Women's Health Annual Visit® 15th ANNIVERSARY

Medical Management of Obesity in Women's Health

Donna H. Ryan, MD

Andrea J. Singer, MD, FACP, CCD

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

1

omnia EDUCATION

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

Women's Health 15th ANNIVERSARY Annual Visit®

2

omnia EDUCATION

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

Women's Health 15th ANNIVERSARY Annual Visit®

3

omnia EDUCATION

Factors that Drive Weight Gain Across the Lifespan

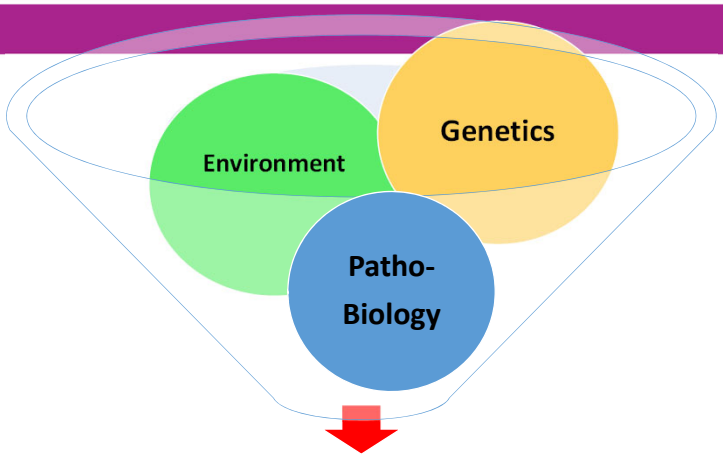
- Medications
- Poor sleep, shift work
- Poor eating behavior/processed foods
- Emotional stress
- Smoking Cessation
- Marriage
- Alterations in the growth trajectory through adolescence
- Post-pregnancy weight retention
- Menopause (body fat distribution)

Women's Health 15th ANNIVERSARY Annual Visit®

4

omnia EDUCATION

Etiology of Obesity



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

Women's Health 15th ANNIVERSARY Annual Visit®

5

omnia EDUCATION

Metabolic and Biologic Adaptations that Defend Body Weight

Old paradigm

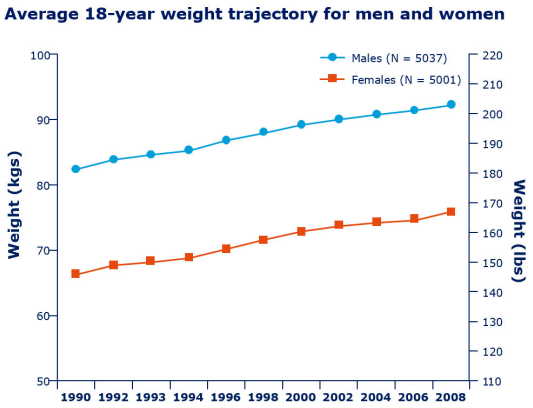
New paradigm

Women's Health 15th ANNIVERSARY Annual Visit®

6

omnia EDUCATION

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



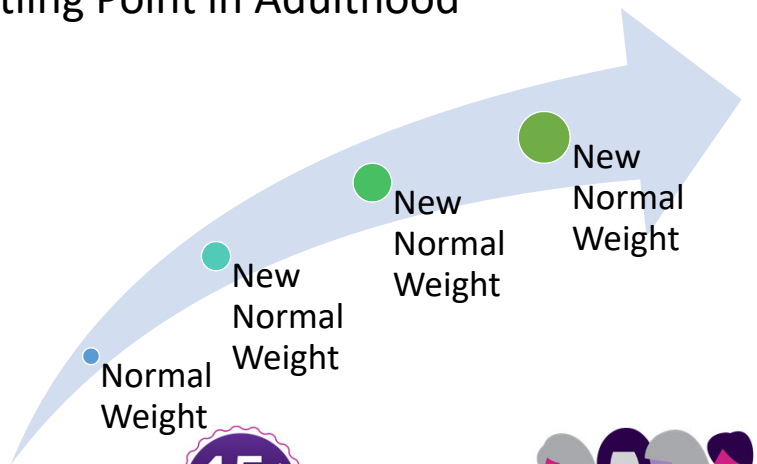
Malhotra R, et al. Obesity 2013; 21: 1923-1934.

Women's Health 15th ANNIVERSARY Annual Visit®

7

omnia EDUCATION

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

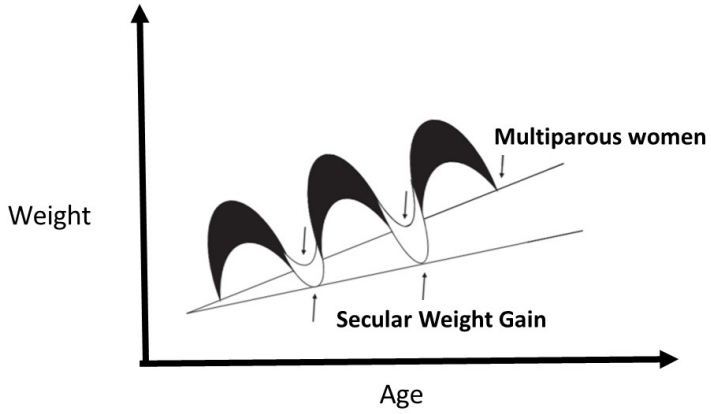


Women's Health 15th ANNIVERSARY Annual Visit®

8

omnia EDUCATION

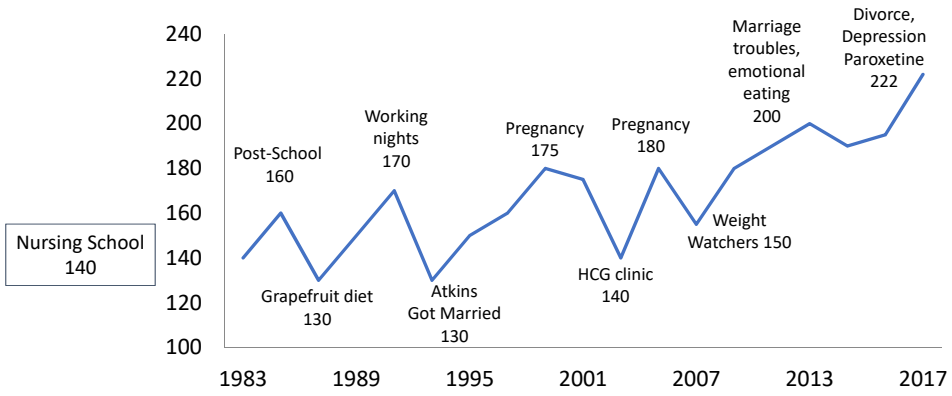
Each Pregnancy Results on Average in ~1 Kg of Weight Gain



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

omnia EDUCATION

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

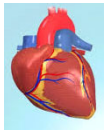
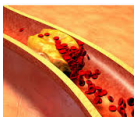


omnia EDUCATION

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

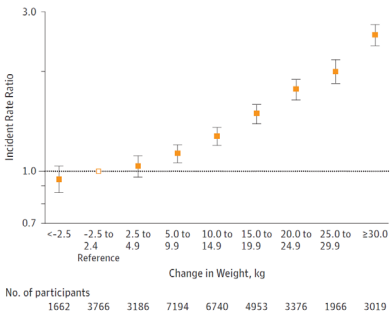

Knowler WC, et al. N Engl J Med. 2002;346:393-403.
Li G, et al. Lancet Diabetes Endocrinol. 2014;2:474-480.
Ryan DH, Curr Obes Rep. 2017;6:187-194.
Wing RR, et al. Diabetes Care. 2011;34:1481-1486.
Foster DG, et al. Arch Intern Med 2009;169:1619-1626.
Warkentin LM, et al. Obes Rev. 2014;15:169-182.

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

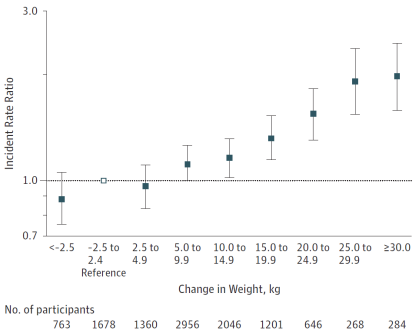
omnia EDUCATION

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.

omnia EDUCATION

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

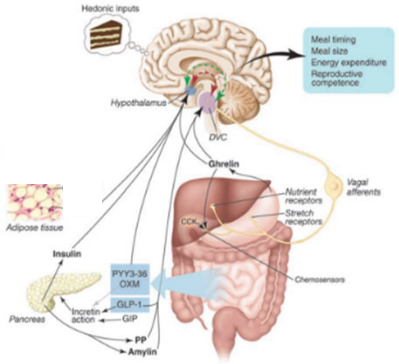
OTC = over the counter; ER = extended release; GABA = gamma-aminobutyric acid

www.accessdata.fda.gov/scripts/cder/drugsatfda

omnia EDUCATION

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.

omnia EDUCATION

GLP-1 Agonist Clinical Data

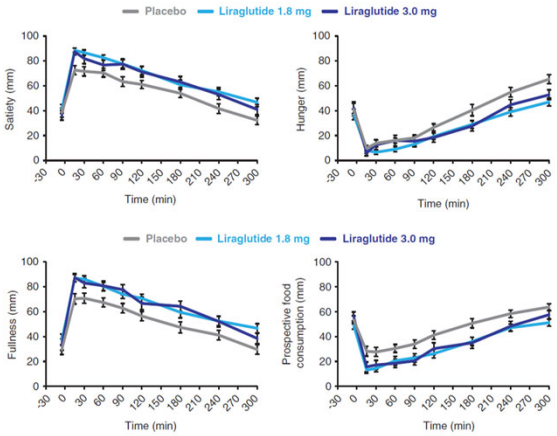
Women's Health 15th ANNIVERSARY Annual Visit®

15

omnia EDUCATION

Liraglutide 1.8 mg and 3.0 mg

- ↓ hunger, prospective food consumption
- ↑ satiety, fullness
- Delays gastric emptying



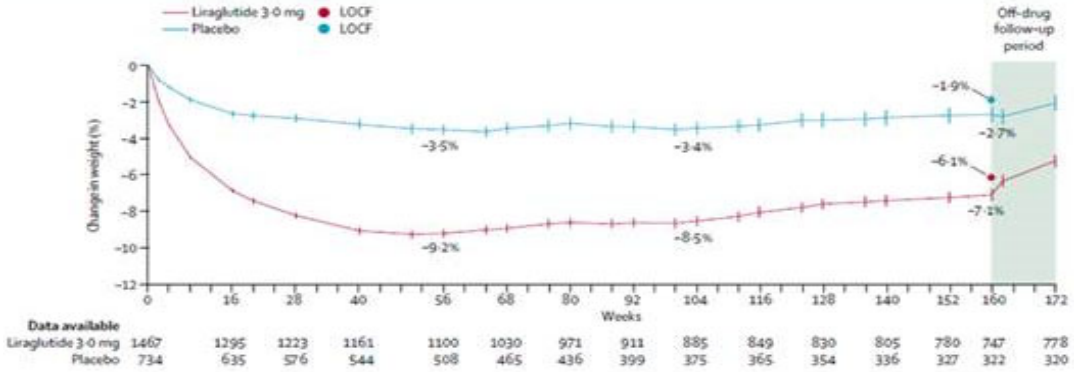
Disclaimer: Liraglutide 1.8mg is not approved for weight management
*Statistical significance P <.05 vs. placebo.
Data for overall includes 100 minus scores for hunger and PFC.
van Can J, et al. Int J Obes (Lond). 2014;38:784-793.

Women's Health 15th ANNIVERSARY Annual Visit®

16

omnia EDUCATION

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



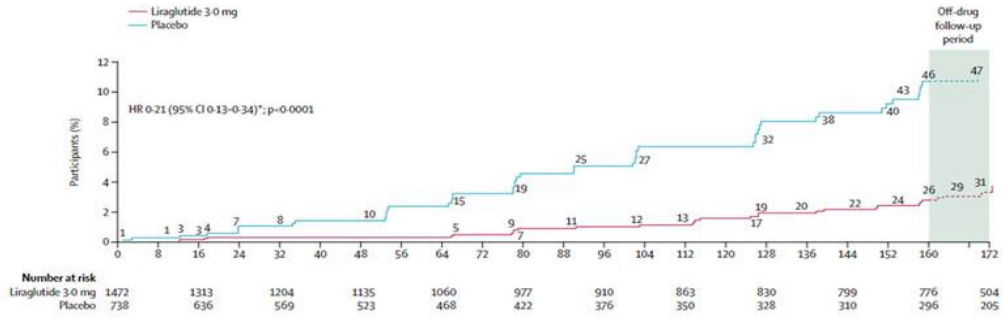
Le Roux C, et al. Lancet. 2017;389:1399-1409.

17

omnia EDUCATION

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.

18

19