

# Medical Management of Obesity in Women's Health

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Identified or perceived conflict of interest has been resolved  
in accordance with ACCME guidelines.

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## Faculty Disclosures

Dr. Ryan has the following disclosures:

**Consulting Fees:** Alyvent, Amgen, Bausch Health, Boehringer Ingelheim, Epitomee, Gila Therapeutics, IFA Celtic, Janssen, KVK Tech, Novo Nordisk, Phenomix, Quintiles, Real Appeal (United Health), ReDesign Health, Sanofi, Scientific Intake

**Commercial Interest Speakers Bureau:** Novo Nordisk

**Contracted Research:** SELECT Steering Committee (Novo Nordisk)

**Ownership Interest:** Gila Therapeutics, Phenomix, Xeno Bioscience, Epitomee, ReDesign Health, Scientific Intake



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# Medical Management of Obesity in Women's Health

## Objectives

- Identify women with obesity and determine their comorbidity risk, with a focus on T2DM and CVD
- Associate the hormonal role in energy regulation and metabolic adaptations to the pathophysiology of obesity in women
- Apply guideline-based algorithms to appropriately individualize treatment for women with obesity that is poorly managed with diet and exercise
- Develop strategies to improve communication and engage patients in shared-decision making during annual health visits

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## Factors that Drive Weight Gain Across the Lifespan

- Medications
- Poor sleep, shift work
- Poor eating behavior/processed foods
- Emotional stress
- Smoking Cessation
- Marriage
- Alterations in the growth trajectory through adolescence
- Post-pregnancy weight retention
- Menopause (body fat distribution)

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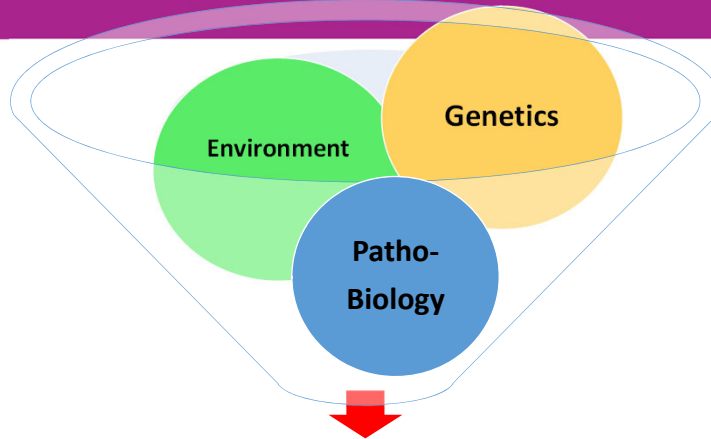
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## Etiology of Obesity



Some individuals are predisposed to develop obesity under current environmental conditions, while others are less susceptible



## Metabolic and Biologic Adaptations that Defend Body Weight

Old paradigm



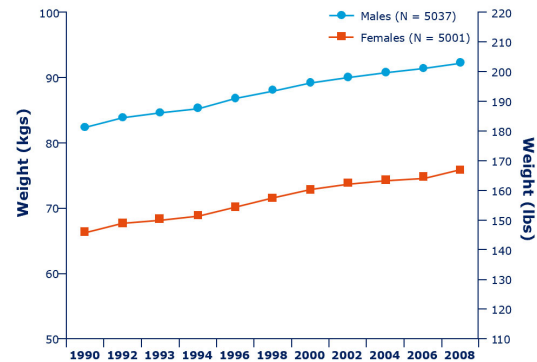
New paradigm



# Medical Management of Obesity in Women's Health

Body Weight and Body Fat  
Are Defended as Weight  
Increases Over the  
Lifespan for 95% of People

Average 18-year weight trajectory for men and women



Malhotra R, et al. Obesity 2013; 21: 1923-1934.

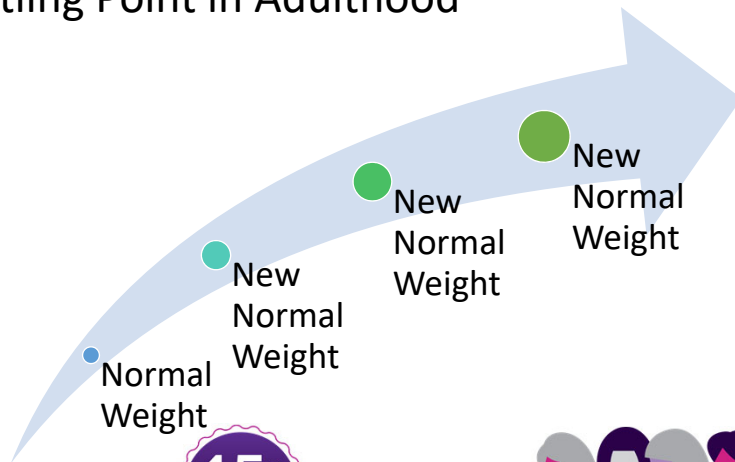
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The Effect of Continued Environmental Pressure on Body  
Weight Settling Point in Adulthood



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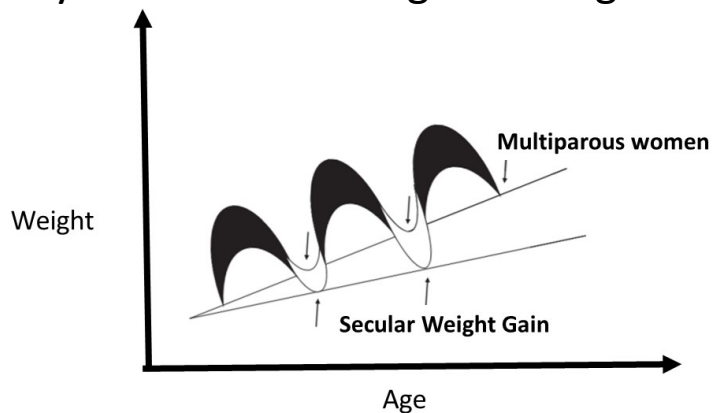


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## Medical Management of Obesity in Women's Health

## Each Pregnancy Results on Average in ~1 Kg of Weight Gain



Melzer K, Schutz Y. International Journal of Obesity. 2010; 34:S44-S52.

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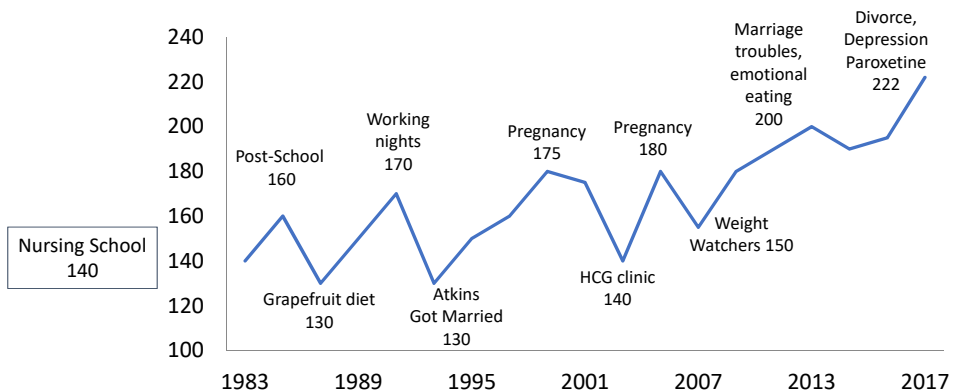


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## On an individual basis, weight across the lifespan often looks like this...



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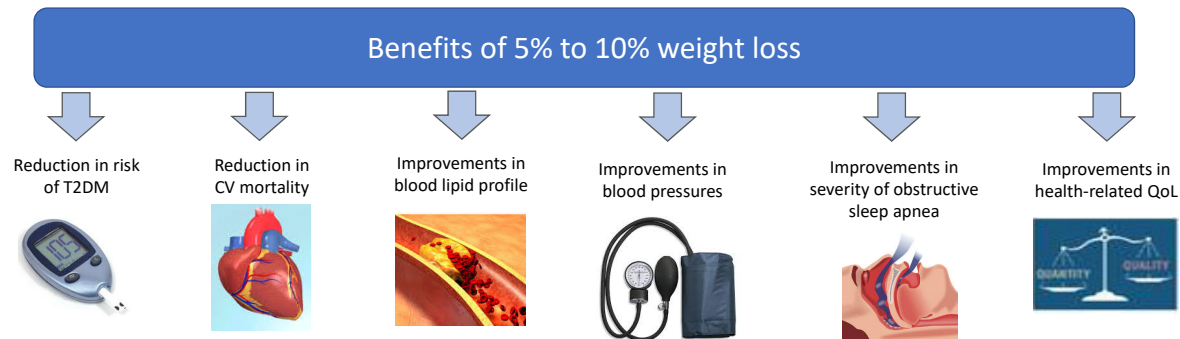
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## Weight Loss Improves Obesity-Related Comorbidity



Knowler WC, et al. N Engl J Med. 2002;346:393-403.  
Li G, et al. Lancet Diabetes Endocrinol. 2014;2:474-480.  
Ryan DH, Curr Obes Rep. 2017;6:187-194.  
Wing RR, et al. Diabetes Care. 2011;34:1481-1486.  
Foster DG, et al. Arch Intern Med 2009;169:1619-1626.  
Warkentin LM, et al. Obes Rev. 2014;15:169-182.

Weight loss may also improve non-alcoholic fatty liver disease and osteoarthritis

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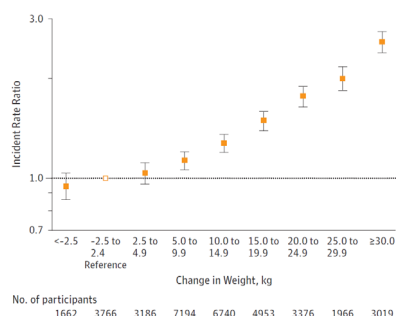


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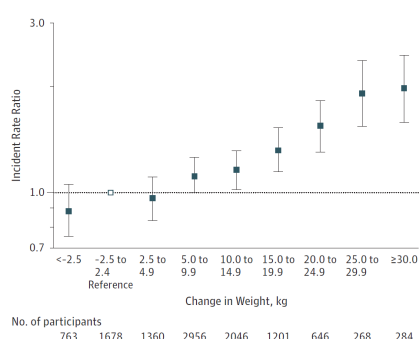


## Weight Gain From Early to Middle Adulthood and Risk for T2DM, CVD, Cancer, Non-traumatic Death

Never smoking women, median follow-up 18 years



Never smoking men, median follow-up 14 years



Zheng Y, Manson JE, Yuan C, et al. JAMA. 2017;318(3):255-269.

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# Medical Management of Obesity in Women's Health

## Pharmacologic Therapies

Agent	Action	Approval by US FDA	Scheduled Drug
Phentermine	• Sympathomimetic amine; norepinephrine release and to lesser extent releases other monoamines	Approved 1959	YES
Orlistat	• Pancreatic lipase inhibitor; Blocks absorption of 30% of ingested dietary fat	Approved 1999 OTC Approved 2006	NO
Lorcaserin	• 5-HT <sub>2C</sub> serotonin agonist • Little affinity for other serotonergic receptors	Approved 2012	YES
Phentermine/ Topiramate ER	• Sympathomimetic • Anticonvulsant (GABA receptor modulator carbonic anhydrase inhibitor, glutamate antagonist)	Approved 2012	YES
Naltrexone ER/ Bupropion ER	• Opioid receptor antagonist • Dopamine/norepinephrine reuptake inhibitor	Approved 2014	NO
Liraglutide	• GLP-1 receptor agonist	Approved 2014	NO

OTC = over the counter; ER = extended release; GABA = gamma-aminobutyric acid

[www.accessdata.fda.gov/scripts/cder/drugsatfda](http://www.accessdata.fda.gov/scripts/cder/drugsatfda)

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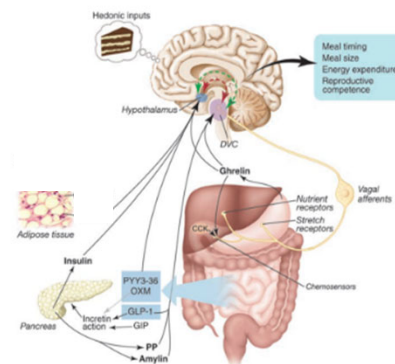
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## New Paradigm: Food intake and Body Fat Regulation Are Largely Biologically Determined

- The brain regulates food intake
  - Homeostatic System – hunger and satiety
  - Reward System – craving and susceptibility to food cues
- Peripheral signals communicate
  - Acute food intake status – **GLP-1, CCK, PYY, ghrelin, amylin, vagus nerve**, etc.
  - Body fat status - **Leptin**
- The brain regulates energy expenditure



CCK = cholecystokinin; GLP-1 = glucagon-like peptide-1; PYY = peptide tyrosine tyrosine.

Berthoud HR, et al. Gastroenterology. 2017;152(7):1728-38.

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# Medical Management of Obesity in Women's Health

## GLP-1 Agonist Clinical Data

**The role of gut hormones in obesity**  
Jessica KW. Ma<sup>1,2</sup>, Justine M. Makrides<sup>1,2,3</sup> and Rachel L. Stalham<sup>1,2,3</sup>

**Abstract**  
The gut hormones ghrelin, leptin, insulin, and GLP-1 regulate energy balance and body weight. Ghrelin stimulates appetite and increases energy intake, while leptin and insulin suppress appetite and decrease energy intake. GLP-1 suppresses appetite and decreases energy intake. The gut hormones ghrelin, leptin, insulin, and GLP-1 are all involved in the regulation of energy balance and body weight. Ghrelin stimulates appetite and increases energy intake, while leptin and insulin suppress appetite and decrease energy intake. GLP-1 suppresses appetite and decreases energy intake.

**The effects of GLP-1 analogues in obese, insulin-using type 2 diabetes in relation to eating behaviour**  
Melanie Rossiter<sup>1,2</sup>, Amy Reed<sup>1,2,3</sup>, Jade Foley<sup>1,2,3</sup>, Heather Woodhouse<sup>1,2</sup>, Steven Brown<sup>1,2,3</sup>, Kate Brophy<sup>1,2,3</sup>

**Abstract**  
Background: Insulin resistance is generally considered to be the major underlying or causative mechanism for the development of type 2 diabetes. However, the role of insulin resistance in the pathogenesis of type 2 diabetes is still unclear. The aim of this study was to investigate the effects of GLP-1 analogues on eating behaviour in obese, insulin-using type 2 diabetes. Methods: A randomised, controlled trial of 12 weeks duration. Participants were randomised to receive either a GLP-1 analogue or placebo. The primary outcome was the change in energy intake. Results: The GLP-1 analogue group showed a significant reduction in energy intake compared to the placebo group. Conclusion: GLP-1 analogues reduce energy intake in obese, insulin-using type 2 diabetes.

**Role of gastrointestinal hormones in feeding behavior and obesity treatment**  
Stephanie Ann Rodriguez<sup>1,2</sup>, Brenda Rodriguez<sup>1,2</sup>, Kay Chen<sup>1,2,3</sup>, Andrea Rodriguez<sup>1,2</sup>, Melissa Rodriguez<sup>1,2</sup>, Lisa Lee<sup>1,2</sup>

**Abstract**  
Gastrointestinal hormones play a key role in the regulation of feeding behavior and energy balance. Ghrelin stimulates appetite and increases energy intake, while leptin and insulin suppress appetite and decrease energy intake. GLP-1 suppresses appetite and decreases energy intake. The gut hormones ghrelin, leptin, insulin, and GLP-1 are all involved in the regulation of energy balance and body weight. Ghrelin stimulates appetite and increases energy intake, while leptin and insulin suppress appetite and decrease energy intake. GLP-1 suppresses appetite and decreases energy intake.

**The Effect of Glucagon-like Peptide-1 (GLP-1) on Obesity**  
David Young, Michael Young and Peter Bell

**Abstract**  
Obesity is a major public health problem. The pathogenesis of obesity is still unclear. The aim of this study was to investigate the effects of GLP-1 on obesity. Methods: A randomised, controlled trial of 12 weeks duration. Participants were randomised to receive either a GLP-1 analogue or placebo. The primary outcome was the change in body weight. Results: The GLP-1 analogue group showed a significant reduction in body weight compared to the placebo group. Conclusion: GLP-1 analogues reduce body weight in obese subjects.

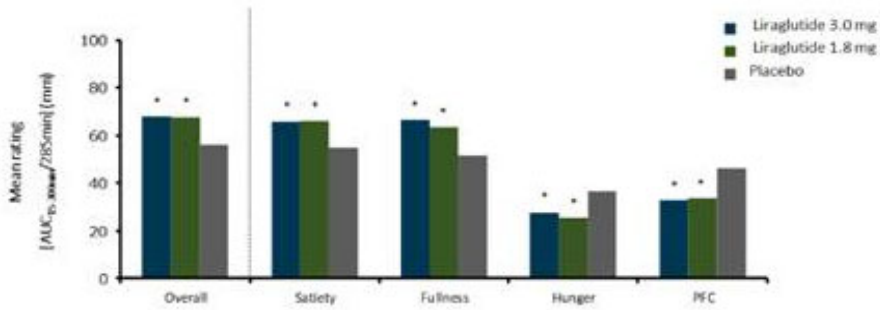
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## Liraglutide Influences All Dimensions of Appetite in Obese Subjects After 5 Weeks of Treatments



5 weeks treatment including 0.6 mg weekly dose escalation. Ratings are AUC<sub>0-100min</sub>/285min reported as FASLS means.

Disclaimer: Liraglutide 1.8mg is not approved for weight management  
 \*Statistical significance P <.05 vs. placebo.  
 Data for overall includes 100 minus scores for hunger and PFC.  
 Adapted from: van Can J, et al. Int J Obes (Lond). 2014;38:784-793.

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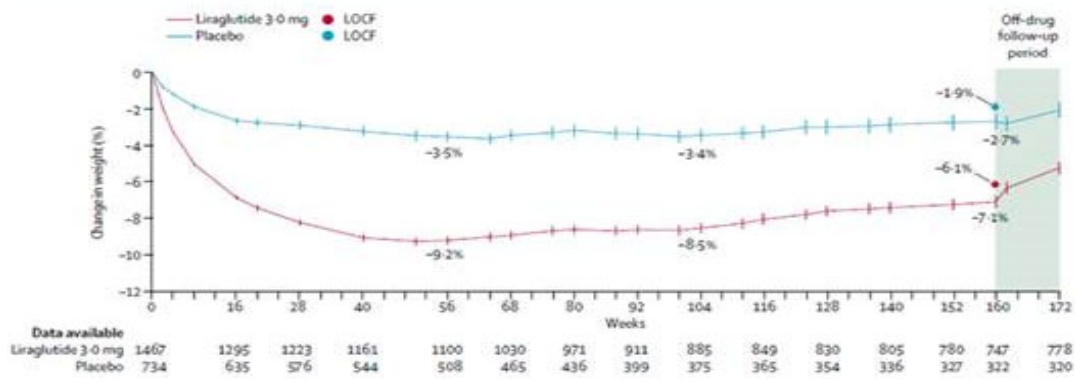
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## SCALE Obesity and Prediabetes: Change in Body Weight (%), Liraglutide 3.0 mg vs. Placebo



Le Roux C, et al. Lancet. 2017;389:1399-1409.

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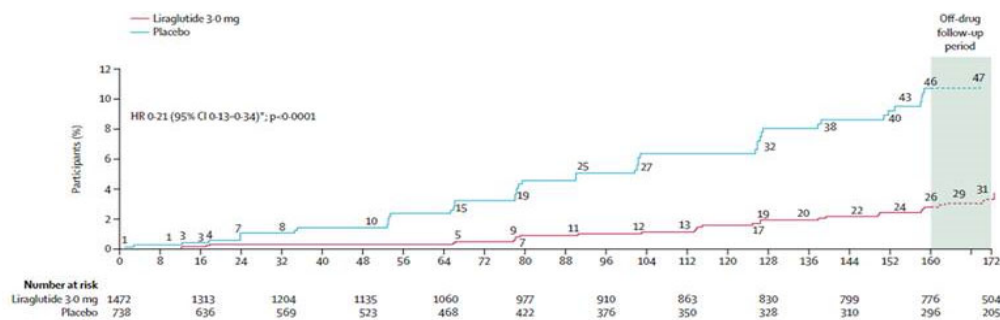


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## 3-Year Assessment of the SCALE Obesity and Prediabetes Trial

This study evaluated the proportion of individuals with prediabetes who were diagnosed with T2DM



Le Roux C, et al. Lancet. 2017;389:1399-1409.

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