Pharmacological and Psychological Interventions for Weight Loss

Morgan T. Sammons, PhD, ABPP

1 CE Credit, Instructional Level: Intermediate
1 Contact Hour (New York Board of Psychology)

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Morgan T. Sammons, PhD, ABPP

Morgan T. Sammons, PhD, ABPP, recently retired as the CEO of the National Register of Health Service Psychologists. He has enjoyed a career as a prescribing psychologist, military psychologist, and has held leadership positions in academia and professional psychology. He is currently a member of the Board of Directors of the Canadian Register of Health Service Psychologists.

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Learning Objectives

1. Describe past and present pharmacological agents for weight loss.
2. Discuss the putative mechanisms of action and efficacy of GLP-1 agonists.
3. Explain the evidence supporting combined psychological/behavioral interventions for weight loss.

Disclosures/Conflicts of Interest

- Dr. Sammons is a member of the Board of Directors of the Canadian Register of Health Service Psychologists.
- NB: This is an overview of drugs and behavioral interventions only. Nothing in this presentation should be construed as clinical advice for direct patient care.
- No other conflicts of interest to disclose.

Amphetamine and amphetamine-like drugs for weight loss

Stimulant drugs for weight loss	Trade names	FDA/Health Canada approved for weight loss?	Comments
Amphetamine-based agents			
Benzphetamine	Regimex, Didrex, others	Yes (US) No (CA)	Schedule I controlled substance in Canada
Phendimetrazine	Bontril, Melfiat, others	Yes (US) No (CA)	Schedule IV controlled substance in Canada
Phentermine	Adipex, Fastin, others	Yes (US) No (CA)	Schedule IV controlled substance in Canada
Diethylpropion	Tenuate and others	Yes (US) No (CA)	Schedule IV controlled substance in Canada
Naltrexone/bupropion	Contrave	Yes (US) Yes (CA)	Bupropion is an amphetamine-like molecule used as antidepressant, naloxone is opiate receptor antagonist controlling feelings of satiety
Phentermine/topiramate	Qysmia	Yes (US) Yes (CA)	Phentermine Schedule IV controlled substance in Canada

GLP-1 (Glucagon-like-peptide) agonists (GLP-1 RAs) for weight loss

GLP-1 agonists	Trade Names	FDA/Health Canada approved for weight loss?	Comments
Liraglutide	Saxenda, Victoza (US) Zultophy (CA)	Yes = Saxenda, Victoza (US) Yes = Saxenda (CA) No = Zultophy (CA)	
Semaglutide	Ozempic, Wegovy (US) Rybelsus (CA)	Yes = Wegovy (US) Yes = Rybelsus (CA) No = Ozempic (US)	
Setmelanotide	IMCIVREE	Yes (US, restricted) No (CA)	Use restricted to genetically mediated enzyme deficiencies
Tirzepatide	Mounjaro	No (US) No (CA)	

LIPID BLOCKERS FOR WEIGHT LOSS

Lipid absorption blockers	Trade names	FDA/Health Canada approved for weight loss?	Comments
Orlistat	Xenical (prescription) Alli (non-prescription)	Yes (US) Yes (CA)	Available as prescribed agent, an OTC medication, and a dietary additive

Mechanism of Action: GLP-1 Receptor agonists

- GLP-1 is an endogenous peptide that has multiple homeostatic functions (heart muscle, brain tissue, others) Synthetic GLP-1 agonists are much more potent that endogenous agonists.
- GLP-1 RAs act on GLP-1 receptors in pancreatic islet cells to stimulate the release of insulin, thereby lowering serum glucose (the incretin effect; or why they are effective for Type 2 but not Type 1 diabetes mellitus).
- GLP-1 RAs block release of glucagon, an endogenous hormone released when serum glucose drops.
- Action at GLP-1 receptors in brain and gut results in slowed gastric emptying and enhanced sensations of satiety (why they are effective in weight loss).
- Unlike other agents for Type 2 diabetes, like exogenous insulin or sulfonylurea [**metformin** and others] risk of hypoglycemia much lower.

GLP-1 agonists subject of intense, sometimes adulatory study

- Recent trial of GLP-1 agonist (semaglutide) in obesity with heart failure: "A low bar".
- As author noted: Obesity worsens any chronic medical condition. Thus, any effective mechanism for weight loss is an effective treatment for diseases complicated by obesity.

- Source: Mandrola, J. (2023). The GLP-1 agonist semaglutide in HFpEF cleared a low bar. Medscape, 26 Aug., 2023.

Efficacy of GLP-1 RAs

- Consistently lower serum glucose than with earlier drugs.
- Consistently greater weight loss than with earlier drugs.
- Tend to be well-tolerated.
- Nausea, vomiting, diarrhea, appetite suppression are the most common side effects; some studies note an increase in upper respiratory symptoms, rare serious side effects include pancreatitis, medullary thyroid cancer, acute kidney injury.

Table: Currently available GLP-1 Receptor Agonists (USA and EU)

Table adapted from Trujillo, A. M., Nuffer, W., & Smith, B. A. (2021). GLP-1 receptor agonists: an updated review of head-to-head clinical studies. Therapeutic Advances in Endocrinological Metabolism. Published online 2021 Mar 9. doi: 10.1177/2042018821997320

	Drug	Approval date (US, EMA)	Homology to native GLP-1 (%)	Dose and frequency	Route	Half-life
Short-acting	Exenatide (Byetta®)	28 April 2005, 20 November 2006	53	5–10 mcg twice daily	SC	2.4 h
	Lixisenatide (Adlyxin®, Lyxumia®)	28 July 2016, 1 February 2013	50	10–20 mcg once daily	SC	3 h
Long-acting	Liraglutide (Victoza®)	25 January 2010, 30 June 2009	97	0.6–1.8 mg once daily	SC	13 h
	Exenatide (Bydureon®)	26 January 2012, 17 June 2011	53	2 mg once weekly	SC	NR
	Dulaglutide (Trulicity®)	18 September 2014, 21 November 2014	90	0.75–1.5 mg once weekly	SC	5 days
	Semaglutide (Ozempic®)	5 December 2017, 8 February 2018	94	0.25–1 mg once weekly	SC	1 week
	Oral Semaglutide (Rybelsus®)	20 September 2019, 3 April 2020	94	3–14 mg once daily	PO	1 week

EMA, European Medicines Agency; FDA, Food and Drug Administration; GLP-1 RA, glucagon-like peptide-1 receptor agonists; NR, not reported; PO, by mouth; SC, subcutaneous; US, United States.

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Components of effective weight loss regimens

- (NB: Bariatric surgery is not discussed in this presentation)
- Management of external/environmental factors (lifestyle changes)
- Management of internal factors (cognitive and emotional changes)
- Pharmacology as indicated

Successful weight loss related to psychological health

- Cognitive factors in long term maintenance of weight loss: lower levels of perceived effort, moderate outcome expectations, higher levels of exercise self-efficacy, higher measured cognitive flexibility, low levels of internal disinhibition and less depression; .
- Behavioral factors mirror cognitive factors. Low levels of internal disinhibition: regular engagement in 1 hour physical exercise daily, consistently lower caloric intake including fewer fat calories, regular breakfast, self-monitoring of weight (weekly), medical interventions as needed
- Source: Salmela, J.,et al. (2023). Eating behavior dimensions and 9-year weight loss maintenance: a sub-study of the Finnish Diabetes prevention study. *International Journal of Obesity,* https://doi.org/10.1038/s41366-023-01300-w, cited in Sammons and Sanzone (submitted).

Intervention strategies for high cognitive inhibition, long-term behavioral change

- Relatively nonspecific: ACT, CBT, mindfulness, relapse prevention strategies all with some efficacy.
- Focus: **encourage agency, embrace reduced change avoidance, enhance autonomous interoceptive awareness and acuity. Regulation of mood and anxiety, enhanced self-efficacy for management external stressors.**
- **Mastery of skills necessary to improve and maintain optimal physical, emotional, and environmental management; resilience fortification.**
- **Longer term engagement in treatment generally yields more positive outcomes.**
- **e.g., Forman E., et. al (2019). Long-term follow-up of the mind your health project: acceptance-based versus standard behavioral treatment for obesity. *Obesity* (Silver Spring). 27, 4, 565 – 571. https://doi.org/10.1002/oby.22412.**

Q&A

- We will now discuss questions that were submitted via the Q&A feature throughout the presentation.
- Due to time constraints, we will not be able to address every question asked.

References/Citations

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