23:467-74; 3. Rutledge T. *Obes Surg* 2011;21:1570-1579; 4. Pitzul, KB et al. *Obes Surg 2014;*24:134-40; 5. Shakory S et al. *Appetite* 2015;91:69-74.

We need to have better ***conversations***.
And we need to offer better ***solutions***.

But how?

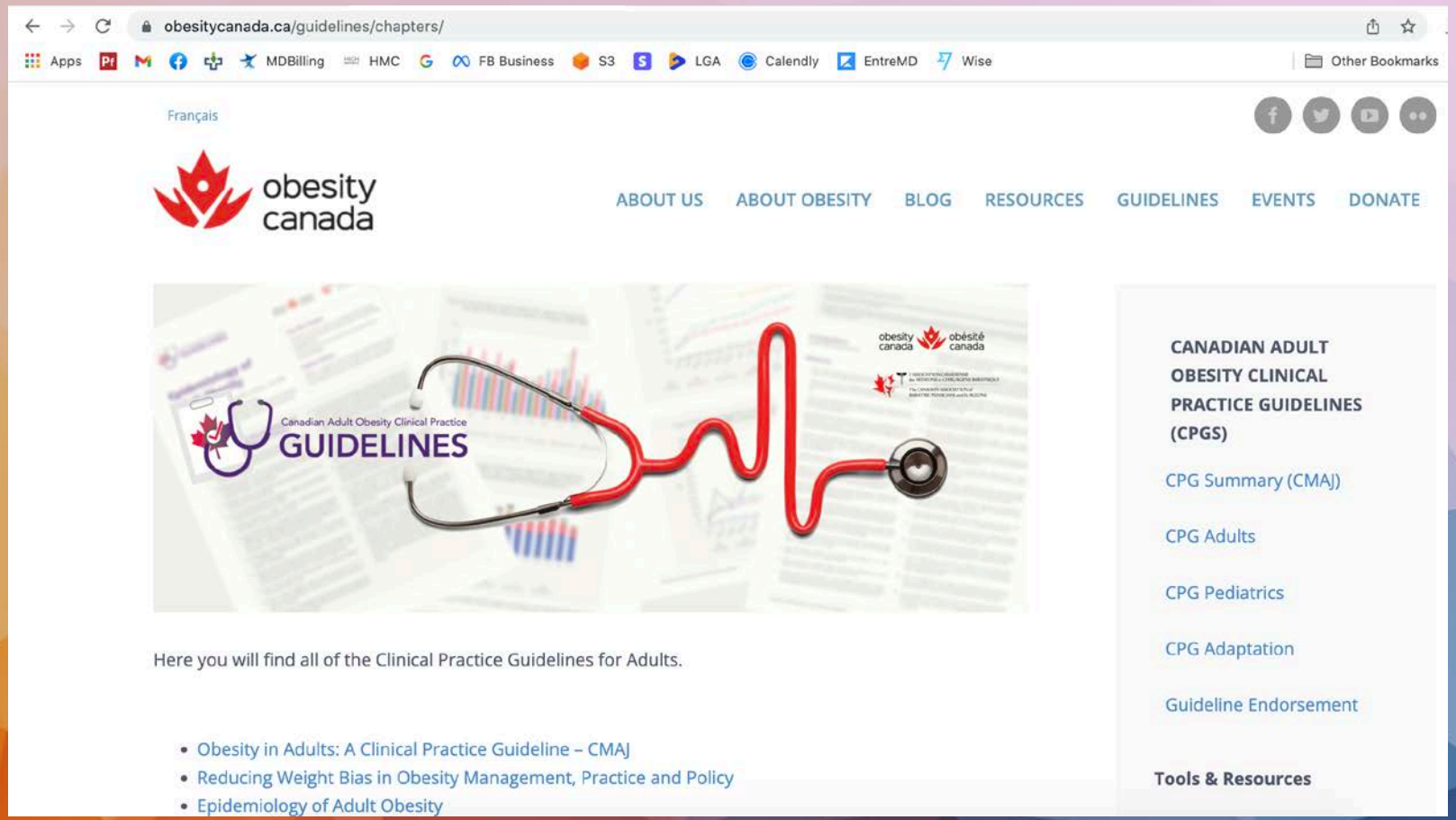
“It’s not your fault.”

“Weight gain can be tough to manage on your own.

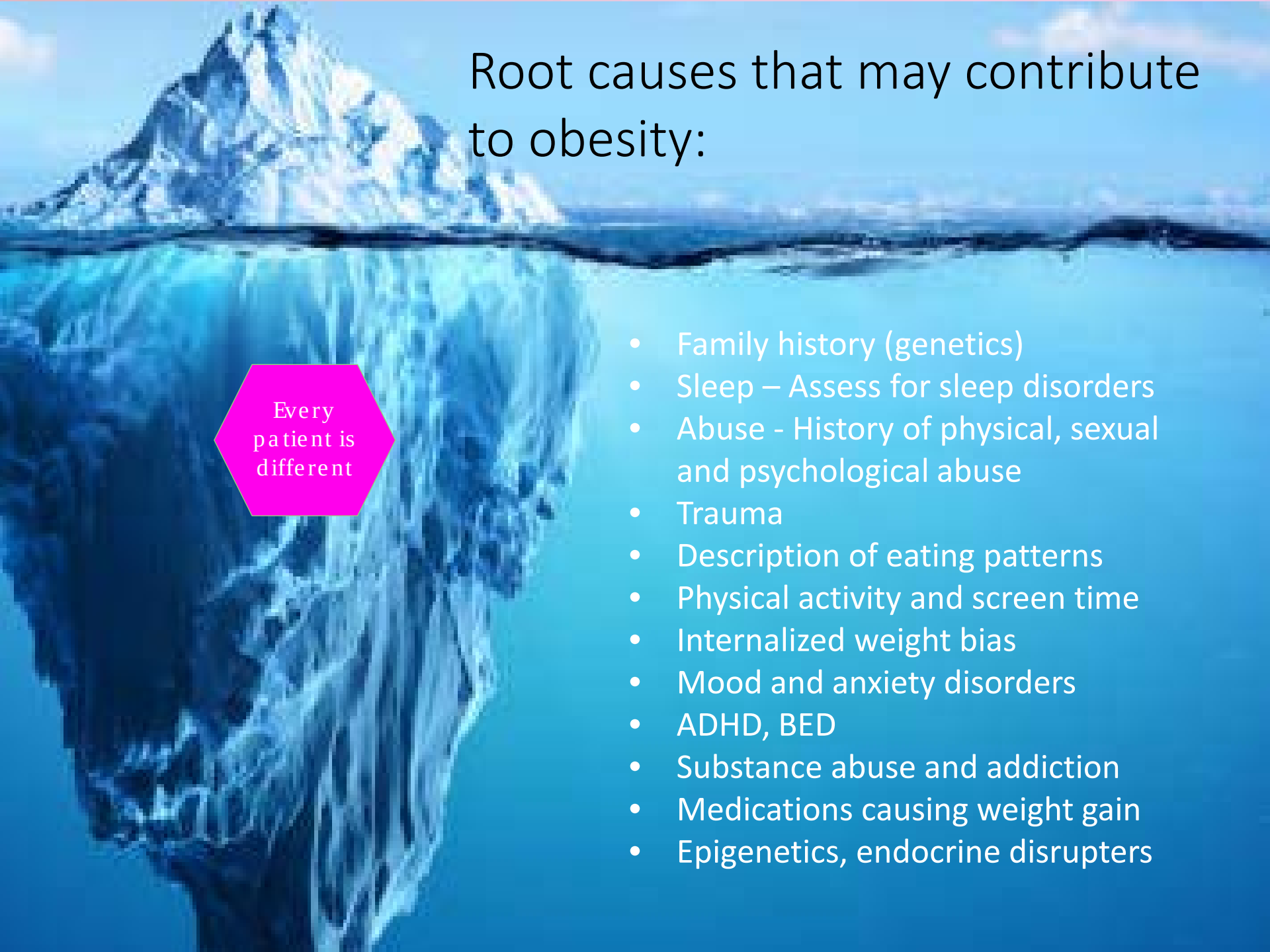
It’s often not as simple as eating less and exercising more. Did you know that genetics and physiology play a huge role in how your body control’s your weight?

If you want support, I’m here to help you.”

Canadian Obesity Clinical Practice Guidelines



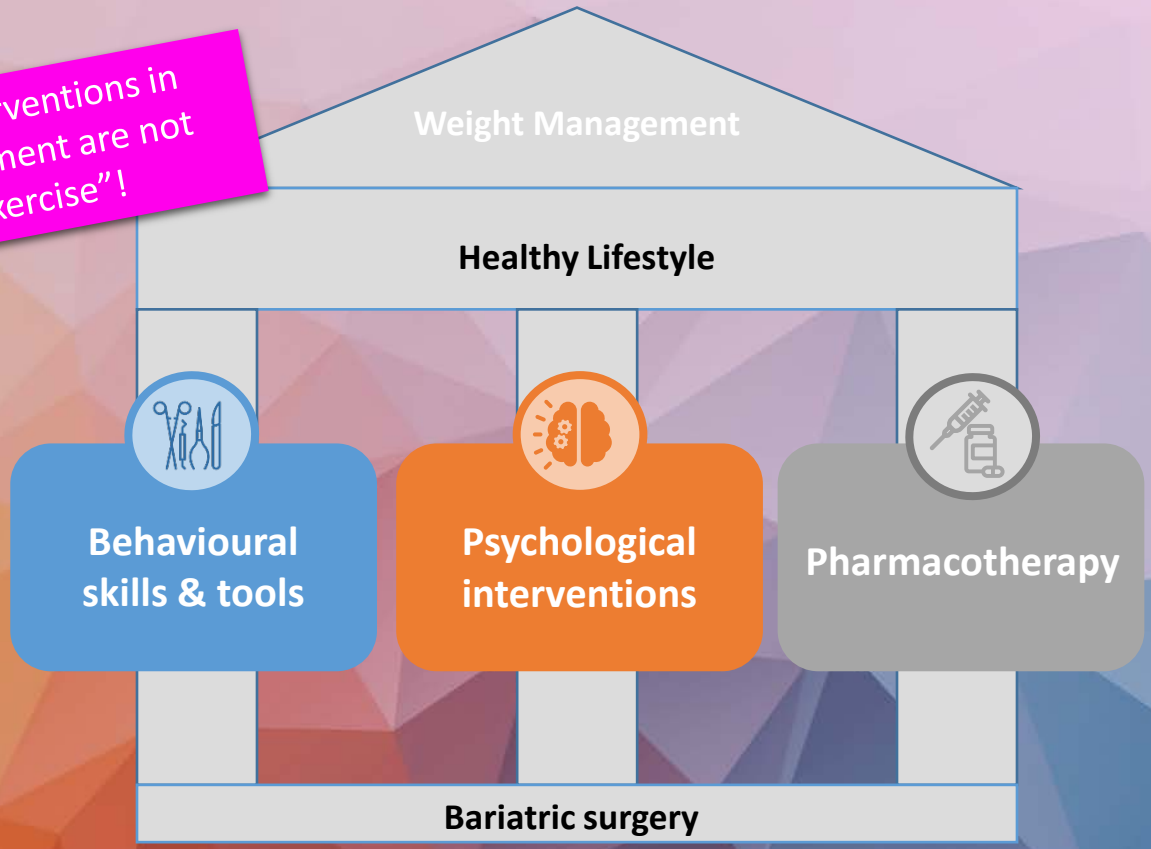
Root causes that may contribute to obesity:



- Family history (genetics)
- Sleep – Assess for sleep disorders
- Abuse - History of physical, sexual and psychological abuse
- Trauma
- Description of eating patterns
- Physical activity and screen time
- Internalized weight bias
- Mood and anxiety disorders
- ADHD, BED
- Substance abuse and addiction
- Medications causing weight gain
- Epigenetics, endocrine disrupters

Effective Obesity Treatment Pillars

Behavioural interventions in obesity management are not "diet and exercise"!



Healthy behaviour is not our default position

Eat more, exercise less.

These are the default position unless we deliberately use psychological skills to resist.

How do we produce lifestyle changes?

A healthier lifestyle is the RESULT of learning behavioural skills and tools that go beyond willpower

- Self-monitoring
- Awareness of wanting
- Mindful eating
- Practising restraint thinking (different from restriction!)
- Developing resilience in the face of setbacks
- Goal setting and action planning (realistic, achievable)
- Problem solving (self-efficacy)
- Intrinsic motivation
- Values-guided committed action

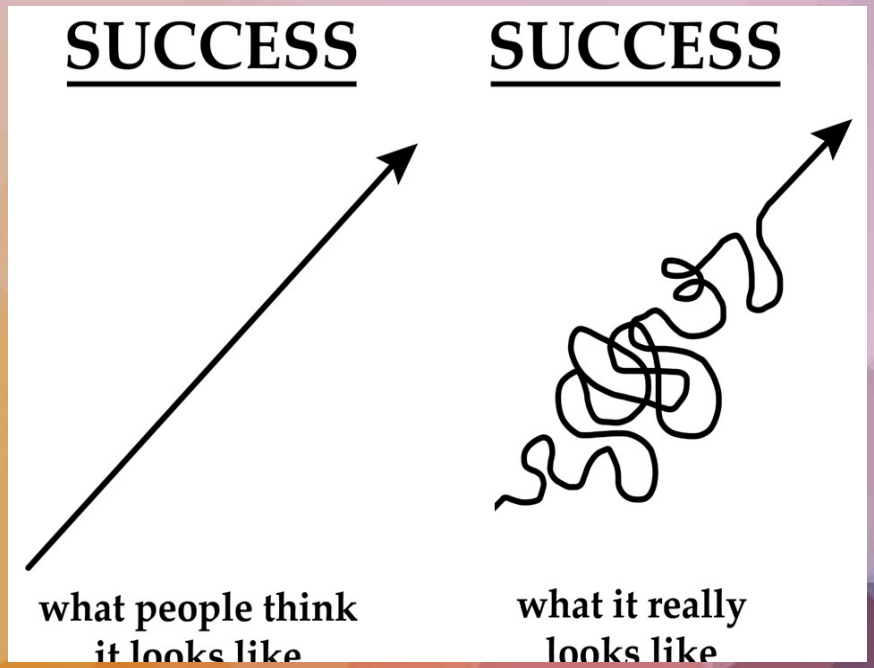
Behavioural interventions in obesity management are not "diet and exercise"

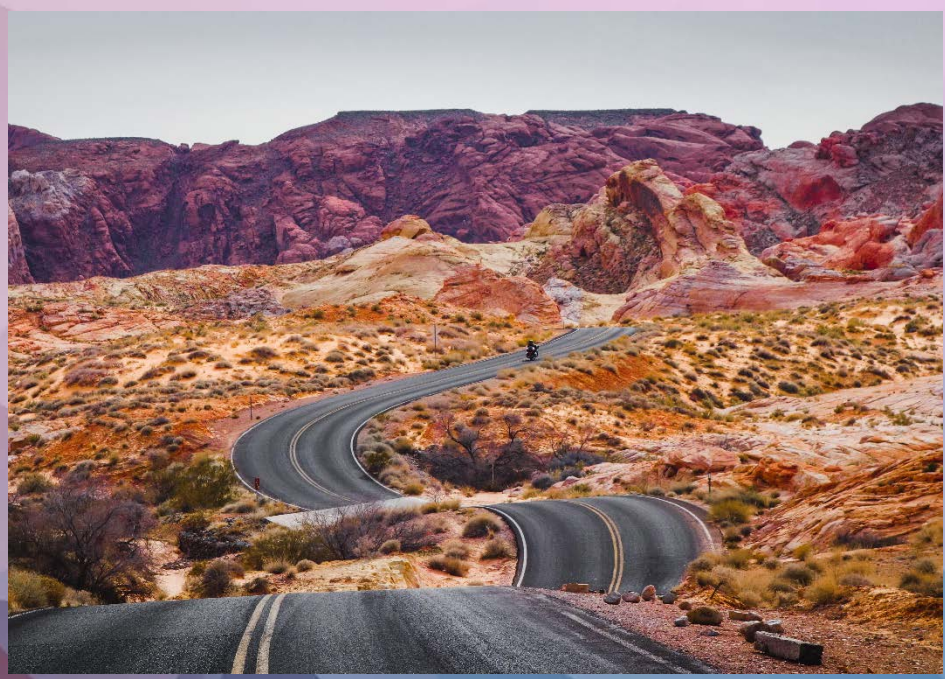
Decisions Ahead of Time.

The power of 1 degree.

1% upgrades.
What is my next best choice?

Resilience: Setbacks are a normal part of the journey

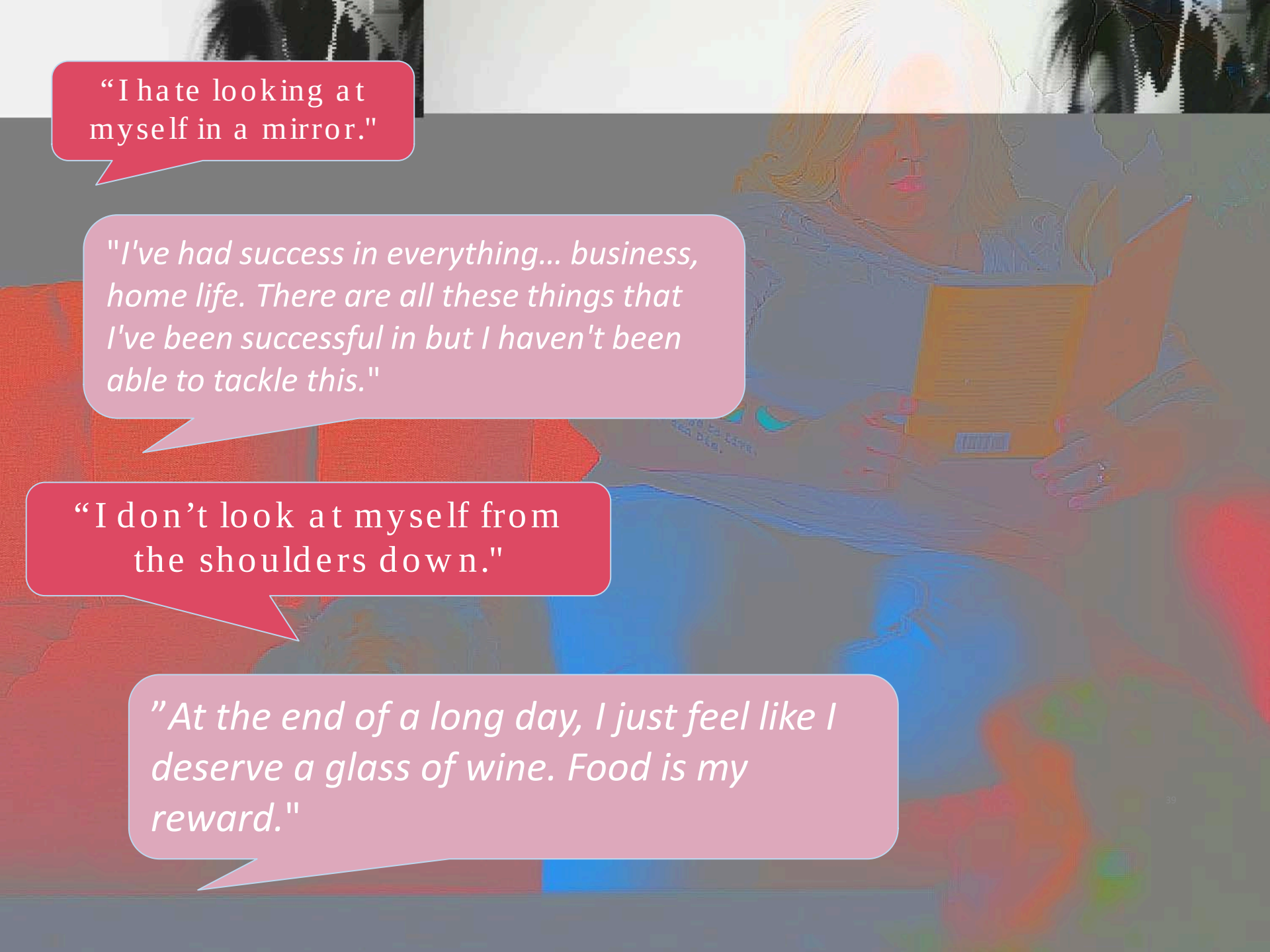




Psychological interventions

- Modify maladaptive thoughts about weight/shape/eating
- Challenge assumptions and unhelpful thinking patterns
- Enhance self-efficacy and coping skills
- Focus on coping and changing thoughts resulting in self-defeating behaviours
- Learn acceptance-based skills to tolerate discomfort and reduction in pleasure, enact commitment to valued behavior, and be mindfully aware during moments of decision-making[1]

1. Forman EM, Butryn ML, Manasse SM, Crosby RD, Goldstein SP, Wyckoff EP, Thomas JG. Acceptance-based versus standard behavioral treatment for obesity: Results from the mind your health randomized controlled trial. Obesity (Silver Spring). 2016 Oct;24(10):2050-6. doi: 10.1002/oby.21601. PMID: 27670400; PMCID: PMC5051349.


“I hate looking at myself in a mirror."
"I've had success in everything... business, home life. There are all these things that I've been successful in but I haven't been able to tackle this."
“I don’t look at myself from the shoulders down."
”At the end of a long day, I just feel like I deserve a glass of wine. Food is my reward."

*“In the past, what I've done is think **'today's a really bad eating day, I've already f'ed it up, I might as well keep going.***

Now I think, I'm going to stop now. I'm able to be more forward thinking and recognize - these are decisions I make.”
- J.H.

*My husband and I finally went on a date last weekend - we **committed before** we went that we would share an appetizer and we shared a small pizza and it was amazing **[planning in advance].***

*I didn't feel guilty **[self-compassion and letting go of guilt]** about eating it, we didn't feel disgusting after we came home. "*

– L.N.

"I actually feel freer now than I have in the past.

I just feel like I can make better choices and I'm not so restricted to that calorie count at the end of the day ***[restraint over restriction].***

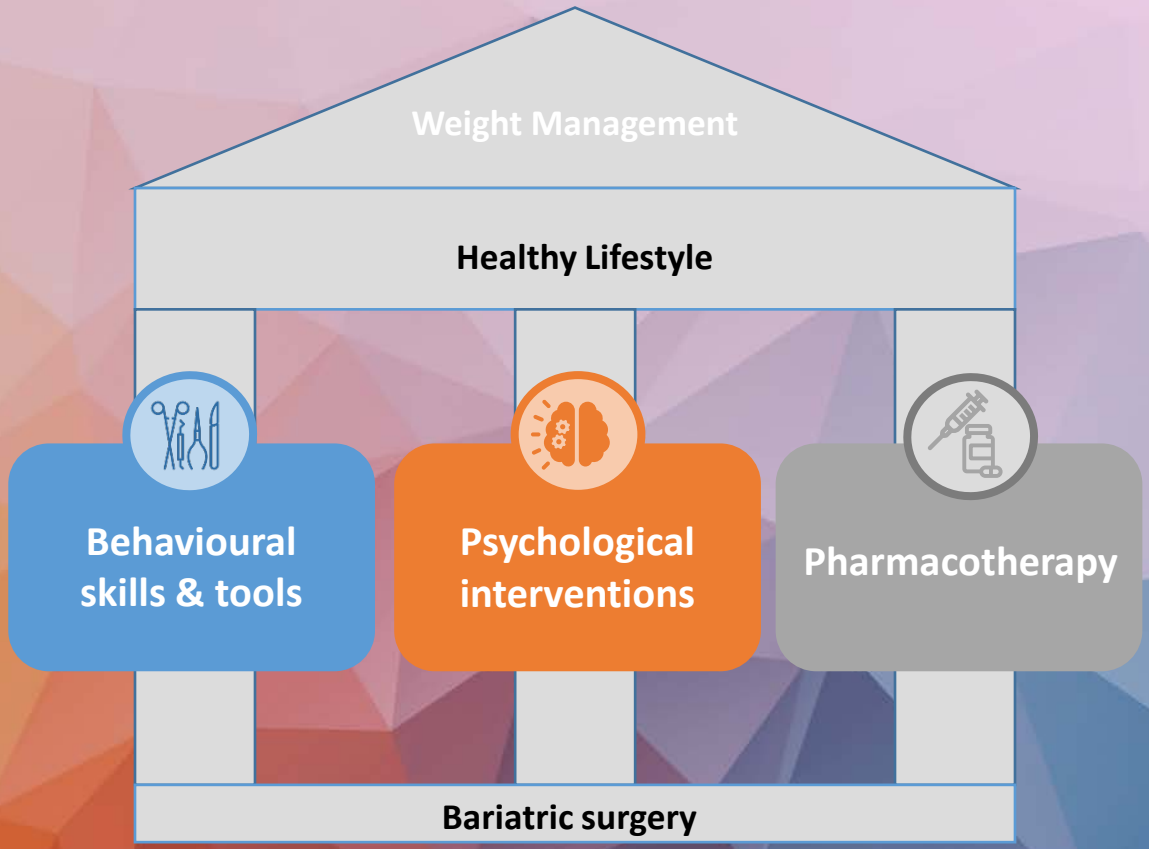
I'm much more balanced in my day - I don't feel like I'm saving up points in the day for a reward at the end of the day." ***[Listening to hunger cues]***

- M.M.

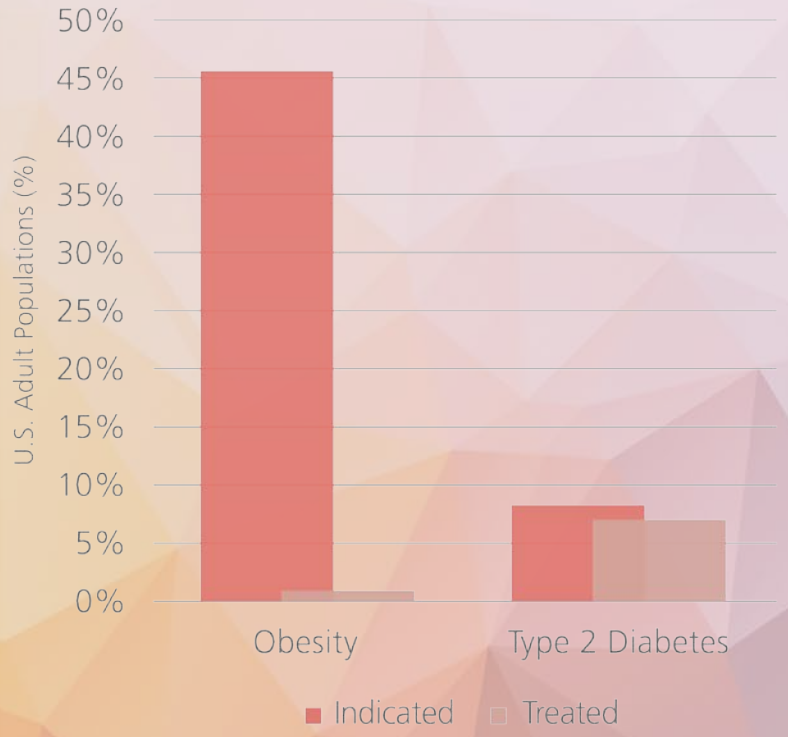
People know what they “should” be doing.
They need to be *empowered* to actually do it.

Shame, blame and punishment never lead to positive action or longterm weight loss.

Let’s treat the physiology



“My doctor doesn’t believe in weight loss medications.”



About 46% of adults are indicated for anti-obesity pharmacotherapy, but <u>only 2% of them receive treatment</u>

Whereas, 8.4% of adults are diagnosed with diabetes—86% receive antihyperglycemic pharmacotherapy

Thomas CE, et al. Low Adoption of Weight Loss Medications: A Comparison of Prescribing Patterns of Antiobesity Pharmacotherapies and SGLT2s. *Obesity* (Silver Spring). 2016;4(9):1955–1961.

Current obesity pharmacotherapy approved for long-term use in Canada

Naltrexone/bupropion[1]
μ-opioid antagonist +
DA/NE reuptake inhibitor

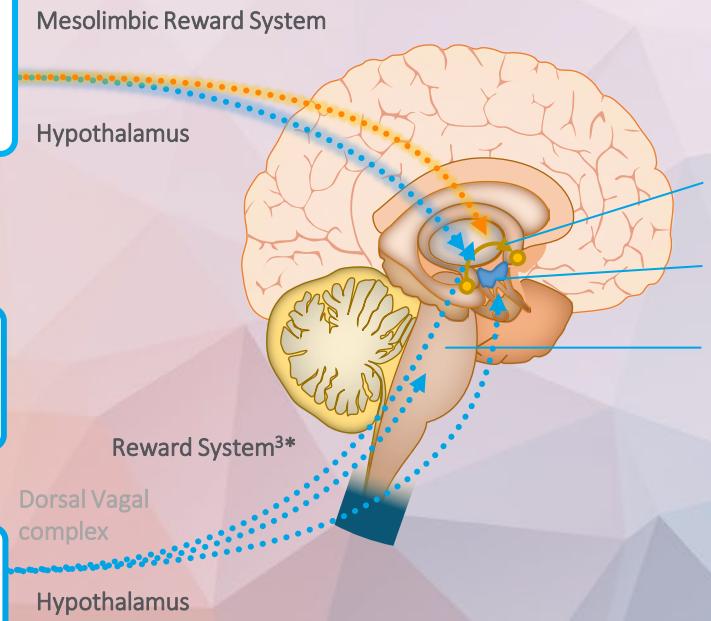
Contrave

Ozempic/Wegovy

Semaglutide
GLP-1 receptor agonist

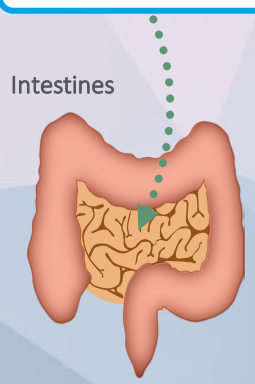
Saxenda

Liraglutide[2]
GLP-1 receptor agonist



Xenical

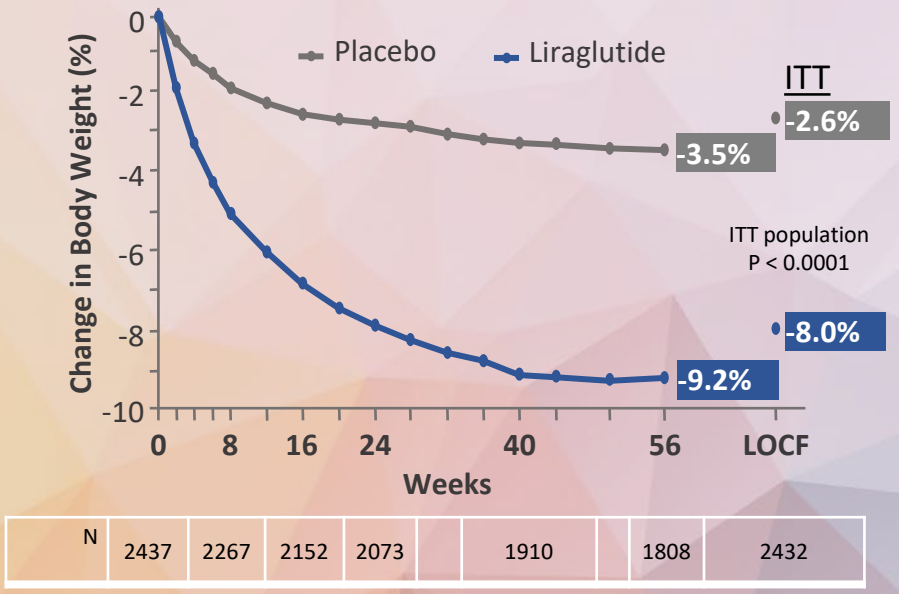
Orlistat[4]
Lipase inhibitor



DA=dopamine; GLP-1=glucagon-like peptide-1; NE=norepinephrine. *GLP-1s have been shown to modulate food reward and hedonic eating

1. Ornellas T, Chavez B. P T. 2011;36(5):255–262; 2. Shah M, Vella A. Rev Endocr Metab Disord. 2014;15(3):181–187; 3. Reproduced from the Canadian Adult Obesity Clinical Practice Guidelines [The Science of Obesity. Lau, C.W., Wharton, S. 1-7, copyright notice] with permission from Obesity Canada/ Obésité Canada; 4. Yanovski SZ et al. JAMA. 2014;311:74-86.

Liraglutide efficacy phase 3 study – SCALE 1



Adverse Event (AE)	Liraglutide n = 3384 (%)	Placebo n = 1941 (%)
Nausea	39	14
Diarrhea	21	10
Constipation	19	9
Vomiting	16	4
Decreased appetite	10	2
Dyspepsia	10	3
Fatigue	8	5
Dizziness	7	5
Abdominal pain	5	3
Increased lipase	5	2
Upper abdominal pain	5	3

Saxenda® Product monograph, July 12, 2017, Novo Nordisk Canada Inc, Mississauga, ON.

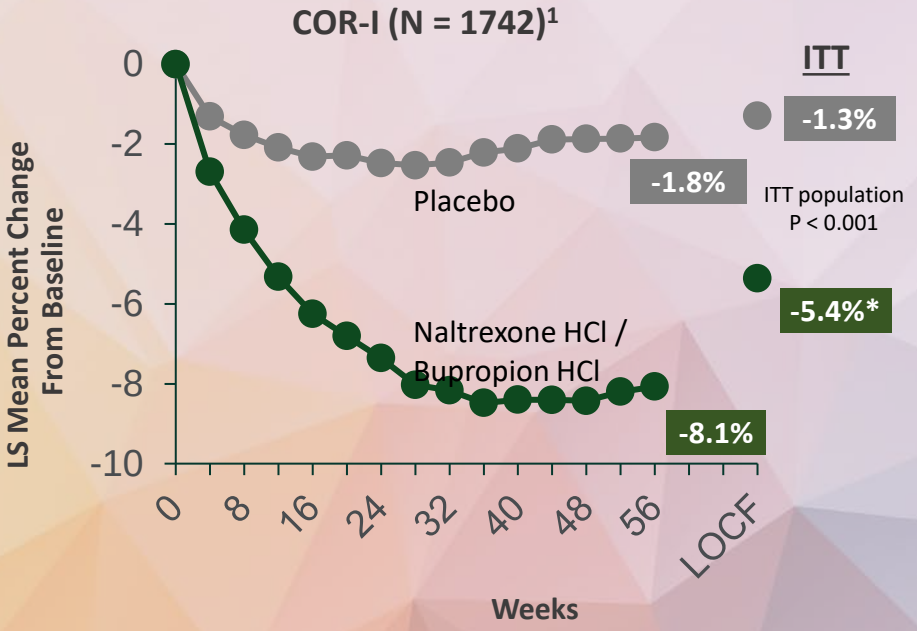
Liraglutide Administration

- Once daily SC injection, usually evening
- Dose titration

0.6mg SC daily x 1 week,
1.2mg SC daily x 1 week,
1.8mg SC daily x 1 week,
2.4mg SC daily x 1 week,
3.0mg SC daily ongoing

- Side effects can be minimized by slower titration
- Click method

Naltrexone/bupropion efficacy phase 3 study – COR-I

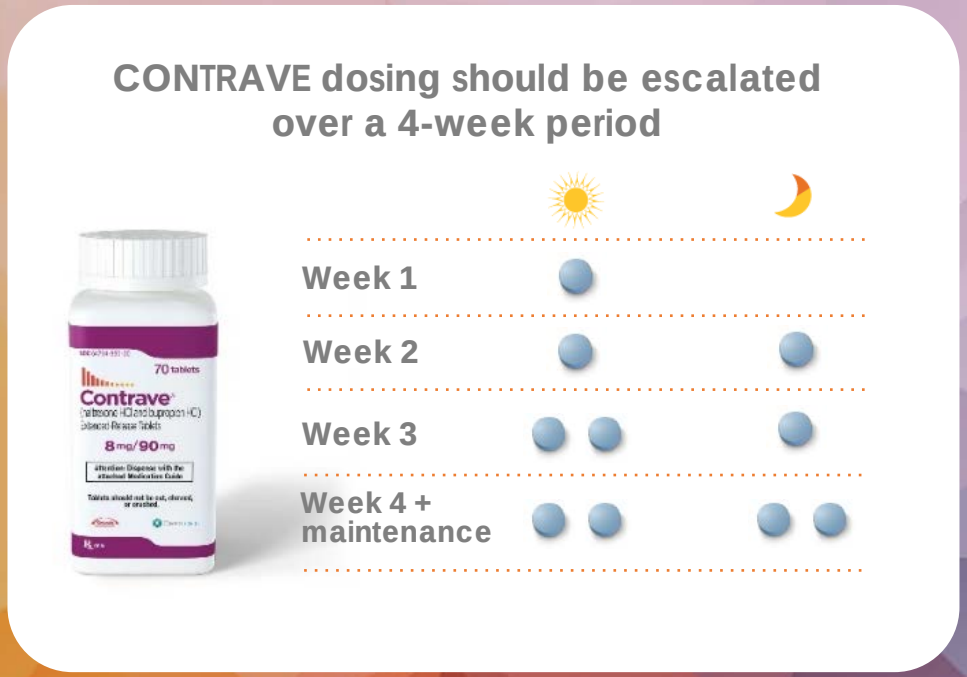


ITT = intent-to-treat

Adverse Reaction[2]	Naltrexone HCl / Bupropion HCl n = 2545 (%)	Placebo n = 1515 (%)
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

1. CONTRAVE® Product monograph, February 12, 2018, Valeant Canada LP; Laval, QC 2. Apovian CM, et al. Obesity..2013;21:935-943

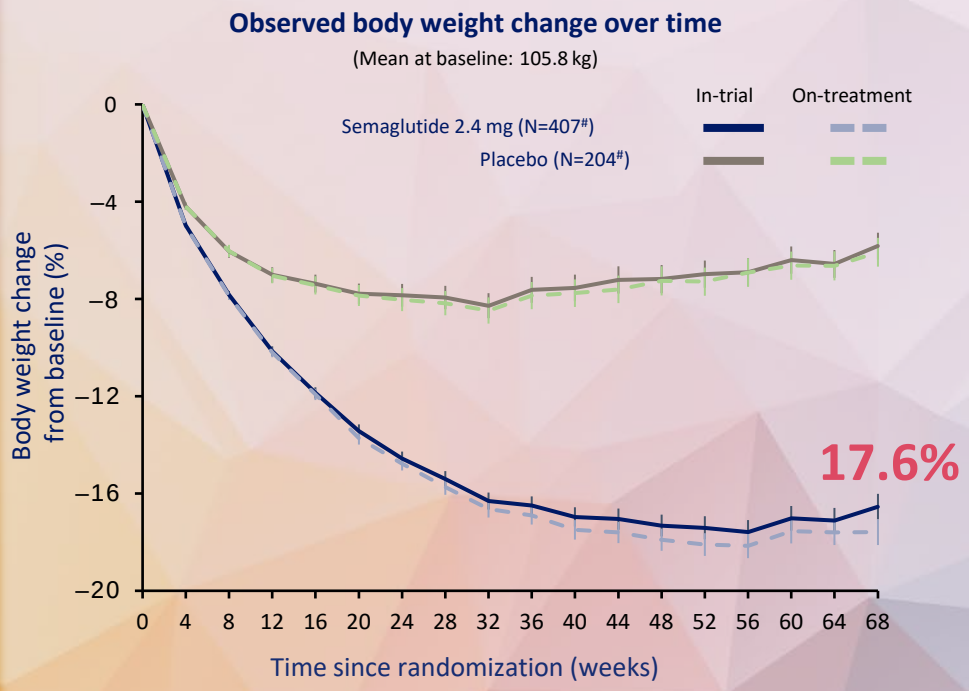
Naltrexone/Bupropion Administration

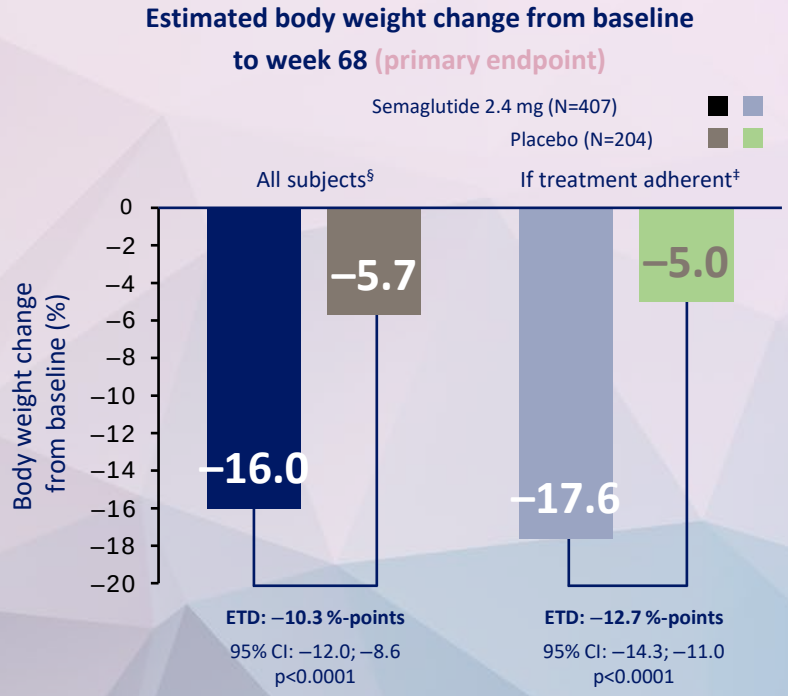


- Slow titration
- Some people may not need full dose
- Take it early evening
- Which patient? Smoking cessation, cravings, depression, binge eating
- Be aware of drug interactions*

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

Semaglutide 2.4mg efficacy – STEP Program





Error bars are +/- standard error of the mean.

#Number of participants at week 0.

§Treatment policy estimand (regardless of treatment adherence).

‡Trial product estimand.

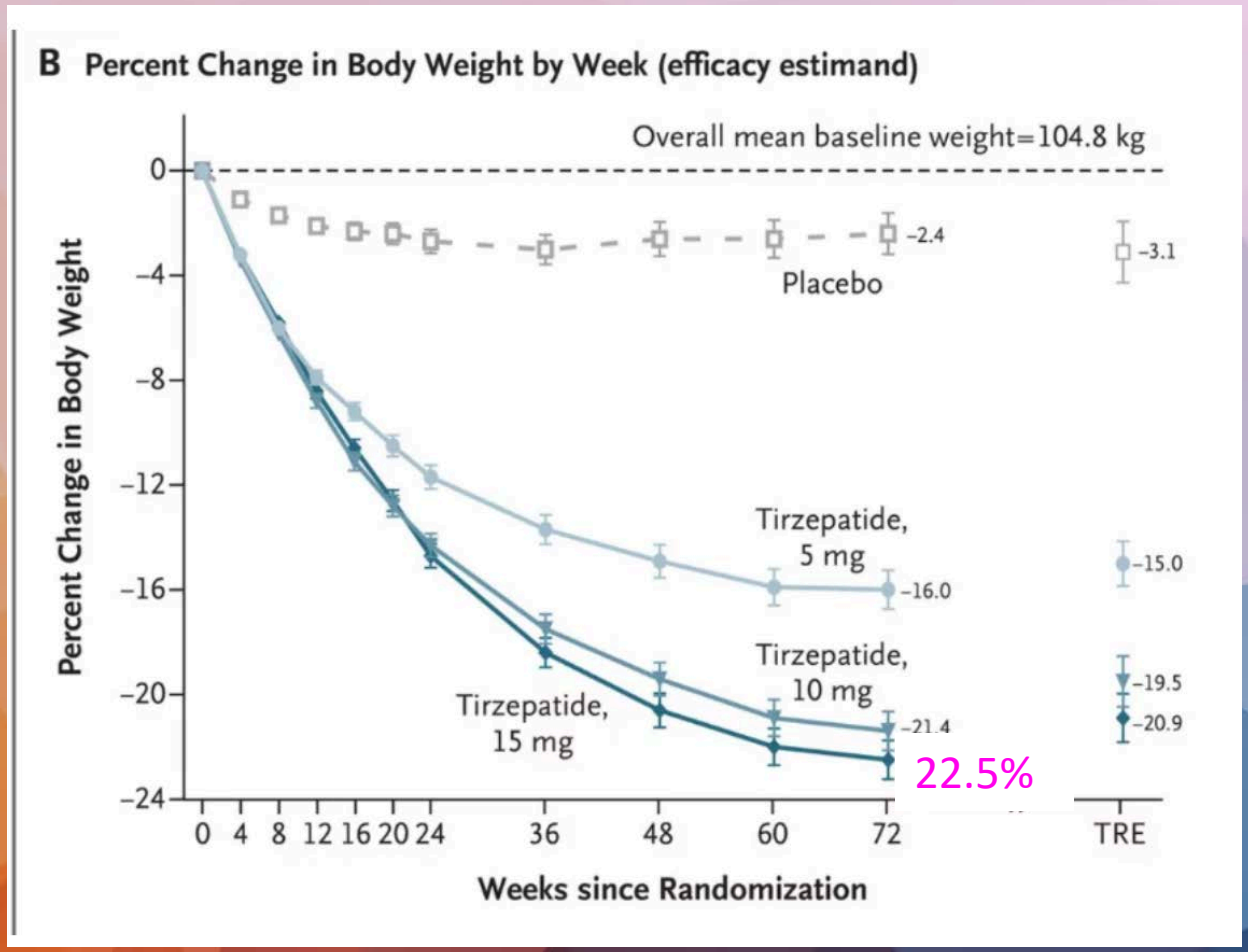
CI, confidence interval; ETD, estimated treatment difference.

Semaglutide Administration

- Once weekly
- SC injection
- Side effects can be minimized by slower titration

https://www.wegovy.com/about-wegovy/dosing-schedule.html

What's coming? Tirzepatide (GLP1 + GIP Dual Agonist)



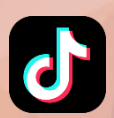
Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, Kiyosue A, Zhang S, Liu B, Bunck MC, Stefanski A; SURMOUNT-1 Investigators. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med. 2022 Jul 21;387(3):205-216. doi: 10.1056/NEJMoa2206038. Epub 2022 Jun 4. PMID: 35658024.

Obesity Paradigm has Changed

Past	Present
Obesity is a risk factor for other chronic diseases. **You need to lose weight.**	**Obesity is a chronic disease with many comorbidities.** **Can we discuss your weight?**
Diet and exercise are the treatment of choice for obesity **Eat less and move more.**	**Identify root causes of weight gain, values that matter and patient-centered health outcomes.** **Let's understand your story and focus on what's important for you.**
With just a bit of willpower, we would not have obesity. **You should try harder.**	**Healthy behaviours are supported by pillars of psychological, behavioural, pharmacological and surgical interventions** **Let's build a treatment plan together.**

Questions and Discussion

Thank you for your time today!

@sashahighmd


High on Life Podcast

Session Evaluation and Reflection

These short forms are important to your learning process and our planning process!

- For **speakers**: Your responses help them understand their strengths and weaknesses, participant learning needs, and teaching outcomes
- For **the CEPD office**:
  - To plan future programs
  - For quality assurance and improvement
  - To demonstrate compliance with national accreditation requirements
- For **YOU**: Reflecting on what you've learned and how you plan to apply it can help you enact change as you return to your professional duties

Use your phone camera to access the evaluation via the QR Code.

Please take 3-5 minutes to fill the evaluation form out. Thank you!