

## SYLLABUS AND COURSE GUIDE

# The Epidemic Within the Pandemic: Managing Complications in Populations with Obesity

**A Free, 90-Minute Live and OnDemand Activity**

**Premier Date: Wednesday, June 30, 2021**

**12:00 PM -1:30 PM ET (live)**

Credit Expiration Date: Thursday, June 30, 2022

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**FACULTY:**

Robert F. Kushner, MD, MS, DABOM (Moderator)

Ken Fujioka, MD

Fatima Cody Stanford, MD, MPH, MPA, MBA, FAAP, FACP, FAHA, FAMWA, FTOS

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## INFORMATION FOR PARTICIPANTS

### Statement of Need

Obesity is increasingly recognized as a multi-causal chronic disease that leads to structural and physiological abnormalities and functional impairments. Despite the growing prevalence and substantial burden of obesity in terms of health-related quality of life (HRQoL), healthcare utilization, and healthcare costs, obesity remains under-diagnosed and under-treated. The recent recognition that obesity is associated with increased risk of morbidity and mortality with coronavirus disease 2019 (COVID-19) shines a light on the fact that obesity is characterized by higher prevalence of physiologic alterations, such as chronic inflammation and impaired respiratory function, when compared to the non-obese state.

This live and OnDemand webcast will include interactive animated 3-D models and a live Q&A session. The discussion, led by expert faculty, will cover pathophysiological features of obesity that influence weight loss, guidelines for screening, diagnosis, and patient counseling, and how to assess efficacy and safety of available and emerging therapies for long-term treatment of obesity.

### Learning Objectives

At the end of this CE activity, participants should be able to:

- Identify pathophysiological features of obesity that influence weight loss and maintenance.
- Apply guidelines for screening, diagnosis, and patient counseling for obesity and obesity-related disorders.
- Assess efficacy and safety of available and emerging therapies for long-term treatment of obesity.

*The following learning objectives pertain only to those requesting CNE or CPE credit:*

- Identify pathophysiological features of obesity that influence weight loss and maintenance.
- Summarize guidelines for screening, diagnosis, and patient counseling for obesity and obesity-related disorders.
- Describe the efficacy and safety of available and emerging therapies for long-term treatment of obesity.

### Financial Support

Supported by an educational grant from Novo Nordisk Inc.

### Target Audience

Primary care physicians, endocrinologists, nurse practitioners, PAs, nurses, and pharmacists

## CREDIT INFORMATION

### CME Credit (Physicians):

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Provider approved by the California Board of Registered Nursing, Provider Number CEP 15510, for 1.5 contact hours.

**Note to Nurse Practitioners:** Nurse Practitioners can apply for *AMA PRA Category 1 Credit*<sup>™</sup> through the American Academy of Nurse Practitioners (AANP). AANP will accept *AMA PRA Category 1 Credit*<sup>™</sup> from organizations accredited by the Accreditation Council for Continuing Medical Education. Nurse practitioners can also apply for credit through their state boards.

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Live: 0376-0000-21-076-L01-P

Enduring: 0376-0000-21-076-H01-P

Type: Knowledge-based

### ABIM MOC Credit:

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.5 medical knowledge MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

**Learning Formats:** Live activity; Enduring material

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### Royal College MOC Credit:

Through an agreement between the Accreditation Council for Continuing Medical Education and the Royal College of Physicians and Surgeons of Canada, medical practitioners participating in the Royal College MOC Program may record completion of accredited activities registered under the ACCME's "CME in Support of MOC" program in Section 3 of the Royal College's MOC Program.

### MIPS Improvement Activity:

This activity counts towards MIPS Improvement Activity requirements under the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA). Clinicians should submit their improvement activities by attestation via the CMS Quality Payment Program website.

**Post-tests, credit request forms, and activity evaluations must be completed online** (requires free account activation), and participants can print their certificate or statement of credit immediately (75% pass rate required). This website supports all browsers except Internet Explorer for Mac. For complete technical requirements and privacy policy, visit <https://www.cmeoutfitters.com/privacy-and-confidentiality-policy>.

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Dr. Kushner reports that he receives research support from Epitech Medical. He is a consultant for Novo Nordisk and WW International, Inc.

Dr. Fujioka reports that he is a consultant for Amgen Inc.; Boehringer Ingelheim; Gelesis; Janssen Global Services, LLC; Novo Nordisk; Phenomix Sciences; Sunovion Pharmaceuticals Inc.; and Takeda Pharmaceuticals U.S.A., Inc. He is on the speakers bureau for Novo Nordisk and Takeda Pharmaceuticals U.S.A., Inc.

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Tony Graham, MD (peer reviewer) has no disclosures to report.

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## FACULTY BIOS

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### **Robert F. Kushner, MD, MS, DABOM (Moderator)**

**Professor, Departments of Medicine and Medical Education  
Northwestern University Feinberg School of Medicine  
Chicago, IL**

Robert Kushner is Professor of Medicine and Medicine Education at Northwestern University Feinberg School of Medicine, and Director of the Center for Lifestyle Medicine in Chicago, IL, USA. After finishing a residency in Internal Medicine at Northwestern University, he went on to complete a post-graduate fellowship in Clinical Nutrition and earned a master's degree in Clinical Nutrition and Nutritional Biology from the University of Chicago. Dr. Kushner is past-President of The Obesity Society (TOS), the American Society for Parenteral and Enteral Nutrition (ASPEN), the American Board of Physician Nutrition Specialists (ABPNS), and a founder and past-Chair of the American Board of Obesity Medicine (ABOM). He was awarded the 2016 Clinician-of-the-Year Award by The Obesity Society, the John X. Thomas, Jr. Best Teachers of Feinberg Award at Northwestern University Feinberg School of Medicine in 2017, and the Friend Award by the Academy of Nutrition and Dietetics Weight Management Group in 2020.

Dr. Kushner has authored over 250 original articles, reviews, books and book chapters covering medical nutrition, medical nutrition education, and obesity, and is an internationally recognized expert on the care of patients who are overweight or obese. He is author/editor of multiple books including Nutrition and Bariatric Surgery (CRC Press, 2015), "Lifestyle Medicine: A Manual for Clinical Practice" (Springer, 2016), Obesity Medicine, Medical Clinics of North America (Elsevier, 2018), Creating a Lifestyle Medicine Center (Springer, 2020), and "Primary Care: Evaluation and Management of Obesity" (Wolter Kluwer, 2022). His latest popular book is "Six Factors to Fit: Weight Loss that Works for You!" (Eat Right Press, 2020). Dr. Kushner's research interests include medical and obesity education, and lifestyle and pharmacological approaches to obesity.



## FACULTY BIOS

### **Ken Fujioka, MD**

**Director, Nutrition and Metabolic Research Center  
Founding Director, Center for Weight Management  
Scripps Clinic Department of Diabetes and Endocrine  
San Diego, CA**

Dr. Ken Fujioka is the director of the Nutrition and Metabolic Research Center and the Center for Weight management at the Scripps Clinic in La Jolla, California. His time is divided equally between clinical research and clinical practice. Dr. Fujioka's research includes diets, medications, bariatric surgery, medical devices, web based weight loss programs, and outcomes in obesity treatment. The Nutrition and Metabolic Research Center has completed over 100 clinical trials in obesity related areas. The Center for Weight Management is a referral based multispecialty center that includes endocrinologists, surgeons, psychologist, dietitians, exercise physiologist, and nurse practitioners. The multispecialty clinic sees over a 1,000 patients a month and is a recognized Center of Excellence treating all forms of obesity, morbid obesity, and eating disorders. Dr. Fujioka has also worked for the Medical Board for the state of California as an expert witness. In 1997 he was asked to define the standard of care in the treatment of obesity. He has published original research, as well as chapters of books and reviews. Additionally, he has worked with multiple government agencies and pharmaceutical companies on drug development and use in clinical practice.

### **Fatima Cody Stanford, MD, MPH, MPA, MBA, FAAP, FACP, FAHA, FAMWA, FTOS**

**Obesity Medicine Physician Scientist  
Department of Medicine, Endocrine Division Director of Equity, Neuroendocrine Unit  
Department of Pediatrics-Endocrinology  
Massachusetts General Hospital and Harvard Medical School  
Nutrition Obesity Research Center at Harvard, Director of Diversity  
Boston, MA**

Dr. Stanford practices and teaches at Massachusetts General Hospital (MGH)/ Harvard Medical School (HMS) as one of the first fellowship-trained obesity medicine physicians in the world. Dr. Stanford received her BS and MPH from Emory University as a MLK Scholar, her MD from the Medical College of Georgia School of Medicine as a Stoney Scholar, and her MPA from the Harvard Kennedy School of Government as a Zuckerman Fellow in the Harvard Center for Public Leadership. She completed her Obesity Medicine & Nutrition Fellowship at MGH/HMS after completing her internal medicine and pediatrics residency at the University of South Carolina. She has served as a health communications fellow at the Centers for Disease Control and Prevention and as a behavioral sciences intern at the American Cancer Society. Upon completion of her MPH, she received the Gold Congressional Award, the highest honor that Congress bestows upon America's youth. Dr. Stanford has completed a medicine and media internship at the Discovery Channel. In addition to being an American Medical Association (AMA) Foundation Leadership Award recipient in 2005 and receiving an AMA Paul Ambrose Award for national leadership among resident physicians in 2009, Dr. Stanford was selected for the AMA Inspirational Physician Award in 2015. The American College of Physicians (ACP) selected her as the 2013 recipient of the Joseph E. Johnson Leadership Award and the Massachusetts ACP selected her for the Young Leadership Award in 2015. She is the 2017 recipient of the HMS Amos Diversity Award and Massachusetts Medical Society (MMS) Award for Women's Health. In 2019, she was selected as the Suffolk District Community Clinician of the Year and for the Reducing Health Disparities Award for MMS. Dr. Stanford was also selected for The Obesity Society Clinician of the Year in 2020. In 2021, she will be awarded the AMA Dr. Edmond and Rima Cabbabe Dedication to the Profession Award which recognizes a physician who demonstrates active and productive improvement to the profession of medicine through community service, advocacy, leadership, teaching, or philanthropy.



## The Epidemic Within the Pandemic: Managing Complications in Populations With Obesity

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activity.

### Today's Activity Is Eligible for ABIM MOC Credit and as a CME for MIPS Improvement Activity

Actively engage in the activity through polling and asking faculty questions.  
Complete your post-test and evaluation at the conclusion of the activity.



Be sure to fill in your **ABIM ID number**  
and **DOB (MM/DD)** on the evaluation  
so we can submit your credit to ABIM



Over the next 90 days, actively work to  
incorporate improvements in your  
clinical practice from this presentation

- Complete the follow-up survey from CME Outfitters in approximately 3 months
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Founding Director, Center for Weight Management  
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## Learning Objective 1

Identify pathophysiologic features of obesity that influence weight loss and maintenance.

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# CME

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### Learning Objective 2

Summarize guidelines for screening, diagnosis, and patient counseling for obesity and obesity-related disorders.

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### Learning Objective 3

Assess efficacy and safety of available and emerging therapies for long-term treatment of obesity.

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### Introduction: When Pandemics Collide

Fatima Cody Stanford, MD, MPH, MPA,  
MBA, FAAP, FACP, FAHA, FAMWA, FTOS

## The Obesity and COVID-19 Pandemics Collide

- Global prevalence of obesity nearly tripled from 1975 to 2016<sup>1</sup>
- By 2025:
  - 2.7 billion adults will be overweight<sup>2</sup>
  - > 1 billion will have obesity<sup>2</sup>
- Obesity is a disease and a risk factor for adverse outcomes in COVID-19<sup>3,4</sup>
  - Triples the risk of hospitalization
  - Increases risk for mechanical ventilation and death



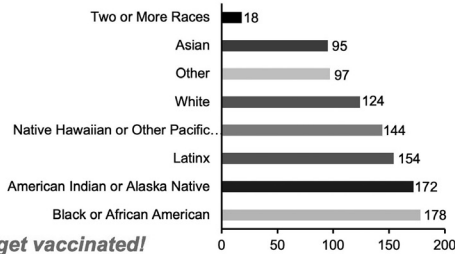
1. World Health Organization (WHO). Obesity and Overweight. <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>. Accessed June 28, 2021.;  
2. World Obesity Federation. Prevalence of Obesity. <https://www.worldobesity.org/about/about-obesity/prevalence-of-obesity>. Accessed June 28, 2021.;  
3. Johns Hopkins University and Medicine Coronavirus Resource Center. Covid-19 Dashboard. <https://coronavirus.jhu.edu/map.html>. Accessed June 28, 2021.;  
4. Centers for Disease Control and Prevention (CDC). Overweight and Obesity. <https://www.cdc.gov/obesity/data/obesity-and-covid-19.html>. Accessed June 28, 2021.

## Obesity and COVID-19 Complications Disproportionately Impact Some Racial and Ethnic Groups

Black, Indigenous, Latinx Americans more likely to experience obesity

- 1.3x more likely in Blacks
- 1.2x more likely in Latinx
- 1.6x more likely in Indigenous Americans
- 4 out of 5 Black or Latinx American women and 50% of American Indian or Alaska Native women have obesity or are overweight

Death from COVID-19 complications per 100,000 people by race or ethnicity through Mar 7, 2021



**Encourage your patients to get vaccinated!**

The COVID Racial Data Tracker. 2021. <https://covidtracking.com/race>. Accessed June 28, 2021; U.S. Department of Health and Human Services Office of Minority Health. [www.minorityhealth.hhs.gov](http://www.minorityhealth.hhs.gov). Accessed June 28, 2021.



## Racial/Ethnic Disparities and Implicit Bias

- Racial inequities in US medical care are pervasive<sup>1</sup>
- Studies suggest provider interactions with patients of color are less patient-centered, with fewer requests for patient input about treatment decisions in general<sup>2</sup>
- Efforts to improve equitable medication uptake and utilization among all racial, ethnic, and socioeconomic groups are needed<sup>3</sup>
- Clinicians need to consider social determinants of health

1. Pokorney SD, et al. *Am Heart J*. 2015;170:141-148.; 2. Buller HR, et al. *N Engl J Med*. 2012;366:1287-1297.; 3. Nathan AS, et al. *Circ Cardiovasc Qual Outcomes*. 2019;12:e005600.



## Patient Voices



I'm relieved to be fully vaccinated now for COVID, but I'm about to give up on losing weight. It's impossible for me to keep it off. — Maria T.

I've worked hard on several occasions to get my weight under control. And I've been successful. The problem is I just can't sustain it. — Jeff H.



### Why is it so Difficult to Sustain Weight Loss?

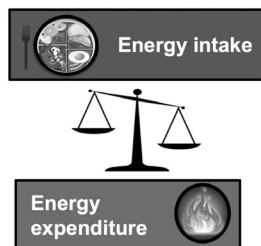
Robert F. Kushner, MD, MS, DABOM

### Learning Objective 1

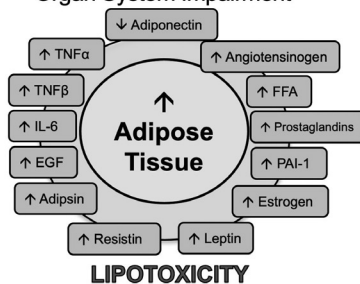
Identify pathophysiologic features of obesity that influence weight loss and maintenance.

## The Pathology of Obesity

### Energy Balance Dysregulation

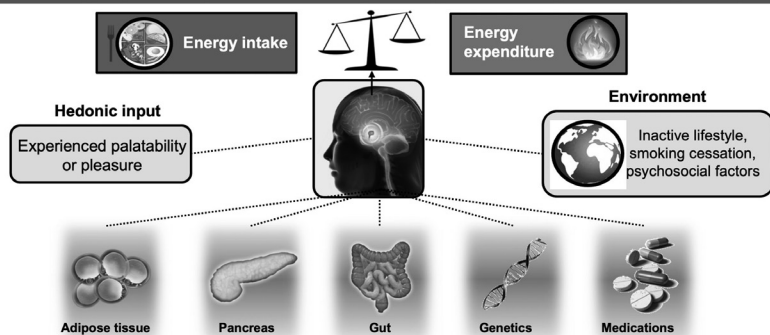


### Organ System Impairment



EGF = epidermal growth factor; FFA = free fatty acids; IL-6 = interleukin 6; PAI-1 = plasminogen activator inhibitor 1; TNF $\alpha$  = tumor necrosis factor alpha; TNF $\beta$  = tumor necrosis factor beta  
Laughlin MR, et al. *Obesity*. 2021;29 (Suppl 1):S1-S50.; Kershaw EE, et al. *Clin Endocrinol Metab*. 2004;89:2548-2556.; Hajer GR, et al. *Eur Heart J*. 2008;29:2959-2971.

## Energy Balance Dysregulation



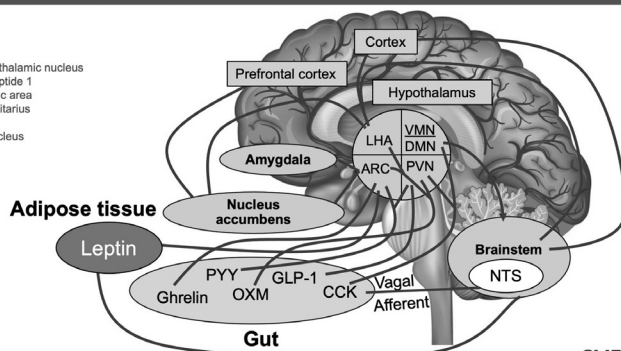
Badman MK, Flier JS. *Science*. 2005;307:1909-1914.; US Department of Health and Human Services. 1998; National Heart, Lung, and Blood Institute (NHLBI). *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*. 1998.

## Animation

### Energy Balance Dysregulation

# Appetite Regulation and the Gut-Brain Axis

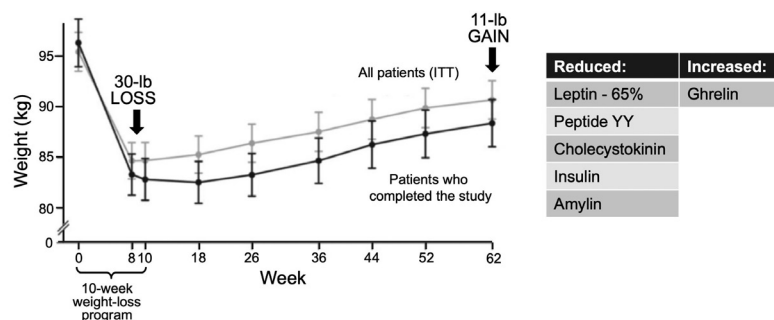
ARC = arcuate nucleus  
CCK = cholecystokinin  
DMN = dorsomedial hypothalamic nucleus  
GLP-1 = glucagon-like peptide 1  
LHA = lateral hypothalamic area  
NTS = nucleus tractus solitarius  
OXM = oxyntomodulin  
PVN = paraventricular nucleus  
PYY = peptide YY



Simpson KA, et al. *Expert Rev Endocrinol Metab.* 2008;3(5):577-592.



## Why Patients Regain: Biologic Adaptations to Weight Loss

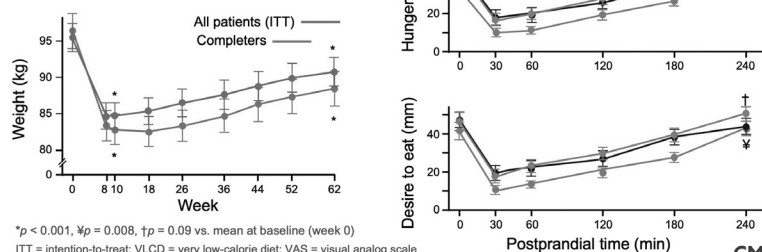


Sumithran P, et al. *N Engl J Med.* 2011;365:1597-1604.



## Hunger Increases in Response to Weight Loss

- 50 individuals with overweight/obesity lost weight on a 10-week VLCD
- Appetite was measured using VAS scores at 0, 10, and 62 weeks



## Why is Obesity Pathological?

Release of adipokines (lipotoxicity)

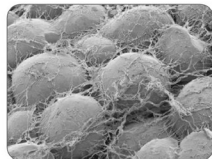
Increased mechanical burden

Increased abdominal pressure

Increased respiratory burden

Fluid and hemodynamic changes/CV burden

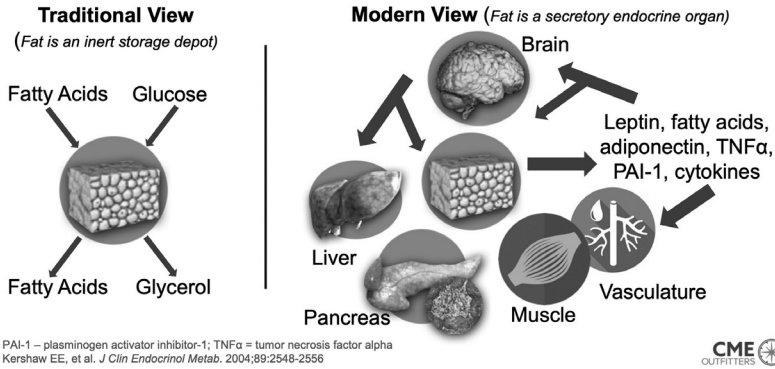
Dietary and physical activity changes associated with obesity



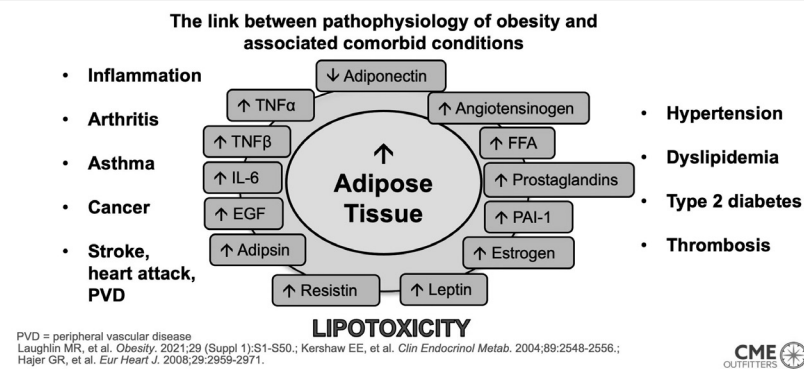
Chait A, den Hartigh LJ. *Front Cardiovasc Med.* 2020; 7:22.



## Adipose Tissue as an Endocrine Organ



## Lipotoxicity: Products of Fat Tissue



## Animation Comorbidities and Consequences of Obesity

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Patient-Centered Screening,  
Diagnosis, and Counseling

Fatima Cody Stanford, MD, MPH, MPA,  
MBA, FAAP, FACP, FAHA, FAMWA, FTOS



### Learning Objective 2

Summarize guidelines for screening, diagnosis, and patient counseling for obesity and obesity-related disorders.

## How is Obesity Defined in Adults?

Weight Status Category	Body Mass Index (kg/m <sup>2</sup> )
Underweight	< 18.5
Normal weight	18.5 – 24.9
Overweight	25.0 – 29.9
Class I obesity	30.0 – 34.9
Class II obesity	35.0 – 39.9
Class III obesity	≥ 40

World Health Organization (WHO). <https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi>. Accessed June 28, 2021.



## Adjustment of BMI Scale for Race, Gender, and Obesity-Related Diseases

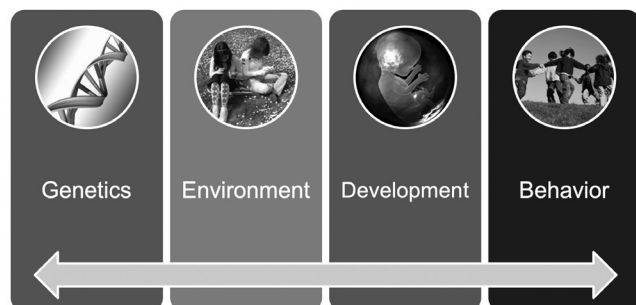
Cutoffs for BMI  
Based on ROC  
Curve Analysis

Obesity Co-Morbidity	BMI (kg/m <sup>2</sup> )					
	Men			Women		
	Black Men	Hispanic Men	White Men	Black Women	Hispanic Women	White Women
Hypertension	28	29	28	31	28	27
Dyslipidemia	27	26	27	29	27	25
Diabetes	29	29	30	33	30	29
≥ 2 Risk Factors	28	29	29	31	30	28
Average	28	28	29	31	29	27

BMI = body mass index; ROC = receiver operating characteristic  
Stanford FC, et al. *Mayo Clin Proc*. 2019;94(2):362-363.



## Obesity: A Multi-factorial Disorder



Gonzalez-Muniesa P, et al. Obesity. *Nat Rev Dis Primers*. 2017; 3:17034.



[illegible]

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graph TD; BM[Biological/Medical] --- FB[Food & Beverage Behavior/Environment]; FB --- MD[Maternal/Developmental]; BM --- S[Social]; FB --- P[Psychological]; MD --- E[Economic]; S --- P; P --- EP[Environmental Pressures on Physical Activity];
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The Obesity Society. <https://www.obesity.org/wp-content/uploads/2020/05/TOS-Reasons-for-obesity-infographic-2015.pdf>. 2015. Accessed June 28, 2021.

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The diagram illustrates the pathophysiology of obesity, categorized into Psychological and Biological/Medical factors. It is structured into three main columns, each representing a different aspect of the condition.

- Psychological Factors (Left Column):** This column is headed by an upward arrow and the word "Intake". It contains three boxes: "Hyperreactivity to Environmental Food Cues", "Delayed Satiety", and "Disordered Eating".
- Biological/Medical Factors (Middle Column):** This column is headed by a downward arrow and the word "Expenditure". It contains three boxes: "Gut Microbiota", "Thermogenesis", and "Physical Disabilities".
- Biological/Medical Factors (Right Column):** This column is headed by an upward arrow and the word "Intake/" followed by a downward arrow and the word "Expenditure". It contains three boxes: "Genetic and Epigenetic Factors", "Age-Related Changes", and "Mood Disturbances".

A legend at the bottom indicates that dark grey boxes represent Psychological factors and light grey boxes represent Biological/Medical factors.

The Obesity Society, <https://www.obesity.org/wp-content/uploads/2020/05/TOS-Reasons-for-obesity-infographic-2015.pdf>, 2015.  
Accessed June 21, 2021.

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The infographic is divided into three main columns. The first column, '↑Intake', lists 'Environmental/Chemical Toxins', 'Pervasive Food Advertising', and 'Large Portion Sizes'. The second column, '↓Expenditure', lists 'Built Environment', 'Sedentary Time', and 'Labor Saving Devices'. The third column, '↑Intake/↓Expenditure', lists 'Stress', 'Weight Cycling', and 'Maternal/Paternal Obesity'. A legend at the bottom identifies six categories: Biological/Medical (light gray), Environmental Pressures on Physical Activity (dark gray), Economic (medium gray), Food-Bev Behavior/Environment (light gray), Psychological (medium gray), and Maternal/Developmental (light gray).

Category	↑Intake	↓Expenditure	↑Intake/↓Expenditure
Biological/Medical			
Environmental Pressures on Physical Activity	Environmental/Chemical Toxins	Built Environment	
Economic			
Food-Bev Behavior/Environment	Pervasive Food Advertising	Sedentary Time	Stress
Psychological			Weight Cycling
Maternal/Developmental	Large Portion Sizes	Labor Saving Devices	Maternal/Paternal Obesity

Biological/Medical    Environmental Pressures on Physical Activity    Economic    Food-Bev Behavior/Environment    Psychological    Maternal/Developmental

The Obesity Society, <https://www.obesity.org/wp-content/uploads/2020/05/TOS-Reasons-for-obesity-infographic-2015.pdf>, 2015. 2015.  
 Accessed April 21, 2021.

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## Initial Steps to Assess Patients with Obesity (AHA/ACC/TOS Guidelines)

Patient Encounter

Measure Height, Weight, and Calculate BMI

Determine Weight Category

Assess/Treat CVD Risk Factors and Obesity-related Comorbidities

Assess Weight and Lifestyle Histories

ACC = American College of Cardiology; AHA = American Heart Association; TOS = The Obesity Society  
Jensen MD, et al. *Circulation*. 2014;129 (Suppl 2):S102-S138.



## Weight Loss Required for CV Health Benefits

CV Risk Factor	Percent Weight Loss
Diabetes (prevention)	3% to 10%
Diabetes (remission)	>15%
Hypertension	3% to >15%
Dyslipidemia	3% to >15%

Cefalu WT, et al. *Diabetes Care*. 2015;38:1567-1582; Lean MJ, et al. *Lancet*. 2016;391:541-553.



## Assess and Treat CVD Risk Factors and Obesity-Related Comorbidities

- History and physical examination
- Clinical and laboratory measurements
  - Blood pressure
  - Fasting blood glucose
  - Fasting lipid panel (expert opinion)
  - Waist circumference measurement (BMI 25 - ≤ 35)
    - (> 88 cm or > 35 in for women and > 102 cm or > 40 in for men)
- Intensive management of CVD risk factors (partial list)
  - Hypertension
  - Dyslipidemia
  - Prediabetes/diabetes
  - Obstructive sleep apnea (OSA)

Jensen MD, et al. *Circulation*. 2014;129 (Suppl 2):S102-S138.



## Assess Weight and Lifestyle Histories

- Ask about history of weight gain and loss over time
- Details of previous weight loss attempts
- Dietary habits
- Physical activity
- Family history of obesity
- Other medical conditions or medications that may affect weight

Jensen MD, et al. *Circulation*. 2014;129 (Suppl 2):S102-S138.



## Next Steps to Assess Patients With Obesity (AHA/ACC/TOS Guidelines)

Assess Need to Lose Weight

Advise to Avoid Weight Gain and Address Other Risk Factors

Assess Readiness to Make Change; Identify Barriers to Success

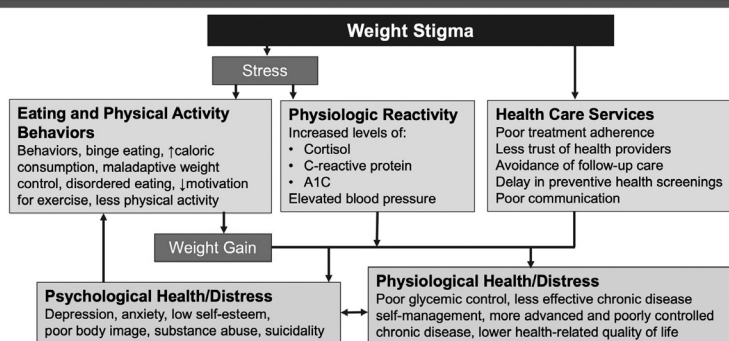
Determine Weight Loss/Health Goals and Intervention Strategies

Comprehensive Lifestyle Therapies Alone or in Conjunction With Adjunctive Therapies

Jensen MD, et al. *Circulation*. 2014;129 (Suppl 2):S102-S138.



## Overcoming Weight Stigma in the Treatment of Obesity



Puhl RM, et al. *Clin Diabetes*. 2016;34(1):44-50.



## 6 A's Model for Weight Management Counseling



Dx = diagnosis; HER = electronic health record; LSW = licensed social worker; OPQRST = onset, precipitating factors, quality of life, remedy, setting, and temporal pattern; RDN = registered dietitian nutritionist; SDH = social determinants of health; SDM = shared decision-making; USPSTF = United States Preventive Services Task Force

Alexander SC, et al. *Fam Med*. 2011;43(3):179-184.; Sturgiss E, Van Weel C. *Canad Fam Phys*. 2017;63:506-508.



## An Important Resource



**Endorsed by** American Board of Obesity Medicine, American Society of Metabolic and Bariatric Surgery, American Association of Clinical Endocrinologists, American Association of Nurse Practitioners, American Medical Group Association, American Academy of Physician Assistants, American College of Physicians, Endocrine Society, Obesity Medicine Association, Obesity Action Coalition, The Obesity Society

- Available for download in the "HCP Resources" tab of this activity

Gallagher C, et al. *Obesity*. 2021;29(5):821-824.



## Treatment Guidelines Based on BMI

- Diet, exercise, and behavior changes in all approaches to managing obesity for BMI  $\geq 25$  kg/m<sup>2</sup> ( $\geq 23.0$  kg/m<sup>2</sup> in Asian Americans)
- Pharmacotherapy indicated for BMI of 27.0 to 29.9 kg/m<sup>2</sup> with  $\geq 1$  comorbidity; or BMI  $\geq 30.0$  kg/m<sup>2</sup> with or without comorbidities
- If response to medication is deemed effective (weight loss  $\geq 5\%$  body weight at 3 months) and safe, it is recommended the medication be continued

Apovian CM, et al. *J Clin Endocrinol Metab.* 2015;100(2):342-362; *Diabetes Care.* 2021; 44(Suppl 1):S100-S110.



### Therapeutic Options for Treating Patients With Obesity

Ken Fujioka, MD



### Learning Objective 3

Assess efficacy and safety of available and emerging therapies for long-term treatment of obesity.

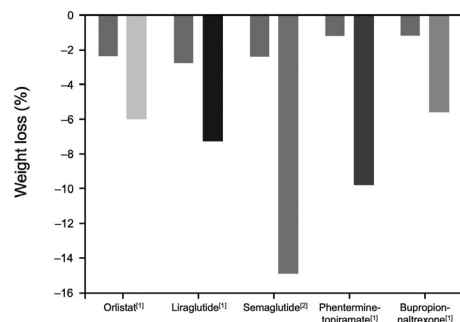
## Pharmacotherapy for Weight Loss (in descending order of FDA approval)

Generic Name	Brand Name	Action	Approval
Semaglutide	Wegovy	GLP-1 receptor agonist	2021
Setmelanotide	Imcivree	Melanocortin (MC4) receptor agonist for POMC, PCSK1, or leptin receptor deficiency	2020
Gelesis100	Plenity	Nonsystemic, superabsorbent hydrogel	2019
Liraglutide	Saxenda	GLP-1 receptor agonist	2014
Naltrexone SR/ Bupropion SR	Contrave	Opioid receptor antagonist/ Dopamine/noradrenaline reuptake inhibitor	2014
Phentermine/ Topiramate ER	Qysmia	Sympathomimetic agent/ Anticonvulsant	2012
Orlistat	Xenical, Alli	Pancreatic lipase inhibitor	1997
Phentermine	Adipex P	Sympathomimetic agent	1956

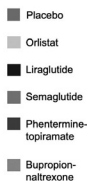
<https://www.accessdata.fda.gov/scripts/cder/drugsatfda>. Accessed June 19, 2021.



## Weight Loss Outcomes with FDA-Approved Medications



Weight loss reflects results at 52 weeks, except for semaglutide, which reflects weight loss at 68 weeks.



1. Khara R, et al. *JAMA*. 2016;315:2424. 2. Wilding JPH, et al. *N Engl J Med*. 2021;384:989.



## Semaglutide for Chronic Weight Management: STEP Phase 3 Trials

	STEP 1 Obesity Trial <sup>1</sup>	STEP 2 T2DM Trial <sup>2</sup>	STEP 3 Intense Behavior Mod <sup>3</sup>	STEP 4 Maintenance Trial <sup>4</sup>
<b>Population</b>	1961 adults with BMI > 30 kg/m <sup>2</sup> or > 27 kg/m <sup>2</sup> with > 1 comorbidity	1595 adults with BMI > 27 kg/m <sup>2</sup> with T2DM	611 adults with BMI > 30 kg/m <sup>2</sup> or > 27 kg/m <sup>2</sup> with > 1 comorbidity	806 adults with BMI > 30 kg/m <sup>2</sup> or > 27 kg/m <sup>2</sup> with > 1 comorbidity entered 20-week run-in*
<b>Randomized</b>	2:1 to semaglutide 2.4 mg vs. placebo	1:1:1 to semaglutide 2.4 mg vs. semaglutide 1.0 mg vs. placebo	2:1 to semaglutide 2.4 mg vs. placebo	2:1 to continued semaglutide 2.4 mg vs. placebo
<b>Background treatment</b>	Both groups: lifestyle intervention	All groups: lifestyle intervention	Both groups: low-calorie diet for 8 weeks and intensive behavioral counseling	Both groups: lifestyle intervention

\*806 who reached 2.4 mg dose entered randomization

STEP = Semaglutide Treatment Effect in People with obesity

1. Wilding JPH, et al. *N Engl J Med*. 2021;384:989. 2. Davies M, et al. *Lancet*. 2021; 397:971-984.

3. Wadden TA, et al. *JAMA*. 2021. 325(14):1403-1413. 4. Rubino, D, et al. *JAMA*. 2021; 325(14):1414-1425.



## Semaglutide for Chronic Weight Management: STEP Phase 3 Trials (cont.)

	STEP 1 (Wilding, et al. 2021) <sup>1</sup>	STEP 2 (Davies, et al. 2021) <sup>2</sup>	STEP 3 (Wadden, et al. 2021) <sup>3</sup>	STEP 4 (Rubino, et al. 2021) <sup>4</sup>
<b>Mean Change in Bodyweight at Week 68</b>				
<b>Semaglutide 2.4 mg</b>	-14.9%	-9.6%*	-16.0%	-7.9% from week 20; -17.4% from baseline
<b>Placebo</b>	-2.4%	-3.4%	-5.7%	+6.9% from week 20; -5.9% from baseline
<b>Proportion of Participants with &gt; 5%</b>				
<b>Semaglutide 2.4 mg</b>	86.4%	68.8%	86.6%	88.7%
<b>Placebo</b>	31.5%	28.5%	47.6%	47.6%

\*Mean change in bodyweight at week 68 was -6.99% for semaglutide 1.0 mg weekly

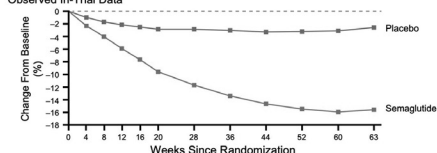
1. Wilding JPH, et al. *N Engl J Med*. 2021;384:989. 2. Davies M, et al. *Lancet*. 2021; 397:971-984.

3. Wadden TA, et al. *JAMA*. 2021. 325(14):1403-1413. 4. Rubino, D, et al. *JAMA*. 2021; 325(14):1414-1425.

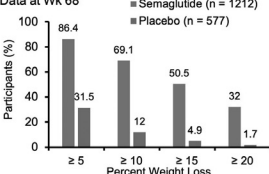


## Effect of Once-Weekly Semaglutide, as Compared with Placebo, on Body Weight: STEP 1 Trial

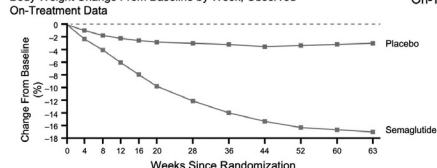
Body Weight Change From Baseline by Week, Observed In-Trial Data



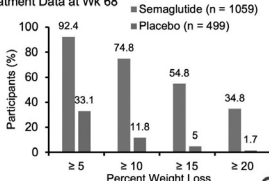
In-Trial Data at Wk 68



Body Weight Change From Baseline by Week, Observed On-Treatment Data



On-Treatment Data at Wk 68



Wilding JPH, et al. *N Engl J Med*. 2021;384:989-1002



## Adverse Reactions Occurring in ≥ 5% of Semaglutide-Treated Patients and More Frequently Than Placebo

Adverse Event	Placebo (%) N = 1261	Semaglutide (%) N = 2116	Adverse Event	Placebo (%) N = 2116	Semaglutide (%) N = 2116
Nausea	16	44	Dyspepsia	3	9
Diarrhea	16	30	Dizziness	4	8
Vomiting	6	24	Abdominal Distension	5	7
Constipation	11	24	Eructation	<1	7
Abdominal Pain	10	20	Hypoglycemia in T2DM	2	6
Headache	10	14	Flatulence	4	6
Fatigue	5	11	Gastroenteritis	4	6

Wilding JPH, et al. *N Engl J Med*. 2021;384:989-1002; WEGOVY™ (semaglutide) injection. Plainsboro, NJ: Novo Nordisk Inc. 2021;



## Patients That Lose Weight “Lose Wait”

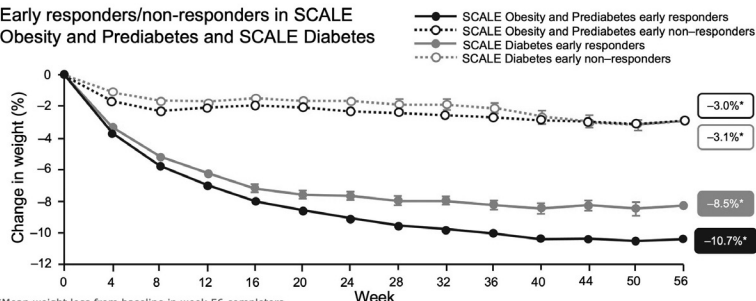
Agent	Study Duration	Time of Early Weight Loss	Weight Loss Threshold for Detection	Responder Definition
Gelesis100	24 weeks	8 weeks	≥ 3%	≥ 5%
Phentermine topiramate	52 weeks	12 weeks	≥ 3%	≥ 5%
Bupropion naltrexone	56 weeks	16 weeks	≥ 5%	≥ 5%
Liraglutide	56 weeks	16 weeks	≥ 4%	≥ 5%

Greenway FL, et al. *Obesity (Silver Spring)*. 2019;27(2):205-216.; Fujioka K, et al. *Int J Obes (London)*. 2016;40(9):1369-1375.; Fujioka K, et al. *Obesity (Silver Spring)*. 2016;24(11):2278-2288.



## Weight Loss With Liraglutide 3.0 mg Over 56 Weeks

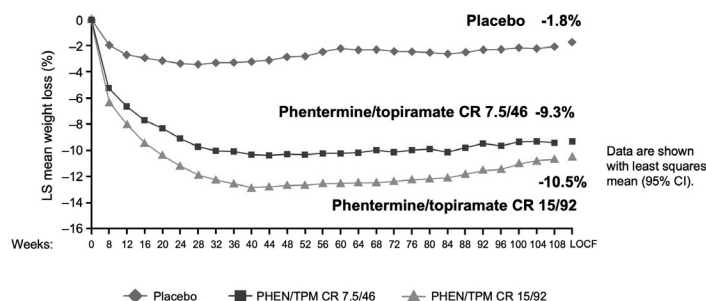
### Early responders/non-responders in SCALE Obesity and Prediabetes and SCALE Diabetes



\*Mean weight loss from baseline in week 56 completers  
Early responders, subjects who achieved ≥ 4% weight loss at 16 weeks; Early non-responders, subjects who achieved < 4% weight loss at 16 weeks  
SCALE = Safety and Clinical Adiposity – Liraglutide Evidence in Individuals with and without diabetes  
Fujioka K, et al. *Obesity*. 2016;24:2278-2288.



## SEQUEL: Effect of Phentermine/Topiramate ER on Weight Loss in Obese Adults Over 2 Years

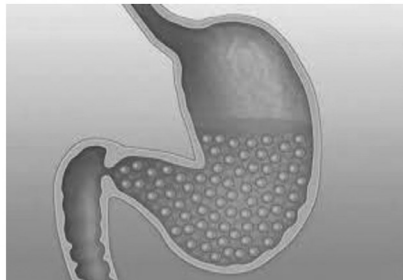


Garvey WT, et al. *Am J Clin Nutr*. 2012;95:297-308.



## Nonsystemic Superabsorbent Oral Hydrogel (Device)

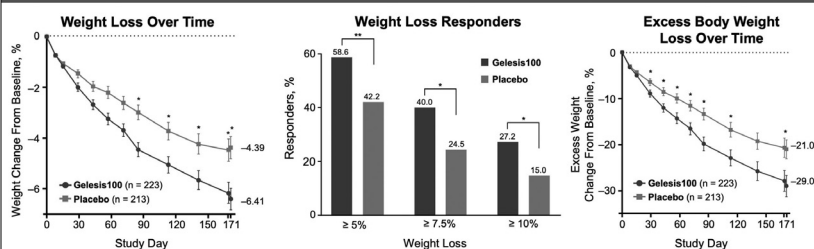
- FDA approved for managing weight in adults with BMI 25-40 kg/m<sup>2</sup> (along with diet and exercise)
- Capsule contains hydrogel particles that expand in the stomach after ingested but are not systemically absorbed
- Taken with 16 oz of water before meals



Greenway FL, et al. *Obesity*. 2019;27:205-216.



## Gelesis Loss of Weight (GLOW) Study



- 24-week, multicenter, randomized double-blind, placebo-controlled study in patients with BMI  $\geq 27$  kg/m<sup>2</sup> and  $\leq 40$  kg/m<sup>2</sup> and fasting plasma glucose  $\geq 90$  and  $\leq 145$  mg/dL
- Co-primary endpoints: placebo-adjusted weight loss and at least 35% of Gelesis100 group achieving

Greenway FL, et al. *Obesity*. 2019;27:205-216.



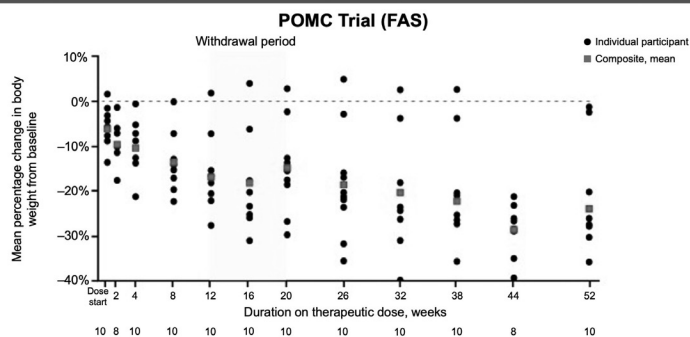
## Single Gene Mutation Induced Severe Obesity

- Age of onset of obesity 6 years or less
- Hyperphagia: binge eating
  - Receptor in brain that signals satiety at end of meal is missing or non-functional
  - Patient literally does not know when to stop eating as they never feel satiated or full
- Can confirm by doing a simple genetic test (oral swab)

Clément K, et al. *Lancet Diabetes Endocrinol*. 2020;12:960-970.



## Key Secondary Endpoint: Mean Percentage Change in Body Weight From Baseline at ~1 Year of Treatment: POMC Trial



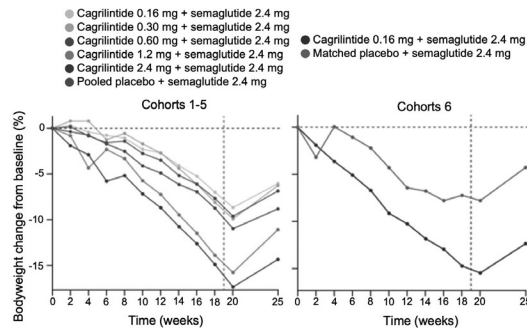
FAS = full analysis set; POMC = proopiomelanocortin  
Clément K, et al. *Lancet Diabetes Endocrinol*. 2020;12:960-970.





# The Future: Multiple Satiety Hormones

- Concomitant treatment with cagrilintide, a long-acting amylin analogue, and semaglutide (2.4 mg)
- Randomized, placebo-controlled, multiple-ascending dose phase 1b trial
- Individuals 18-55 years of age with BMI 27.0-39.9 kg/m
- Treatment well tolerated with acceptable safety profile
- Longer trials needed to fully assess efficacy/safety



Enobio LB, et al. *Lancet*. 2021;10286:1736-1748.



## Summary: Safety and Tolerability of Agents for Treating Obesity

Agent	Contraindications	AEs (partial list – see PIs)
Semaglutide	MEN2: personal/family Hx of MTC; <b>pregnancy</b> [stop semaglutide ≥2 months before planned pregnancies to account for long half-life]	Nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia
Liraglutide	MEN2: personal/family history of MTC (potential risk of thyroid C-cell tumor); <b>pregnancy</b>	GI AEs, constipation, vomiting, injection site reaction
Naltrexone SR/ Bupropion SR	Chronic opioid use; uncontrolled HTN; seizure disorders; anorexia nervosa; bulimia; other bupropion drugs; MAOI use; <b>pregnancy</b>	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth
Phentermine/ Topiramate ER	Glaucoma; hyperthyroidism; use during/within 14 days of MAOI use; <b>pregnancy</b> [risk of fetal malformation, including cleft palate or cleft lip]	Paresthesia, dizziness, dysgeusia, insomnia, constipation, dry mouth

AEs = adverse effects; HTN = hypertension; MAOI = monoamine oxidase inhibitor; MEN2 = multiple endocrine neoplasia syndrome; MTC = medullary thyroid carcinoma; PI = product information  
<https://www.accessdata.fda.gov/scripts/cder/drugsatfda>. Accessed June 19, 2021.



## Summary: Safety and Tolerability of Agents for Treating Obesity

Agent	Contraindications	AEs (partial list – see PIs)
Orlistat	Chronic malabsorption syndrome; cholestasis; <b>pregnancy</b>	Abdominal pain/discomfort; oily spotting/stool; fecal urgency
Setmelanotide	None	Injection site reactions, skin hyperpigmentation, nausea, headache, diarrhea, abdominal pain, depression, URI, spontaneous penile erection
Gelesis100	<b>Pregnancy</b> , allergies to cellulose, citric acid; esophageal anatomic anomalies, strictures, prior GI surgery complications	Abdominal pain, constipation, flatulence, infrequent bowel movements, abdominal distension, diarrhea, nausea

<https://www.accessdata.fda.gov/scripts/cder/drugsatfda>. Accessed June 19, 2021.



## SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Encourage patients with obesity to get fully vaccinated for COVID-19
- Ensure equitable clinical interactions with all patients and avoid stigmatizing language
- Apply the 6 A's model for weight management counseling
- Partner with patients and employ shared-decision making to improve adherence to therapies and improve outcomes
- Prescribe therapies for weight loss, when indicated, that consider energy balance dysregulation and the underlying biologic/metabolic adaptations to weight loss



## To Ask a Question

Please click on the *Ask Question* tab and type your question. Please include the faculty member's name if the question is specifically for him/her.

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CME Outfitters

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Questions & Answers

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Participants can print their certificate or statement of credit immediately.

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## CME for MIPS Improvement Activity

Required Steps to Claim CME Credit as an MIPS Improvement Activity

- Complete activity post-test and evaluation at the link provided
- Over the next 90 days, actively work to incorporate improvements in your clinical practice from this presentation
- Complete the follow-up survey from CME Outfitters in approximately 3 months

**CME Outfitters will send you confirmation of your participation to submit to CMS attesting to your completion of a CME for MIPS Improvement Activity**

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## ATTENDANCE FORM FOR GROUPS

Please complete and FAX to 614.929.3600

Activity Title and Faculty:

### The Epidemic Within the Pandemic: Managing Complications in Populations with Obesity

with Robert F. Kushner, MD, MS, DABOM (Moderator); Ken Fujioka, MD; Fatima Cody Stanford, MD, MPH, MPA, MBA, FAAP, FACP, FAHA, FAMWA, FTOS

Site/Institution Name: \_\_\_\_\_

☐ Office-based    ☐ Hospital    ☐ Clinic    ☐ Managed Care    ☐ Small Group Practice (less than 5)

Practice Setting    ☐ Large Group Practice (more than 5)    ☐ Other \_\_\_\_\_

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Site Coordinator: \_\_\_\_\_ Phone: \_\_\_\_\_

Fax: \_\_\_\_\_ Email: \_\_\_\_\_

Completion Date: \_\_\_\_\_ We participated in: \_\_\_\_\_

#### Attendee Name (please print)

#### Please Circle Discipline

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_____	MD	DO	PA	NP	RN	Pharm	Other	_____
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