Women's Health Annual Visit® 15th ANNIVERSARY

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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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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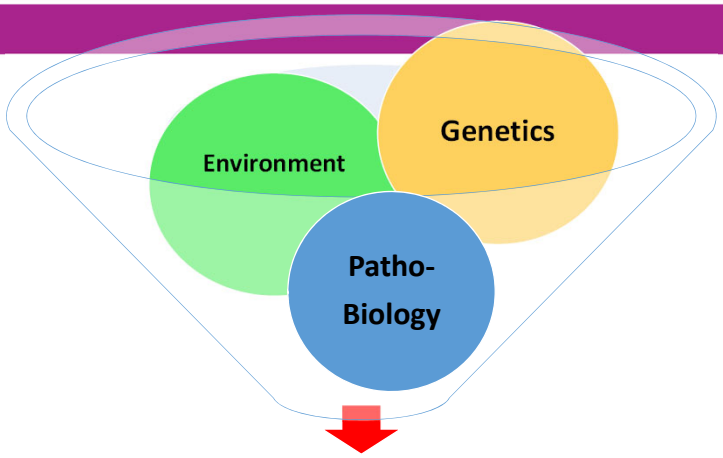
Etiology of Obesity



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

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Metabolic and Biologic Adaptations that Defend Body Weight

Old paradigm

New paradigm

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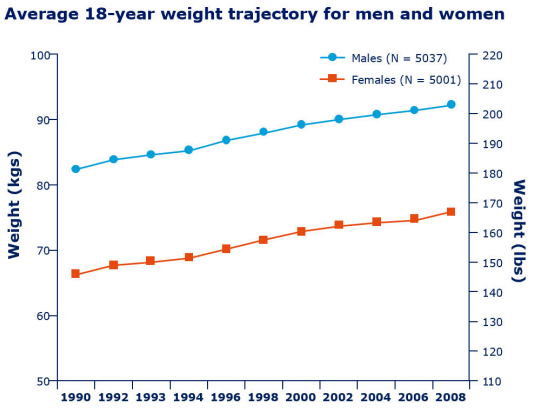
Body Weight and Body Fat Are Defended as Weight Increases Over the Lifespan for 95% of People



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

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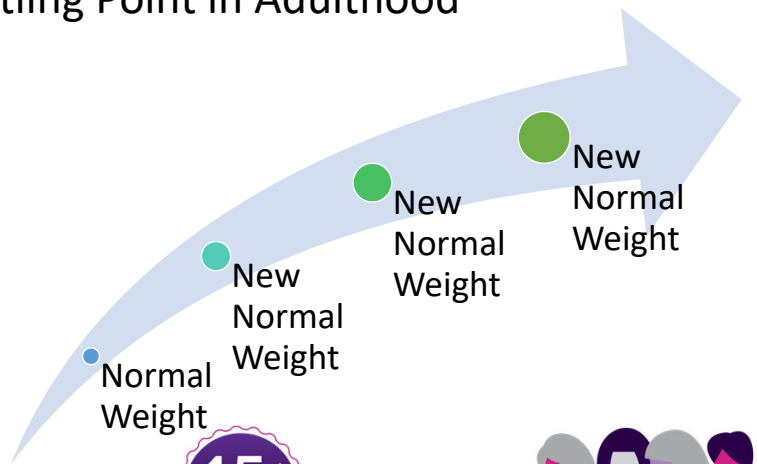
The Effect of Continued Environmental Pressure on Body Weight Settling Point in Adulthood



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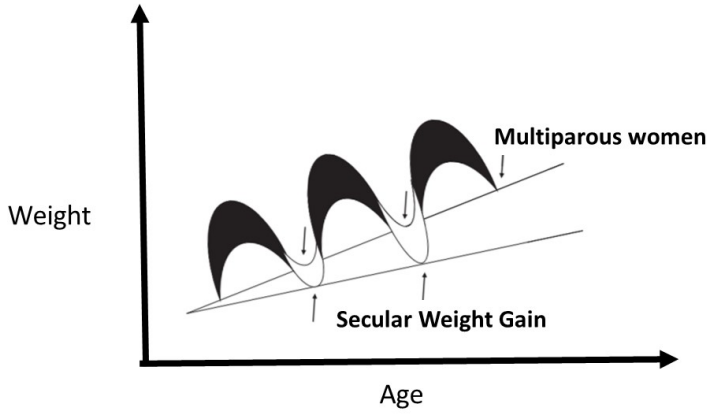
Each Pregnancy Results on Average in ~1 Kg of Weight Gain



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

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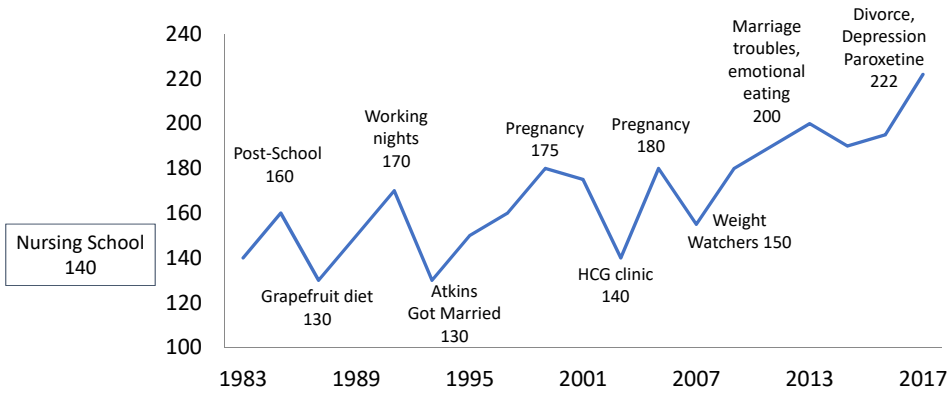
On an individual basis, weight across the lifespan often looks like this…



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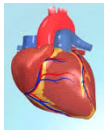
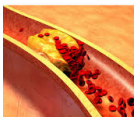
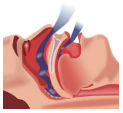
Weight Loss Improves Obesity-Related Comorbidity

Benefits of 5% to 10% weight loss

- Reduction in risk of T2DM
- Reduction in CV mortality
- Improvements in blood lipid profile
- Improvements in blood pressures
- Improvements in severity of obstructive sleep apnea
- Improvements in health-related QoL




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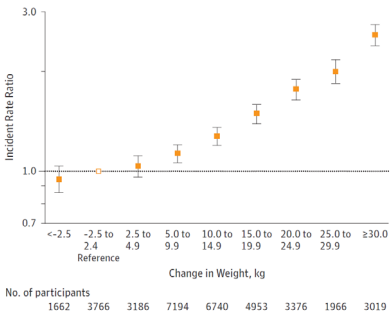
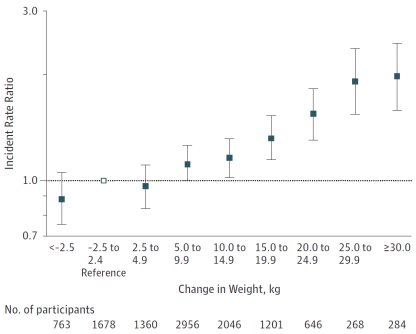
Weight Gain From Early to Middle Adulthood and Risk for T2DM, CVD, Cancer, Non-traumatic Death

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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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_{2C} 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

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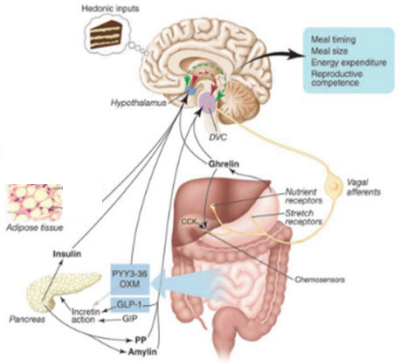
New Paradigm: Food intake and Body Fat Regulation Are Largely Biologically Determined

- 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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GLP-1 Agonist Clinical Data

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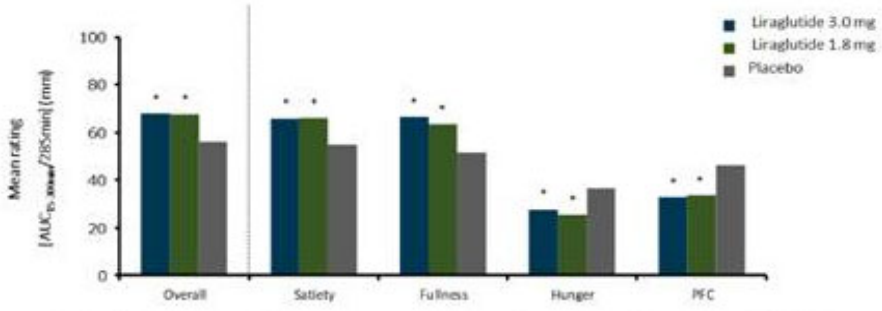
Liraglutide Influences All Dimensions of Appetite in Obese Subjects After 5 Weeks of Treatments



5 weeks treatment including 0.6 mg weekly dose escalation . Ratings are $AUC_{15\text{-}100mm}$/285min reported as FAS LS-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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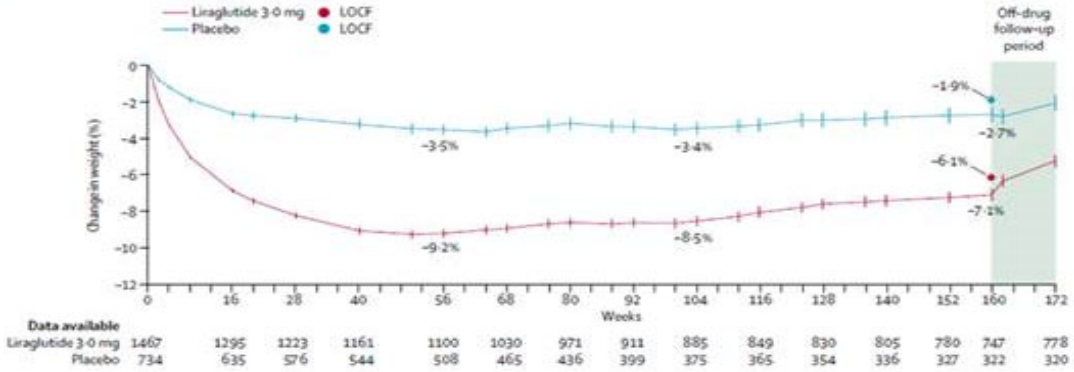
SCALE Obesity and Prediabetes: Change in Body Weight (%), Liraglutide 3.0 mg vs. Placebo



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

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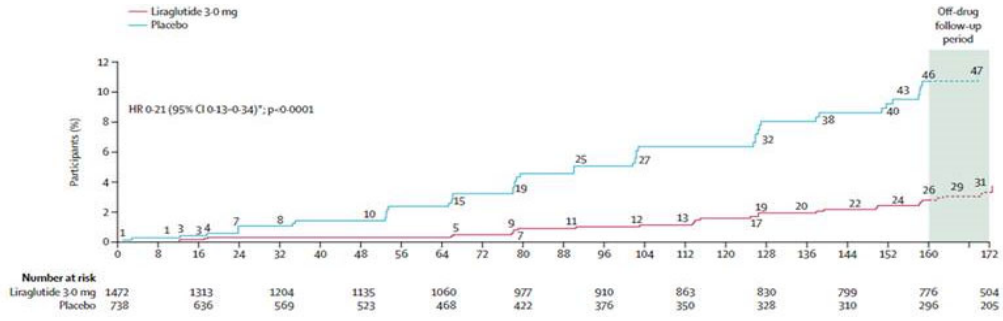
3-Year Assessment of the SCALE Obesity and Prediabetes Trial

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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