Facilitating Changes in Behavior – Meeting the Needs of Patients and Providers

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Director, Center for Lifestyle Medicine, Northwestern Medicine
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Multifaceted Approaches to Optimize Care for Patients with Obesity

Lifestyle Counseling Rates Among PCPs
NAMCS (n=32,519 records)

NAMCS = National Ambulatory Medical Care Survey

Percent of Patients Receiving PCP Advice by Obesity Classification


Traditional Medical Model

Mr. Smith, you are a 52-year-old man with hypertension, prediabetes, and GERD. I can treat these problems. If you were able to lose some weight that would help too.
Current Hierarchical Provision of Obesity Care by HCPs – Obesity as a ‘Secondary Issue’

- Specialist
- Counsel & Treat
- Assess & Refer
- Identify & Give Advice
  “Lose Weight”
- Don’t Ask: Don’t Tell

HCP = health care provider

Weight Management is Embedded within the Office Visit

- Embeddedness = observed tendency among health care providers to see weight as an issue within other types of medical visits rather than presenting as a discreet issue

A Paradigm Shift

Mr. Smith, you are a 52-year-old man who is overweight. Medically, we call this obesity. You now have developed hypertension, prediabetes, and GERD, all complications of obesity. Unless we focus on your weight, you are at risk of developing many more medical problems. What do you think?
Proposed Hierarchical Provision of Obesity Care by HCPs – Obesity as a ‘Primary Issue’

- Specialist
- Counsel & Treat
- Identify, Assess, & Refer

HCP = health care provider

Practice Issues (Barriers)
- Functioning in an acute care model
- Limitation of time
- Few available resources
- Inadequate reimbursement
- Lack of effective teamwork
- Insufficient training

Bias

What are the Barriers?

Closing the Obesity Gap

Gap in Training & Practice

Importance

Provision of Care
Multifaceted Approaches to Optimize Care for Patients with Obesity

Developing Professional Competence

- “The habitual and judicious use of communication, knowledge, technical skills, clinical reasoning, emotions, values, and reflection in daily practice for the benefit of the individual and community being served.”
- “Competence builds on a foundation of basic clinical skills, scientific knowledge, and moral development.”


Patient-Physician Communication


<table>
<thead>
<tr>
<th>Patient Power/Interest</th>
<th>Physician Power/Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Low</td>
<td>Low</td>
</tr>
</tbody>
</table>

Mutuality
- "Shared decision-making"

Paternalism
- "Do what I say!"

Consumerism
- "What ever you want"

Dysfunctional
- "Don't ask: Don't tell"

The 5 A’s Counseling Framework

USPSTF | Adaptation for Obesity
---|---
Assess | Ask
Advise | Assess
Agree | Advise
Assist | Agree
Arrange | Assist


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### The 5 A’s Counseling Framework

| Ask/Assess | • Weight history  
|           | • Contributions to weight gain  
|           | • Past treatment attempts  
|           | • Diet and physical activity patterns  
|           | • Physical examination and pertinent laboratory tests |
| Advise    | • Perception of health problems associated with excess weight  
|           | • Explain complications of excess weight  
|           | • Explain benefit of weight loss to improve health  
|           | • Explore treatment options  
|           | • Provide strategies for weight management |
| Agree     | • Decide upon a collaborative-based treatment plan |
| Assist    | • Discuss potential barriers to implement treatment plan  
|           | • Provide handouts |
| Arrange   | • Discuss follow up plans and/or referrals |

### Motivational Interviewing (MI)

- Motivational interviewing is a collaborative, goal-oriented approach of communication to elicit behavior change in patients.
- The approach is designed to identify and resolve ambivalence toward a specific goal by connecting necessary changes to incentives that reduce barriers for change.

### Motivational Interviewing Skills

- Ask  
  - Ask open-ended questions inviting the patient to consider how and why they might change.
- Listen  
  - Understand the patient’s experience and summarize with reflective listening.
- Inform  
  - Ask permission to provide information, then ask what the implications might be for the patient.

Moving to a New Paradigm in Obesity Care

- Assess and treat obesity-related comorbid conditions
- Assess motivation for weight management
- HCP provides weight management
- HCP referral for weight management
- HCP and colleagues offer collaborative care
- HCP referral to obesity medicine specialist
- LM counseling, (pharmacotherapy)
- Commercial or web-based, RD, disease management
- (NP, PA, RN, RD, PsyD, coaches), LM counseling, pharmacotherapy
- Team approach, LM counseling, VLCD, pharmacotherapy, bariatric surgery


Conclusion

- Obesity care is currently embedded within the office visit.
- Making obesity a primary concern will require increased competency in obesity care along with changes in the medical practice system.
- Use of the 5 A's counseling framework and motivational interviewing (MI) is intended to facilitate behavior change.
Achieving a Comfort Zone with Pharmacotherapy

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Medical Director, Strategies To Overcome and Prevent (STOP) Obesity Alliance
George Washington University
Washington, DC
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Obesity Is Significantly Under-Treated

Multifaceted Approaches to Optimize Care for Patients with Obesity

**FDA-Approved Obesity Pharmacotherapy Options**

- Phentermine (and other noradrenergic agents)
- Orlistat
- Lorcaserin
- Phentermine / topiramate ER
- Naltrexone SR / bupropion SR
- Liraglutide 3.0 mg

*Indications: Adjunct to behavioral modification in BMI >30 kg/m² or 27-30 kg/m² with comorbidities*

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**Phentermine**

- Sympathomimetic amine
- Approved 1959
- Short-term use; schedule IV
- Dosing: 15-37.5mg qAM
- Contraindications/warnings: Pregnancy, nursing, MAOI use, glaucoma, drug abuse history, hyperthyroidism, uncontrolled hypertension, tachycardia, history of CAD, CHF, stroke

**Orlistat**

- Lipase inhibitor
- Approved 1999
- Long-term use; not scheduled
- 120 mg TID with meals (Rx) or 60 mg TID (OTC)
- Use MVI with fat-soluble vitamins at bedtime
- Contraindications: pregnancy, chronic malabsorption syndrome, cholestasis
- Gastrointestinal AEs

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**Lorcaserin**

- Selective 5HT-2c receptor agonist
- Increases satiety
- Approved in 2012
- Long-term use; schedule IV
- Single dose: 10 mg BID; discontinue if <5% BWL after 12 weeks
- Contraindications: pregnancy
- Warnings: coadministration with serotonergic agents; valvular heart disease; psychiatric disorders; priapism

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**Lorcaserin: Weight Change over 2 Years**

![Graph showing weight change over 2 years with Lorcaserin and Placebo groups compared.](image)

**Key Secondary Endpoints**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Lorcaserin</th>
<th>Placebo</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumference (cm)</td>
<td>↓ -6.8</td>
<td>-3.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP/DBP (mm Hg)</td>
<td>↓ -1.4/-1.1</td>
<td>-0.8/-0.6</td>
<td>0.04/0.01</td>
</tr>
<tr>
<td>Cholesterol (% Δ)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>↓ -0.90</td>
<td>0.57</td>
<td>0.001</td>
</tr>
<tr>
<td>LDL</td>
<td>↓ 2.87</td>
<td>4.03</td>
<td>0.049</td>
</tr>
<tr>
<td>HDL</td>
<td>↓ 0.05</td>
<td>-0.21</td>
<td>0.72</td>
</tr>
<tr>
<td>Triglycerides (%)</td>
<td>↓ -6.15</td>
<td>-0.14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>A1c</td>
<td>↓ -0.9</td>
<td>-0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>↓ -2.0</td>
<td>-1.6</td>
<td>0.049</td>
</tr>
<tr>
<td>Beck depression II</td>
<td>↓ -1.1</td>
<td>-0.9</td>
<td>0.26</td>
</tr>
</tbody>
</table>

Lorcaserin: Adverse Events Reported by 5% or More in Any Group

<table>
<thead>
<tr>
<th></th>
<th>Lorcaserin (N = 3195)</th>
<th>Placebo (N = 3185)</th>
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</thead>
<tbody>
<tr>
<td>Headache</td>
<td>537 (16.8)</td>
<td>321 (10.1)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>270 (8.5)</td>
<td>122 (3.8)</td>
</tr>
<tr>
<td>Nausea</td>
<td>264 (8.3)</td>
<td>170 (5.3)</td>
</tr>
<tr>
<td>Constipation</td>
<td>186 (5.8)</td>
<td>125 (3.9)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>229 (7.2)</td>
<td>114 (3.6)</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>169 (5.3)</td>
<td>74 (2.3)</td>
</tr>
</tbody>
</table>


Phentermine / Topiramate ER

- Phentermine: blunts appetite
- Topiramate: prolongs satiety
- Approved in 2012
- Long-term use; schedule IV
- 4 fixed doses (3.75/23mg increments)
- Titrate if <3% weight loss at 12 wk
- REMS: teratogenicity
- Contraindications: pregnancy, glaucoma, MAOIs, hyperthyroidism


Phentermine / Topiramate ER Prevents Progression to T2DM

Multifaceted Approaches to Optimize Care for Patients with Obesity

Patients with Extreme Obesity (BMI >45)

Weight loss of ≥5%
Placebo (n=1561), %
Phentermine/Topiramate ER 3.75 mg/23 mg (n=240), %
Phentermine/Topiramate ER 7.5 mg/46 mg (n=498), %
Phentermine/Topiramate ER 15 mg/92 mg (n=1580), %

**P<.01 vs. placebo**
**P<.001 vs. placebo**

Phentermine/Topiramate ER: Adverse Reactions Leading to Treatment Discontinuation

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Placebo (n=1561), %</th>
<th>Phentermine/Topiramate ER 3.75 mg/23 mg (n=240), %</th>
<th>Phentermine/Topiramate ER 7.5 mg/46 mg (n=498), %</th>
<th>Phentermine/Topiramate ER 15 mg/92 mg (n=1580), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vision blurred</td>
<td>0.5</td>
<td>2.1</td>
<td>0.8</td>
<td>0.7</td>
</tr>
<tr>
<td>Headache</td>
<td>0.6</td>
<td>1.7</td>
<td>0.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Irritability</td>
<td>0.1</td>
<td>0.8</td>
<td>0.8</td>
<td>1.1</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0.2</td>
<td>0.4</td>
<td>1.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Parasthesia</td>
<td>0.0</td>
<td>0.4</td>
<td>1.0</td>
<td>1.1</td>
</tr>
<tr>
<td>Insomnia</td>
<td>0.4</td>
<td>0.0</td>
<td>0.4</td>
<td>1.6</td>
</tr>
<tr>
<td>Depression</td>
<td>0.2</td>
<td>0.0</td>
<td>0.8</td>
<td>1.3</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.3</td>
<td>0.0</td>
<td>0.2</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Naltrexone SR / Bupropion SR: Mechanism of Action

Weight Loss

Naltrexone

Bupropion

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**Naltrexone SR / Bupropion SR**

- **Bupropion**: Dopamine/norepinephrine reuptake inhibitor
- **Naltrexone**: opioid receptor antagonist
- **Approved 2014**
- **Long-term use: not controlled**
- **Dosing (8 mg / 90 mg tabs): titrate weekly to 2 BID**
- **Consider discontinuation if <5% weight loss after 12 weeks**
- **Contraindications**: pregnancy, seizures, uncontrolled HTN, chronic opioid use, MAOI use


**Naltrexone SR / Bupropion SR : Patients Completing 1 Year of Treatment**

![Graph showing weight change comparison between Naltrexone SR/Bupropion SR and Placebo over 1 year of treatment.]

Subjects discontinuing due to AE:

<table>
<thead>
<tr>
<th></th>
<th>Naltrexone SR/bupropion SR 32/360 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>32.5%</td>
<td>6.7%</td>
</tr>
<tr>
<td>Constipation</td>
<td>19.2%</td>
<td>7.2%</td>
</tr>
<tr>
<td>Headache</td>
<td>17.6%</td>
<td>10.4%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10.7%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>9.9%</td>
<td>3.4%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>9.2%</td>
<td>5.9%</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>8.1%</td>
<td>2.3%</td>
</tr>
</tbody>
</table>

**Subjects discontinuing due to AE:**

<table>
<thead>
<tr>
<th></th>
<th>Overall 24%</th>
<th>Placebo 12%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>5.3%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Headache</td>
<td>1.7%</td>
<td>1.1%</td>
</tr>
</tbody>
</table>


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**Liraglutide 3.0 mg**

- GLP-1 receptor agonist
- Multiple actions; effect on weight is primarily via POMC neurons
- Liraglutide 1.8 mg: type 2 diabetes
- Liraglutide 3.0 mg: obesity treatment
- Long-term use; not controlled
- Dosing: SC; titrate weekly by 0.6 mg
- Discontinue if <4% loss at 16 weeks
- REMS: medullary thyroid carcinoma, acute pancreatitis

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**Liraglutide 3.0 mg for Weight Maintenance**


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**Liraglutide 3.0 mg**

<table>
<thead>
<tr>
<th></th>
<th>Liraglutide 3.0 mg</th>
<th>Placebo</th>
<th>Discontinuation</th>
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<tbody>
<tr>
<td>Nausea</td>
<td>39</td>
<td>14</td>
<td>2.9</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>21</td>
<td>10</td>
<td>1.4</td>
</tr>
<tr>
<td>Vomiting</td>
<td>16</td>
<td>4</td>
<td>1.7</td>
</tr>
<tr>
<td>Constipation</td>
<td>19</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Dypepsia</td>
<td>9</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Hypoglycemia in T2DM</td>
<td>23</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>14</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>7</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Increased lipase</td>
<td>5</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Overall discontinuation: 9.8% vs 4.3%

Combination Therapy

- Placebo alone
- Medication alone
- Lifestyle modification alone
- Medication + brief therapy
- Combined therapy

Adapted from Wadden, et al. NEJM 2005.

Thank you
Scott Kahan, MD, MPH
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Multifaceted Approaches to Optimize Care for Patients with Obesity

Thursday, November 5, 2015

Activity Chair
Robert F. Kushner, MD, MS, FACP, FTOS

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Getting Back to the Basics – Patient Selection for Pharmacotherapy

Ken Fujioka, MD
Director of Nutrition and Metabolic Research
Scripps Clinic Dept. of Endocrine

Addressing Individual Patient Needs and Preferences

• Treat obesity like any disease and work it up like a disease
• History
  – cause of obesity
    • Portion control, snacking, binge, low activity level, craving of specific foods etc.
  – comorbid diseases
  – current meds
  – patient expectations – on weight loss
  – personal profile – wants to get pregnant?

Physical

• General: is the patient depressed
• BMI: is it over 35 kg/m² with a co-morbidity
• Waist circumference
• Thyroid exam - nodule?
• Cardiac – Heart rate and blood pressure
**Treatment Plan**

- **Medications**
  - Diabetic meds with weight loss
    - GLP-1 receptor agonists, SGLT-2 inhibitors
  - Weight loss medications
    - Lorcaserin, Phentermine / Topiramate ER, Naltrexone SR / Bupropion SR, Liraglutide 3.0 mg
- **Bariatric Surgery**
  - Sleeve gastrectomy vs bypass
- **Failed bariatric surgery**
  - Conversion to bypass
  - Add weight loss medications
- **Everyone gets Diet and Lifestyle modification**

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**Lorcaserin**

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**Mechanism**

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Mechanism

Discontinuation Rates Due to Drug AEs

- Placebo – 6.7%
- Lorcaserin – 8.6%
  - Headache – 1.3% vs 0.8%
  - Depression – 0.9% vs 0.5%
  - Dizziness – 0.7% vs 0.2%

Clinical Practice Pearls

- This is a safe drug with no stimulating effects
  - Can be considered in the Cardiovascular patient #
- If you have a patient on SSRIs or other serotonin medications then use with caution
- Hypoglycemia a risk in diabetic patients on sulfonylureas and insulin
- The patient with portion control issues or Satiety
Topiramate

- Very potent weight loss agent
  - Positive studies in Binge Eating
- Significant number of potential Adverse Events
  - REMS program: potential for teratogenicity, cleft lip and cleft palate
    - Increased heart rate
    - Suicide and mood and sleep disorders
    - Acute myopia and glaucoma
    - Cognitive impairment
    - Metabolic acidosis
    - Creatinine elevations

Phentermine / Topiramate ER: EQUIP and CONQUER
Most Commonly Reported Treatment Emergent Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event (%) (N=3749)</th>
<th>Placebo</th>
<th>PHEN/TPM ER 3.75/23</th>
<th>PHEN/TPM ER 7.5/46</th>
<th>PHEN/TPM ER 15/92</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paresthesia</td>
<td>1.9</td>
<td>4.2</td>
<td>13.7</td>
<td>19.9</td>
</tr>
<tr>
<td>Drymouth</td>
<td>2.8</td>
<td>6.7</td>
<td>13.5</td>
<td>19.1</td>
</tr>
<tr>
<td>Constipation</td>
<td>6.1</td>
<td>7.9</td>
<td>15.1</td>
<td>16.1</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>12.4</td>
<td>15.4</td>
<td>12.8</td>
<td>13.5</td>
</tr>
<tr>
<td>Headache</td>
<td>9.3</td>
<td>10.4</td>
<td>7.0</td>
<td>18.6</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>1.1</td>
<td>1.3</td>
<td>7.4</td>
<td>5.4</td>
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<tr>
<td>Nasopharyngitis</td>
<td>8.0</td>
<td>12.5</td>
<td>10.5</td>
<td>5.4</td>
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<tr>
<td>Insomnia</td>
<td>4.7</td>
<td>5.5</td>
<td>5.7</td>
<td>5.4</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3.4</td>
<td>2.9</td>
<td>7.2</td>
<td>8.5</td>
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<tr>
<td>Sweats</td>
<td>6.3</td>
<td>7.5</td>
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<td>7.8</td>
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<tr>
<td>Nausea</td>
<td>4.4</td>
<td>5.8</td>
<td>3.6</td>
<td>7.2</td>
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<tr>
<td>Back pain</td>
<td>5.1</td>
<td>5.4</td>
<td>5.6</td>
<td>6.6</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4.3</td>
<td>5.0</td>
<td>4.4</td>
<td>5.9</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>3.5</td>
<td>5.0</td>
<td>4.0</td>
<td>5.4</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.9</td>
<td>5.5</td>
<td>6.4</td>
<td>5.6</td>
</tr>
</tbody>
</table>

Clinical Pearls and Phentermine / Topiramate ER

- Balance of excellent weight loss with the potential for more clinical adverse events
- In the pivotal trials they did allow pts on SSRIs to be in the study
- Topiramate has positive data in binge eating
- Despite the fact that this medication contains a sympathomimetic it did not typically increase blood pressure but does increase pulse
  - Not recommended for known cardiovascular patients
- Recommend the middle 7.5 / 46 mg dose
  - Weight loss at 2 years very similar to highest dose
  - If the pt needs to stop they do not have to taper down

Naltrexone SR / Bupropion SR

Mechanism
Mechanism

Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline
Apovian CM, Aronne LJ, Bessesen DH. J Clin Endocrinol Metab. 2015;100: 342–362

COR-1: Change in Selected Items from the Control of Eating Questionnaire at Week 56


*P < .05 vs placebo.

Table 3. Adverse Reactions Reported by Obese or Overweight Patients With an Incidence (%) of at Least 2% Among Patients Treated With Naltrexone SR / Bupropion SR and More Common than with Placebo

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Placebo (n=511)</th>
<th>Naltrexone 16 mg plus bupropion (n=471)</th>
<th>Naltrexone 32 mg plus bupropion (n=471)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>5.7</td>
<td>6.9</td>
<td>8.9</td>
</tr>
<tr>
<td>Headache</td>
<td>4.3</td>
<td>5.1</td>
<td>6.4</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1.0</td>
<td>2.9</td>
<td>3.2</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1.0</td>
<td>2.2</td>
<td>2.9</td>
</tr>
<tr>
<td>Insomnia</td>
<td>3.9</td>
<td>4.2</td>
<td>4.9</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>1.0</td>
<td>1.9</td>
<td>2.3</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0.6</td>
<td>1.4</td>
<td>1.8</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>0.0</td>
<td>0.2</td>
<td>0.8</td>
</tr>
<tr>
<td>Other</td>
<td>0.2</td>
<td>0.4</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Adverse Events

- Nausea
  - Forced Titration in studies
- Constipation
- Headache
- Vomiting
- Dizziness
- Insomnia
  - Take second dose late afternoon
- Dry mouth

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### Drug-Drug and Other Interactions

- Ticlopidine and Clopidogrel (Plavix)
  - Decrease dose to 1 BID
- Seizure risk with bupropion thus do not give to patients with a seizure history
- 1 to 2 mm Hg rise in blood pressure and pulse (check BP the first 12 weeks)
- Do not give to patient on chronic opioids

### Clinical Pearls

**Naltrexone SR / Bupropion SR**

- Bupropion a known anti-depressant thus useful in the depressed patient
  - Be cautious with combining with other depression meds (potential for interaction)
- Has the potential to work on “Cravings” and food reward type eating
- Recommend slow titration, (or back titration) and may not need to go to the highest dose
- If patient has insomnia may need to take second dose earlier in the day

### Liraglutide 3.0 mg
Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline
Apovian CM, Aronne LJ, Bessesen DH. J Clin Endocrinol Metab. 2015;100:342-362

Liraglutide 3.0 mg Delayed Time to Onset of T2DM

The time of onset of T2DM occurs in between the first of the two required registrations of elevated HbA1c, FPG, or 2-hour OGTT plasma glucose, and the diabetes assessment visit prior to the first registration. The estimated survival time is based on an analysis of time to onset of T2DM using a Kaplan-Meier approach that includes treatment, sex, and baseline BMI stratum as fixed factors and baseline FPG value as a covariate. BMI, body mass index; FAS, full analysis set; FPG, fasting plasma glucose; HbA1c, glycosylated hemoglobin; HR, hazard ratio; NNT, number needed to treat; OGTT, oral glucose tolerance test; T2DM, type 2 diabetes mellitus.

In-Roux et al. Obesity Week 2015, 2-6 November 2015, Poster T-P-LB-3843
Subjects with Normoglycemia Over Time

![Graph showing the proportion of participants with normoglycemia over time.]

- Measured at OGTT visits: 0–172 weeks
- Liraglutide 3.0 mg
- Placebo
- Odds ratio for normoglycemia at week 160
  - Liraglutide 3.0 mg/Placebo: 3.6 (95% CI [3.0; 4.4], p<0.0001)

Contraindications and Potential Adverse Events

- Personal or family history of medullary thyroid carcinoma
- Multiple Endocrine Neoplasia syndrome type 2
- Gastro paresis
- Pancreatitis
- Increased heart rate (0.9% HR > 100)

Clinical Pearls: Liraglutide 3.0

- Part of the feedback pathway that regulates weight and food intake: thus hitting multiple receptors for appetite regulation (Satiety and time to next feeding)
- Non-stimulating and in this author’s opinion useful in the cardiovascular patient
- Titrate slowly as GI side effects are common
  - Don’t be afraid to back titrate
- May not need top dose to get effective weight loss
- Drug of choice in the pre-diabetic and diabetic
- Patient that has already lost some weight on their own

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Contraindications & Cautions

<table>
<thead>
<tr>
<th>Clinical scenario</th>
<th>Avoid/caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated seizure risk</td>
<td>Naltrexone SR / bupropion SR</td>
</tr>
<tr>
<td>h/o recurrent kidney stones</td>
<td>Phentermine / topiramate ER, orlistat</td>
</tr>
<tr>
<td>h/o glaucoma</td>
<td>Phentermine / topiramate ER</td>
</tr>
<tr>
<td>Uncontrolled hypertension</td>
<td>Naltrexone SR / bupropion SR</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>Phentermine</td>
</tr>
<tr>
<td>Moderate-severe renal impairment</td>
<td>Do not exceed half-dose: Phentermine / topiramate ER, naltrexone SR / bupropion SR Caution: liraglutide 3.0 mg, lorcaserin</td>
</tr>
<tr>
<td>Moderate-severe hepatic impairment</td>
<td>Do not exceed half-dose: Phentermine / topiramate ER, naltrexone SR / bupropion SR Caution: liraglutide 3.0 mg, lorcaserin</td>
</tr>
<tr>
<td>SSRI use</td>
<td>Caution: lorcaserin</td>
</tr>
</tbody>
</table>

Dual Benefits

<table>
<thead>
<tr>
<th>Obesity and...</th>
<th>Consider, but not explicitly approved...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>Naltrexone SR / bupropion SR</td>
</tr>
<tr>
<td>Depression</td>
<td>Naltrexone SR / bupropion SR</td>
</tr>
<tr>
<td>Migraines</td>
<td>Phentermine / topiramate ER</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Liraglutide 3.0 mg</td>
</tr>
<tr>
<td>Chronic constipation</td>
<td>Orlistat</td>
</tr>
<tr>
<td>Elevated LDL</td>
<td>Orlistat</td>
</tr>
</tbody>
</table>

Choosing Between Options

- Drug factors
  - Contraindications
  - Dual benefits
  - Studied populations

- Patient factors
  - Patient preferences
  - Adverse events
  - Prior experiences
  - Access

- Healthcare Provider factors
  - Provider knowledge/comfort