Looking Past the Scale: Strategies to Promote Weight Loss and Reduce Co-Morbidities in Your Obese Patients

February 7, 2013
Fort Lauderdale, Florida

Educational Partner:
CME Incite, LLC
Session 5: Looking Past the Scale: Strategies to Promote Weight Loss and Reduce Co-Morbidities in Your Obese Patients

Learning Objectives

1. Evaluate the effect of obesity on the whole patient, focusing on identification of patients with increased body mass indices and the associated co-morbidities.
2. Identify strategies to engage both male and female patients in open dialogues about the benefits of weight reduction, highlighting the essential components of weight management and the importance of setting realistic weight-loss goals.
3. Compare the safety and efficacy of currently available and novel agents in development for the treatment of obesity.

Faculty

Timothy Church, MD, MPH, PhD
Professor and Director
Laboratory of Preventive Medicine
Pennington Biomedical Research Center
Baton Rouge, Louisiana

Dr Timothy Church is the John S. McIlhenny Endowed Chair, professor and director of the Laboratory of Preventive Medicine at the Pennington Biomedical Research Center in Baton Rouge, Louisiana. Dr Church earned his medical degree and structural and cellular biology doctorate degree from Tulane University School of Medicine in New Orleans. He completed a residency in preventive medicine at Tulane, where he also earned a master’s degree in public health.

Dr Church is a principal investigator, co-principal investigator, or investigator on a number of National Institutes of Health (NIH) and industry grants, most of which address issues related to exercise, weight, and health. His research areas of interest included diabetes, hypertension, quality-of-life issues, cancer survivorship, and maintenance of function in the elderly. Dr Church has authored more than 150 peer-reviewed publications and received several awards for his research.

Donna H. Ryan, MD
Professor Emeritus Pennington Biomedical Research Center
Baton Rouge, Louisiana

Dr Donna H. Ryan is Professor Emeritus at the Pennington Biomedical Research Center in Baton Rouge, Louisiana, where she served as associate executive director for clinical research for more than 20 years. She has been actively engaged in obesity and nutrition research for the last 20 years.

Dr Ryan served as 2009–2010 president of The Obesity Society, an organization of more than 2000 North American scientists. She co-chairs the panel that is currently revising the National Institutes of Health (NIH)–sponsored Guidelines for the Evaluation and Management of Overweight and Obesity, or Obesity II.

Dr Ryan’s research interests include many aspects of obesity management and prevention, including obesity pharmacotherapy, evaluation of weight-loss diets of different macronutrient composition, practical or pragmatic clinical trials to evaluate primary care approaches to obesity management, and translational research engaging third-party payors in obesity intervention.

Dr Ryan was funded for more than 20 years by the United States Department of Defense to oversee a military nutrition research project in which she collaborated with the US Army Research Institute for Environmental Medicine’s Military Nutrition Division. She was co-principal investigator for the NIH-funded Clinical Nutrition Research Center at Pennington and co-principal investigator for the National Institute of Diabetes and Digestive and Kidney Diseases–sponsored Look AHEAD (Action for Health in Diabetes) study that addresses weight loss in persons with type 2 diabetes. Dr Ryan conceived a statewide Clinical Translational Science Center, awarded in 2012, that encompasses 9 Louisiana research institutions. She inaugurated LSU ICON (Improving Clinical Outcomes Network), a project to improve clinical outcomes in 11 Louisiana State University hospitals.

Since retiring from active service in February 2012, Dr. Ryan continues in public service around obesity issues with the NIH and nonprofits, consults with the drug and device industry, and is actively engaged in continuing medical education.
Faculty Financial Disclosure Statements
The presenting faculty reports the following:
Dr Church serves as a consultant for VIVUS, Inc.; an advisory board member for Jenny Craig, Inc.; and a board member for Catapult Health.
Dr Ryan serves as an advisor to Arena Pharmaceuticals, Inc.; Eisai Co., Ltd.; and Novo Nordisk Inc.; and as a consultant for Scientific Intake Limited Co.

Education Partner Financial Disclosure Statement
The content collaborators at CME Incite report the following:
Priya Wanchoo, MBBS; Rose O'Connor, PhD; and Monique Pond, PhD, have no financial relationships to disclose.

Suggested Reading List
Looking Past the Scale: Strategies to Promote Weight Loss and Reduce Comorbidities in Your Obese Patients

February 7, 2013
Fort Lauderdale, FL

Drugs List

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>liraglutide</td>
<td>NA</td>
</tr>
<tr>
<td>lorcaserin</td>
<td>Belviq</td>
</tr>
<tr>
<td>metformin</td>
<td>Fortamet, Glucophage, Glumetza, etc.</td>
</tr>
<tr>
<td>naltrexone/bupropion SR</td>
<td>Contrave</td>
</tr>
<tr>
<td>orlistat</td>
<td>Alli, Xenical</td>
</tr>
<tr>
<td>paroxetine</td>
<td>Paxil</td>
</tr>
<tr>
<td>phentermine</td>
<td>Adipex-P, Phentermine, Zantryl, etc.</td>
</tr>
<tr>
<td>phentermine/topiramate ER</td>
<td>Qysmia</td>
</tr>
</tbody>
</table>

Learning Objectives

- Evaluate the effect of obesity on the whole patient, focusing on identification of patients with increased BMI and the associated comorbidities
- Identify strategies to engage both male and female patients in open dialogues about the benefits of weight reduction, highlighting the essential components of weight management and the importance of setting realistic weight loss goals
- Compare the safety and efficacy of currently available and novel agents in development for the treatment of obesity

BMI = Body Mass Index

Pretest Question 1

Which waist circumference is an indicator of high risk for developing weight-related comorbidities, especially type 2 diabetes, in adults?

1. Men >35 inches, women >30 inches
2. Men and women >35 inches
3. Men >40 inches, women >35 inches
4. Men and women >40 inches

Pretest Question 2

What is a realistic percent weight loss outcome at 6 months from nonsurgical weight loss treatment?

1. <1%
2. 3% to 5%
3. 5% to 10%
4. 15% to 20%
5. Unsure

Demographic Question

Approximately how many obese patients in the last 60 days have you counseled about losing weight?

1. None
2. 1-5
3. 6-10
4. 11-20
5. Over 20
Pretest Question 3

If an obese (BMI 32) person with hypertension has been unsuccessful in his/her weight loss goals (5% reduction) after 6 months of lifestyle modification, what would be the next strategy to recommend for weight loss?

1. Continue lifestyle modifications for another 6 months
2. Increase daily exercise time
3. Consider pharmacotherapy
4. Schedule bariatric surgery
5. Unsure

Pretest Question 4

Which of the following pharmacotherapies for chronic weight management have been FDA approved in 2012?

1. Liraglutide
2. Phentermine/topiramate ER
3. Liraglutide and phentermine/topiramate ER
4. Lorcaserin and phentermine/topiramate ER
5. Unsure

Addressing Obesity in Your Waiting Room: Consequences for the Patient as a Whole

Timothy Church, MD, MPH, PhD
Professor and Director
Laboratory of Preventive Medicine
Pennington Biomedical Research Center
Baton Rouge, LA

Goals for this Presentation

- Assess obesity in clinical practice
- Discuss health benefits of weight loss in overweight and obese patients
- Communicate realistic weight loss goals with your patients

Assessing Obesity in Clinical Practice

<table>
<thead>
<tr>
<th>BMI=weight (kg)/height (m²)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal weight</td>
</tr>
<tr>
<td>Overweight</td>
</tr>
<tr>
<td>Obesity class 1</td>
</tr>
<tr>
<td>Obesity class 2</td>
</tr>
<tr>
<td>Obesity class 3</td>
</tr>
</tbody>
</table>

*World Health Organization defines overweight as BMI ≥25 and obese as BMI ≥30.

Obesity Trends* Among US Adults, BRFSS 1990-2000-2010

BRFSS = Behavioral Risk Factor Surveillance System

More than Two Thirds of US Adults Are Overweight or Obese

BMI >25

25% increase


Prevalence of Overweight (BMI ≥25) by Sex and Race (Age ≥20 Years)

NHES     NHANESI   NHANESII  NHANESIII

Prevalence of Overweight (BMI ≥25) by Sex and Race (Age ≥20 Years)


Coronary heart disease
Gallbladder disease
Gout
Diabetes
Osteoarthritis
Hypertension
Dyslipidemia
Cataracts
Skin
Pancreatitis
Idiopathic intracranial hypertension
Cataracts
Coronary heart disease
Diabetes
Hypertension
Gynecologic abnormalities
Abnormal menses
Infertility
Polycystic ovarian syndrome
Osteoarthritis
Phlebitis
Venous
Stasis
Pulmonary disease
Abnormal function
Obstructive sleep apnea
Hyperventilation syndrome
Gallbladder disease
Nonalcoholic fatty liver disease
Steatosis
Steatohepatitis
Cirrhosis
Cancer
Breast
Uterus
Cervix
Prostate
Kidney
Skin
Gout

Medical Complications of Obesity

“How do we assess obesity?”

Assessing Obesity in Clinical Practice

Waist circumference indicates high risk*
Men >40 inches
Women >35 inches
Indirect measure of central adiposity, correlated with visceral fat
Excess abdominal fat is an independent predictor of risk factors and morbidity

ARS Question

Do you measure patient waist circumference along with other vital signs at every patient visit?

1. Yes
2. No

*WHO waist circumference cutoff varies by race/ethnicity.

WHO = World Health Organization.
Measuring Waist Circumference

- Locate upper hip bone and top of right iliac crest
- Place measuring tape around abdomen at level of iliac crest, keeping it parallel to the floor
- Ensure tape is snug but not compressing the skin


Overweight Individuals at Greater Risk for Developing Chronic Conditions

Increased abdominal adiposity highly correlated with insulin resistance and, ultimately, type 2 diabetes

US Prevalence of Obesity and Weight-Related Comorbidities

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30+</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BMI ≥ 30 kg/m² or ≥ 27 kg/m² with a weight-related comorbidity
- 88% (97 million) have at least one weight-related comorbidity
- 19.8% (~21.9 million) have 3 comorbidities
- Diagnosed and treated for comorbidity
- 91% (101 million) have been diagnosed in the past or are currently on drug therapy

What are the health benefits of weight reduction?

Diabetes Prevention Program 4-Year Study Results: Progression From IGT to T2DM

Is it possible to prevent type 2 diabetes?

<table>
<thead>
<tr>
<th>Diabetes Incidence per 100 Person-Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet + Exercise</td>
</tr>
<tr>
<td>n=1079</td>
</tr>
<tr>
<td>4.8</td>
</tr>
<tr>
<td>Metformin (850mg BID)</td>
</tr>
<tr>
<td>n=1073</td>
</tr>
<tr>
<td>7.8</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
<tr>
<td>n=1082</td>
</tr>
<tr>
<td>11.0</td>
</tr>
</tbody>
</table>

The goal of intensive lifestyle intervention was 7% reduction in baseline body weight through low-calorie, low-fat diet and moderate intensity exercise for ≥150 minutes per week.

The goal of intensive lifestyle intervention was 5% reduction in baseline body weight through diet with <30% calories from fat, <10% calories from saturated fat, ≥15 mg fiber intake, and moderate-intensity exercise for ≥30 minutes/day.

7-Year Follow-up of the Finnish Diabetes Prevention Study

The goal of intensive lifestyle intervention was 5% reduction in baseline body weight through diet with <30% calories from fat, <10% calories from saturated fat, ≥15 mg fiber intake, and moderate-intensity exercise for ≥30 minutes/day.

Relative risk reduction.


7-Year Follow-up of the Finnish Diabetes Prevention Study


Increased abdominal adiposity highly correlated with insulin resistance and, ultimately, type 2 diabetes

Dietary intake
- 1200-1500 kcal/day <250 lb
- 1500-1800 kcal/day >250 lb
- <30% calories from fat
- Meal replacements*

Physical activity
- Gradual increases
- 175 minutes/week
- 10,000 steps

*Menu plans provided for those who declined meal replacements.

Look AHEAD Study Lifestyle Intervention Recommendations for Intervention in Overweight and Obese Adults With T2DM

Physical activity
- Gradual increases
- 175 minutes/week
- 10,000 steps

“How do we effectively communicate with our overweight patients?”

Reinforce Weight Loss Goals and Importance of Follow-up
- Ask your patient, “What are YOUR goals?”
- Patients typically seek weight losses
  - ~30% reduction in body weight
  - 10% reduction in baseline body weight can equate to “failure” for many patients
- Reinforce realistic expectations
  - Encourage continued adherence to lifestyle and behavioral changes

Weight Loss Benefits at 1 Year: Effect on Cardiovascular and Diabetes Measures

<table>
<thead>
<tr>
<th></th>
<th>DSE</th>
<th>ILI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=2463</td>
<td>n=2496</td>
</tr>
<tr>
<td></td>
<td>(0.7% weight loss)</td>
<td>(8.6% weight loss)</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>-0.14</td>
<td>-0.64*</td>
</tr>
<tr>
<td>Glucose (mg %)</td>
<td>-7.2</td>
<td>-21.5*</td>
</tr>
<tr>
<td>% on diabetes meds</td>
<td>+2.2</td>
<td>-7.8*</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>-2.8</td>
<td>-6.8*</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>-1.8</td>
<td>-3.0*</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>-5.7</td>
<td>-5.2</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>+1.4</td>
<td>+3.4*</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>-14.6</td>
<td>-30.3*</td>
</tr>
</tbody>
</table>

*P = 0.001

N=5145 overweight and obese adults with type 2 diabetes.

DSE=diabetes support and education; ILI=intensive lifestyle intervention.

Set Realistic Goals With Your Patient
- Accept steady, incremental progress to goal
- Focus on behaviors such as reducing caloric intake and increasing physical activity
  - Short-term goal: 5% to 10% loss at 6 months
  - Interim goal: maintenance
  - Long-term goal (if desired): additional energy deficit recalculated for next weight loss goal

Goal: decrease body weight by 5%-10% from baseline

Reinforce Weight Loss Goals and Importance of Follow-up

Key Practice Takeaways
- Identify and engage high-risk overweight patients
- Recognize the health benefits that can be achieved by weight reduction
- Open communication with overweight patients is vitally important


Case Study 1

Meet Joe

Patient: Joe
- Age: 49 years
- Occupation: Bus driver
- Marital Status: Married
- Lifestyle: Mostly sedentary, 1 pack-a-day smoker

Relevant Medical History
- Hypertension
- Mixed hyperlipidemia
- BMI: 35 (5'10", 243 lbs)

Calculating BMI:
Joe – 5’10”, 243 lbs

At 5’10”, 243 lbs, Joe’s calculated BMI is 35, which is considered obese.

Following Joe

Current Medications
- Calcium channel blocker
- Diuretic
- Statin

Main Complaint During Office Visit
- Frequent headaches
- Joe’s blood pressure at the time of the exam was 160/110

Conversation With the Practitioner
- Are you taking your medications as prescribed?
- Do you have a high-sodium diet?
- Now would be a great time to discuss how your weight may be contributing to your uncontrolled blood pressure

ARS Question

What advice would you give Joe regarding weight management when he presents to you during this office visit?

1. Discuss the benefits of losing weight and realistic weight loss goals
2. Recommend that Joe begins a smoking cessation program prior to any weight loss programs
3. Prescribe pharmacotherapy adjunct to lifestyle modifications
4. Discuss the benefits of bariatric surgery on reducing weight-related comorbidities

ARS Question

What would you recommend to Joe at his 6-month follow-up where you discover he has successfully lost 20 lbs (8.2% reduction, new BMI 32) through pharmacotherapy and diet modifications?

1. Congratulate patient and discuss weight maintenance as next phase of weight loss
2. Increase his daily exercise time
3. Continue with diet modifications and pharmacotherapy
4. Begin dose-reducing his antihypertensive and cholesterol-lowering medications
A Toolbox of Safe and Effective Ways to Achieve Weight Loss

Donna Ryan, MD
Professor Emeritus
Pennington Biomedical Research Center
Baton Rouge, Louisiana

Goals for this Presentation

- Lifestyle intervention
  - Changes in diet and physical activity
  - Use of pedometer and other self-monitoring tools
- Pharmacotherapy
  - Review of currently available treatment options
- Bariatric surgery
  - Realistic expectations and benefit-to-risk ratio

Obesity Treatment Guidelines

<table>
<thead>
<tr>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet, physical activity, and behavior</td>
<td>Appropriate NHLBI Guidelines</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>Not appropriate</td>
<td>with comorbidities</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery*</td>
<td>Not appropriate</td>
<td>Not appropriate</td>
<td>LAGB approved for patients with ≥2 comorbidity</td>
<td>+</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Bariatric surgeries require lifestyle medical follow-up.

FDA approved gastric band surgery for patients with BMI ≥30 and one weight related medical condition (February 2011).

Goals for this Presentation

- Recommendations for low-calorie diet
  - Maximum of 30% of total calories from total fat
  - Minimum of 15% of total calories from protein
  - Maximum of 10% of total calories from saturated fat
- Other effective diet plans
  - Mediterranean diet – moderate fat, restricted calories, rich in vegetables but low in red meat
  - Low-carbohydrate diet – low carbs, nonrestricted calories, aims for 20 g of carbs per day gradually increasing to max of 120 g per day
  - DASH diet – 9 servings of fruits/vegetables per day
- Successful weight loss habits include
  - Eating breakfast
  - Reduced portion sizes
  - Increased fruits and vegetables
  - Reading food labels

The diet will not “work” unless an energy (calorie) deficit is created

Weight Loss Interventions Result in Sustained Weight Change Over 24 Months

Percentage Reduction in Initial Weight Over 4 Years in ILI and DSE Groups: Look AHEAD

Dietary Interventions:
Changes in Diet

- ILI=intensive lifestyle intervention; DSE=diabetes support and education.

P<0.0001

Retention at 4 years: ILI=91.1%
DSE=93.1%

The Right Tool for the Right Job

- One size does not fit all
- Commercial weight loss programs are an option, including several with supporting data
- The programs “work” if the participants remain committed to the program, but dropout rates are high and steady

Advancing Therapy: Pharmacology

Previously Available Pharmacotherapies

<table>
<thead>
<tr>
<th>Agent</th>
<th>PHENTERMINE</th>
<th>ORLISTAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism</td>
<td>Central Noradrenergic</td>
<td>Peripheral Pancreatic Lipase Inhibitor</td>
</tr>
<tr>
<td>Approval</td>
<td>Short-term use</td>
<td>Long-term use Not scheduled Also available OTC</td>
</tr>
<tr>
<td>Cost</td>
<td>$</td>
<td>$$$</td>
</tr>
<tr>
<td>Common Adverse Effects</td>
<td>Restlessness</td>
<td>Insomnia Increase in pulse Increase in blood pressure</td>
</tr>
</tbody>
</table>

Recently Approved Pharmacotherapy

<table>
<thead>
<tr>
<th>Agent</th>
<th>Phentermine/topiramate ER 1,2</th>
<th>Lorcaserin 3,4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Status</td>
<td>Approved July 2012</td>
<td>Approved June 2012</td>
</tr>
<tr>
<td>Mechanism</td>
<td>PHEN stimulates norepinephrine release from hypothalamic neurons; TPM is an anticonvulsant</td>
<td>Selectively targets the 5-HT2C receptor</td>
</tr>
<tr>
<td>Follow-up Duration</td>
<td>56 (108*) weeks</td>
<td>52 (154*) weeks</td>
</tr>
<tr>
<td>Common Adverse Effects</td>
<td>Dry mouth Tingling Constipation Altered taste sensation Upper respiratory infection</td>
<td>Headache Dizziness Nausea</td>
</tr>
</tbody>
</table>

Recent approved Pharmacotherapy

Study Design: 56-Week Study Followed by 52-Week Extension

Placebo-controlled, double-blind

<table>
<thead>
<tr>
<th>Treatment (56 weeks)</th>
<th>Treatment (52 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo n=994</td>
<td>Placebo n=227</td>
</tr>
<tr>
<td>7.5 mg phentermine/46 mg topiramate (PHEN/TPM ER 7.5/46) n=448</td>
<td>7.5 mg phentermine/46 mg topiramate (PHEN/TPM ER 7.5/46) n=153</td>
</tr>
<tr>
<td>15 mg phentermine/92 mg topiramate (PHEN/TPM ER 15/92) n=995</td>
<td>15 mg phentermine/92 mg topiramate (PHEN/TPM ER 15/92) n=295</td>
</tr>
</tbody>
</table>

All subjects participated in a lifestyle modification program


*2 year extension data available.
Weight Change Over 1 Year With Phentermine/Topiramate ER

Gadde KM, et al.

*P<0.0001 vs placebo

-9.6% for Cs
-12.4% for Cs
-1.6% for Cs

Waist circumference decreased
3.6 inches for PHEN/TPM ER
15/92 group and
3.0 inches for PHEN/TPM ER
7.5/46 group vs
0.9 inches for placebo group

Completers Population:

ITT-LOCF

Weight Change Over 2 Years With Phentermine/Topiramate ER

Garvey WT, et al.

Data are shown with least squares mean (95% CI).

PHEN/TPM ER 7.5/46
PHEN/TPM ER 15/92
PHEN/TPM
ER 7.5/46
PHEN/TPM
ER 15/92

-9.3% for Cs
-10.7% for Cs
-2.2% for Cs

Completers Population

ITT-LOCF

Effect of Phentermine/Topiramate ER on Blood Pressure and Lipid Levels After 56 Weeks

Gadde KM, et al.
Lancet. 2011;377:1341-1352. All P values are vs placebo.

**P<0.01
***P<0.001
****P<0.0001

Fasting Glucose

Placebo
PHEN/TPM ER 7.5 mg plus topiramate 46.0 mg
PHEN/TPM ER 15.0 mg plus topiramate 92.0 mg

Change (mmol/L)

Effect of Phentermine/Topiramate ER on Glycemic Parameters After 56 Weeks

Gadde KM, et al.
Lancet. 2011;377:1341-1352. All P values are vs placebo.

Fasting Insulin

Glycated Hemoglobin

HOMA-IR=Homeostasis Model of Assessment-Insulin Resistance.

Change (%)

Fasting Glucose

5.1 (0.73 µU/mL)
-27.6****
(-3.97 µU/mL)
-24.0***
(-3.45 µU/mL)

Change (pmol/L)

HOMA-IR

5.1 (0.73 µU/mL)
-27.6****
(-3.97 µU/mL)
-24.0***
(-3.45 µU/mL)

Data are presented from the intention-to-treat analysis with LOCF. Least-squares means ± 95% CI

Phentermine/Topiramate ER Safety Data

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Placebo (%) (n=993)</th>
<th>PHEN/TPM ER 7.5/46 (%) (n=498)</th>
<th>PHEN/TPM ER 15/92 (%) (n=994)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry mouth</td>
<td>2 13</td>
<td>&lt;0.0001</td>
<td>21</td>
</tr>
<tr>
<td>Constipation</td>
<td>6 15</td>
<td>&lt;0.0001</td>
<td>17</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>1 7</td>
<td>&lt;0.0001</td>
<td>10</td>
</tr>
<tr>
<td>Insomnia</td>
<td>5 6</td>
<td>0.3832</td>
<td>10</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3 7</td>
<td>0.0005</td>
<td>10</td>
</tr>
<tr>
<td>Back pain</td>
<td>5 6</td>
<td>0.0199</td>
<td>7</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 4</td>
<td>0.6754</td>
<td>7</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>4 4</td>
<td>0.7729</td>
<td>6</td>
</tr>
</tbody>
</table>

Data are presented from the intention-to-treat analysis with LOCF. Least-squares means ± 95% CI

REMS Training for PHEN/TPM ER

- PHEN/TPM ER is contraindicated during pregnancy
- PHEN/TPM ER has been approved with a REMS training program to inform clinicians and patients about
  - Increased risk of congenital malformation, specifically orofacial clefts, in infants exposed to PHEN/TPM ER during the first trimester of pregnancy
  - Importance of pregnancy prevention for females of reproductive potential receiving PHEN/TPM ER
  - Need to discontinue PHEN/TPM ER immediately if pregnancy occurs

REMS=Risk Evaluation and Mitigation Strategy
**Study Design: 52-Week Study Followed by 52-Week Extension**

Placebo-controlled, double-blind

- Patients with BMI 27-45 kg/m² with ≥1 co-existing condition
- Randomization (N=3182)
- Treatment (52 weeks)
  - Placebo
    - n=1587
  - Lorcaserin 10 mg BID
    - n=1595

- Randomization (N=839)
- Treatment (52 weeks)
  - Placebo
    - n=684
  - Placebo
    - n=275
  - Lorcaserin 10 mg BID
    - n=564

All subjects participated in a lifestyle modification program

---

**Weight Change Over 1 Year With Lorcaserin Therapy**

- Waist circumference decreased 2.7 inches for lorcaserin group vs 1.5 inches for placebo group

- Placebo
  - n=1587
  - Lorcaserin 10 mg BID
  - n=1595

- Placebo
  - n=684
  - Placebo
  - n=275
  - Lorcaserin 10 mg BID
  - n=564

- Study Week (ITT-LOCF Population)

**Effect of Lorcaserin on Metabolic Measures in Obese Adults After 1 Year**

- Change (mm Hg)

- Placebo
  - SBP
  - DBP

- Lorcaserin 10 mg BID
  - TC
  - LDL-C
  - HDL-C

Data are presented from the intention-to-treat analysis with LOCF imputation. Means ± SE.

**Effect of Lorcaserin on Glycemic Parameters in Obese Adults After 1 Year**

- Fasting Glucose (mg/dL)
- Fasting Insulin (µU/mL)
- HbA1c (%)
- HOMA-IR

Data are presented from the intention-to-treat analysis with LOCF imputation. Means ± SE.

**Weight Change With Lorcaserin Over 2 Years (ITT-LOCF Population)**

- Year 1
- Year 2

<table>
<thead>
<tr>
<th>Study Week (ITT-LOCF Population)</th>
<th>Placebo in Years 1 and 2</th>
<th>Lorcaserin in Year 1, placebo in Year 2</th>
<th>Lorcaserin in Years 1 and 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-12 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-18 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24-30 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-36 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36-42 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>42-48 months</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Only included patients who continued the study past year 1

---

**Lorcaserin Safety Data**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Lorcaserin 10 mg BID n=1595, Year 1 (%)</th>
<th>Lorcaserin 10 mg BID n=573, Years 1 and 2 (%)</th>
<th>Placebo n=1584, Year 1 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>287 (18.0)</td>
<td>310 (53.9)</td>
<td>97 (6.2)</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>83 (5.4)</td>
<td>109 (19.2)</td>
<td>37 (2.3)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>95 (6.1)</td>
<td>143 (25.1)</td>
<td>44 (2.8)</td>
</tr>
<tr>
<td>Constipation</td>
<td>79 (5.1)</td>
<td>132 (23.0)</td>
<td>75 (4.7)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>70 (4.4)</td>
<td>132 (23.0)</td>
<td>75 (4.7)</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>79 (5.1)</td>
<td>132 (23.0)</td>
<td>75 (4.7)</td>
</tr>
<tr>
<td>Influenza</td>
<td>72 (4.5)</td>
<td>132 (23.0)</td>
<td>75 (4.7)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>79 (5.1)</td>
<td>132 (23.0)</td>
<td>75 (4.7)</td>
</tr>
</tbody>
</table>

Population includes all patients who received ≥1 dose of lorcaserin or placebo
Lorcaserin Warnings

- Lorcaserin is contraindicated in pregnancy
- Warnings:
  - Should not be used in patients who are taking SSRIs or SNRIs, TCAs, triptans and tryptophan

Emerging Pharmacotherapy

<table>
<thead>
<tr>
<th>Agent</th>
<th>Naltrexone/BupSR1</th>
<th>Liraglutide2-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Status</td>
<td>FDA requested additional Phase 3 data</td>
<td>In Phase 3 clinical trials</td>
</tr>
<tr>
<td>Mechanism</td>
<td>Naltrexone, opioid receptor antagonist; Bup, norepinephrine-dopamine reuptake inhibitor</td>
<td>Glucagon-like peptide-1 analogues</td>
</tr>
<tr>
<td>Follow-up Duration</td>
<td>56 weeks</td>
<td>56 weeks</td>
</tr>
<tr>
<td>Common AEs</td>
<td>Nausea, Headache, Constipation, Diarrhea, Vomiting, Dry mouth</td>
<td>Nausea, Vomiting, Gastrointestinal effects</td>
</tr>
</tbody>
</table>

Bariatric Surgery

- Indications
  - BMI >40 kg/m² or
  - BMI 35–39.9 kg/m² and cardiopulmonary disease, diabetes, or lifestyle impairment
  - Failure to achieve adequate weight loss with nonsurgical treatment
- Contraindications
  - History of noncompliance with medical care
  - Certain psychiatric illnesses: personality disorder, uncontrolled depression, suicidal ideation, active substance abuse
  - Unlikely to survive surgery

Current Bariatric Surgical Procedures

<table>
<thead>
<tr>
<th>Adjustable Gastric Band</th>
<th>Gastric Sleeve</th>
<th>Gastric Bypass</th>
<th>Bilipancreatic Diversification With a Duodenal Switch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>$24,500-$26,000*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reversible?</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Weight loss</td>
<td>+++</td>
<td>+++</td>
<td>No</td>
</tr>
<tr>
<td>Safety</td>
<td>++++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Other issues</td>
<td>Requires compliance for greatest efficacy</td>
<td>Newest</td>
<td>Additional vitamin and mineral supplements may be required to offset malabsorption</td>
</tr>
</tbody>
</table>

*Total cost for all types of open bariatric surgery; laparoscopic surgery total cost ~$17,000.

References:
Decreased Mortality in Severely Obese Patients Who Underwent Bariatric Surgery


Postoperative mortality and morbidity

Acute complications

- Hemorrhage, leaks, obstruction, infection

Long-term complications

- Nutritional deficiency
- Potential weight regain
- Internal hernias

Potential Complications of Surgical Weight Loss

Pories W. J Clin Endocrinol Metab. 2008;93:S89-S96.

A waist circumference of >40 in men and >35 in women indicates increased risk for comorbidity development.

5% to 10% reduction in weight is clinically meaningful and will improve patient health.

Lifestyle modifications that incorporate diet, physical activity, and behavioral components can result in clinically meaningful weight loss.

Overweight or obese patients at high risk are potential candidates for pharmacotherapy.

The newly approved pharmacotherapy agents, lorcaserin and phentermine/topiramate ER, are potential new treatment options.

Best Practice Pearls

- Which waist circumference is an indicator of high risk for developing weight related co-morbidities, especially type 2 diabetes, in adults?
  1. Men >35 inches, women >30 inches
  2. Men and women >35 inches
  3. Men >40 inches, women >35 inches
  4. Men and women >40 inches

Post-test Question 1

What is a realistic percent weight loss outcome at 6 months from nonsurgical weight loss treatment?

1. <1%
2. 3% to 5%
3. 5% to 10%
4. 15% to 20%
5. Unsure

Post-test Question 2

If an obese (BMI 32) person with hypertension has been unsuccessful in his/her weight loss goals (5% reduction) after 6 months of lifestyle modification, what would be the next strategy to recommend for weight loss?

1. Continue lifestyle modifications for another 6 months
2. Increase daily exercise time
3. Consider pharmacotherapy
4. Schedule bariatric surgery
5. Unsure

Post-test Question 3
Post-test Question 4

Which of the following pharmacotherapies for chronic weight management have been FDA approved in 2012?

1. Liraglutide
2. Phentermine/topiramate ER
3. Liraglutide and phentermine/topiramate ER
4. Lorcaserin and phentermine/topiramate ER
5. Unsure

Case Study 2

Meet Karen

Patient: Karen

- Age: 34 years
- Occupation: Dental hygienist
- Marital Status: Recently married
- Lifestyle: Attempted an exercise regimen prior to her wedding 6 months ago, but has since been to the gym only a few times; nonsmoker

Relevant Medical History

- Impaired fasting glucose level
- BMI: 31 (5'4", 180 lbs)

Following Karen

Current Medications

- SSRI (paroxetine) – began about 1 year ago during stressful wedding planning

Main Complaint During Office Visit

- Weight Gain
  - Within the last year she gained 20 lbs – which she attributes to the stress of wedding planning and the subsequent celebrations associated with her wedding and honeymoon

Conversation With the Practitioner

- When was your last glucose test?
- Are you taking your SSRI as prescribed?
- Now would be a great time to discuss the benefits of weight reductions on your overall health

ARS Question

What would be your first course of action when Karen presents to you for advice about how to lose weight?

1. Discuss her reasons for losing weight and realistic weight loss goals
2. Recommend that Karen try to wean off her SSRI, which may be causing additional weight gain
3. Immediately begin a structured weight loss program
4. Prescribe pharmacotherapy, including counseling about using contraception if taking certain weight loss therapies, along with lifestyle modifications

ARS Question

How would you counsel Karen when she suggests that she and her husband would like to start a family soon?

1. Highlight the importance of being at a healthy weight when she becomes pregnant
2. Delay becoming pregnant until she has reached her realistic weight loss goals
3. Recommend weaning off the SSRI, regaining a healthy weight through any appropriate means, and then begin trying to conceive
4. Advise using effective contraception if she chooses to take certain weight loss medications since they could cause fetal harm
Karen presents at age 54 years; diagnosed with T2DM 3 years ago and BMI now 34 (5'4", 197 lbs). Although she walks a mile a day and is mindful of her diet, her weight continues to creep higher. Which would be the best course of action?

1. Consultation with a nutritionist to discuss diet modifications
2. A structured weight loss program
3. Pharmacotherapy adjunct with lifestyle modifications
4. Bariatric surgery

What if Karen were older? Would it change your weight management approach?

Questions?