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.

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
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

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


The Effect of Continued Environmental Pressure on Body Weight Settling Point in Adulthood
Each Pregnancy Results on Average in ~1 Kg of Weight Gain


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

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


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

Pharmacologic Therapies

<table>
<thead>
<tr>
<th>Agent</th>
<th>Action</th>
<th>Approval by US FDA</th>
<th>Scheduled Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td>Sympathomimetic amine; norepinephrine release and to lesser extent releases other monoamines</td>
<td>Approved 1959</td>
<td>YES</td>
</tr>
<tr>
<td>Orlistat</td>
<td>Pancreatic lipase inhibitor; Blocks absorption of 30% of ingested dietary fat</td>
<td>Approved 1999</td>
<td>NO</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>5-HT2C serotonin agonist; Little affinity for other serotonergic receptors</td>
<td>Approved 2006</td>
<td>YES</td>
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<tr>
<td>Phentermine/Topiramate ER</td>
<td>Sympathomimetic; Anticonvulsant (GABA receptor modulator carbonic anhydrase inhibitor, glutamate antagonist)</td>
<td>Approved 2012</td>
<td>YES</td>
</tr>
<tr>
<td>Naltrexone ER/Bupropion ER</td>
<td>Opioid receptor antagonist; Dopamine/norepinephrine reuptake inhibitor</td>
<td>Approved 2014</td>
<td>NO</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>GLP-1 receptor agonist</td>
<td>Approved 2014</td>
<td>NO</td>
</tr>
</tbody>
</table>

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

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

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.

GLP-1 Agonist Clinical Data

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.

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


3-Year Assessment of the SCALE Obesity and Prediabetes Trial

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