Current Concepts in Obesity Medicine

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Disclosures

• Novo Nordisk: Speaker's Bureau
Objectives

• Learn the diagnostic criteria for the disease of obesity
• Understand why losing weight and keeping it off is so challenging
• Realize the importance of individualizing patients’ obesity treatment plans
• Review the evidence on treatment options
Meet Jonathan…

144% Weight Gain over 27 years

No Sustained Treatment
Meet Frank…

**46% Weight Loss over 10 years**

*No Surgery*

*Nearly No Medications*

*Sustained Behavioral Intervention*

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36 years old
Metabolic Syndrome
Sleep Apnea

46 years old
Met. Syndrome
Resolved
Sleep Apnea
Improved

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Weight (lbs): 443 256.9 289.4 290 304.8 316 270 238

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Weight (lbs)
What is obesity?
Abnormal or excessive fat accumulation that presents a risk to health.

A crude population measure of obesity is the body mass index (BMI), a person's weight (in kilograms) divided by the square of his or her height (in meters).

Resolved, that our American Medical Association recognize obesity as a disease state with multiple pathophysiological aspects requiring a range of interventions to advance obesity treatment and prevention.
How do we classify weight?

<table>
<thead>
<tr>
<th>BMI (Body Mass Index)</th>
<th>Weight Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.5 – 24.9</td>
<td>“Normal”</td>
</tr>
<tr>
<td>25 – 29.9</td>
<td>Overweight</td>
</tr>
<tr>
<td>30 – 34.9</td>
<td>Obesity Class I</td>
</tr>
<tr>
<td>35 – 39.9</td>
<td>Obesity Class II</td>
</tr>
<tr>
<td>40 or more</td>
<td>Obesity Class III</td>
</tr>
</tbody>
</table>

### Years of life lost to obesity

<table>
<thead>
<tr>
<th>BMI</th>
<th>Healthy Weight</th>
<th>Overweight</th>
<th>Obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30+</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Healthy Weight**
- **Overweight**
- **Obesity**

- **BMI 30-35**
  - Life Expectancy Reduced
  - 2-4 Years

- **BMI 40-50**
  - Life Expectancy Reduced
  - 8-10 Years

Each 5 kg/m\(^2\) increase in BMI

**~40% higher mortality rate**

For ischemic heart disease, stroke, vascular diseases

Obesity Cost $1.42 Trillion in 2014

- 14.3% of Healthcare Spending
- 320,000 Deaths
- 5% Weight Loss for those with BMI ≥ 40 saves $2137 / year

236 known Obesity Comorbidities

- Type 2 Diabetes\textsuperscript{2} and pre-diabetes\textsuperscript{3}, Hypertension, Stroke, Dyslipidemia, CHF\textsuperscript{2}, Infertility\textsuperscript{6}

- 13 types of Cancer\textsuperscript{2}

- Obstructive Sleep Apnea\textsuperscript{5}, Osteoarthritis\textsuperscript{2}

- Depression\textsuperscript{1}, Decreased Quality of life

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Health Benefits of 5% - 10% Weight Loss

- **DECREASED RISK** of Type 2 Diabetes by 58% (or more)\(^1\),\(^4\)
- **REDUCES** Sleep Apnea\(^3\)
- **REDUCES** Osteoarthritis\(^5\)
- **IMPROVED** Quality of life\(^2\)

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Screen all adults for obesity

Patients with BMI of 30 or more should be offered or referred to intensive, multi-component behavioral interventions.  Grade B
How do we treat obesity?
Person-first language reduced weight bias

DO Say

“Patients with:”

• Unhealthy Weight
• Weight Problems

DON’T Say

“Obese Patients”

• Obese
• Fat
• Extremely Obese
• Morbidly Obese

~20% of patients who perceive weight stigma from their health care provider will avoid future appointments or seek out a new provider.

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Are HCP’s engaging in a discussion about weight?

- Comfortable Talking About Weight
- Diagnosed with obesity
- Follow-up Appointment

Isn’t weight management easy?

Calories In

Calories Out

?
Counting Calories Is Not Enough to Achieve Long-term Weight Loss

Decreased caloric intake + Increased energy expenditure ≠ Long-term Weight loss

CNS pathways sense changes in weight and body energy stores and exert opposing effects on energy balance to promote homeostasis.

Explain that obesity is a **chronic disease**

**DO**

Explaining to a person that obesity is a chronic disease helps that individual move forward with proper treatment.

Part of that treatment is provider and patient acceptance that “It’s not their fault.”

**DON’T**

Conversely, telling a patient to “eat less, move more” reinforces that obesity is a lifestyle choice resulting from dietary indiscretion and laziness.

This is not consistent with current medical evidence.
Effective Treatment Strategies

- Intensive Lifestyle Intervention
- Medical Supervision
- Bariatric Surgery
- Weight Loss Medications
- Structured Food Plans & Meal Replacements
Treatment | 25-26.9 | 27-29.9 | 30-34.9 | 35-39.9 | ≥40
--- | --- | --- | --- | --- | ---
Diet, physical activity and behavior therapy | Yes, with comorbidity | Yes, with comorbidity | Yes | Yes | Yes
Pharmacotherapy | Yes, with comorbidity | | Yes | Yes | Yes
Surgery | | | Yes, with comorbidity | | Yes

- **Diet and Activity remain the cornerstone of weight loss interventions**
- **Participation in a long-term (>1 year) comprehensive weight-loss maintenance program is strongly recommended**
- **Surgery may be appropriate if inadequate response to diet, physical activity, behavior therapy and pharmacotherapy.**
Intensive Lifestyle Intervention

% Reduction in initial weight

% Of Visits Attended

- Quartile 1
  - 4.60%
  - 51%

- Quartile 2
  - 7.40%
  - 82%

- Quartile 3
  - 9.60%
  - 93%

- Quartile 4
  - 11.00%
  - 99%

Meal Replacements

Meal Replacements

• For every 100,000 patients treated with full meal replacement, it is estimated that this will prevent:
  – 50 heart attacks
  – 75 strokes
  – 899 cases of type 2 diabetes
  – 26 cancers

Physical Activity

Minutes of Physical Activity per week

<table>
<thead>
<tr>
<th>Quartile</th>
<th>Reduction in Initial Weight</th>
<th>Minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.40%</td>
<td>26 min</td>
</tr>
<tr>
<td>2</td>
<td>7.10%</td>
<td>85 min</td>
</tr>
<tr>
<td>3</td>
<td>9.00%</td>
<td>149 min</td>
</tr>
<tr>
<td>4</td>
<td>11.90%</td>
<td>287 min</td>
</tr>
</tbody>
</table>

Habits of successful MAINTAINERS (≥30 pounds x ≥1 year)

1. **Low-calorie**
   1,300 to 1,680 kilocalories per day

2. **Consistent food intake from day to day, and eat 4-5 times daily**

3. **Eat breakfast every day**

4. **Physically activity**
   60 to 90 minutes exercise per day at moderate intensity, or
   11,000 to 12,000 steps per day (6 miles)

5. **Self-monitoring: weigh weekly or daily**
   Even a small amount of regain => corrective action (calories, activity)

6. **TV viewing: less than 10 hours per week**
Pharmacotherapy for obesity
• Other Medications
  – Consider the weight effects of **ALL** of the medications that a person is taking
  – Consideration **MUST** be given for **IATROGENIC** weight gain caused by medications

• Anti-Obesity Medications
## Medication Selection

<table>
<thead>
<tr>
<th>Disease</th>
<th>Avoid</th>
<th>Choose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Paroxetine</td>
<td>Bupropion (wt loss)</td>
</tr>
<tr>
<td></td>
<td>Amitryptiline</td>
<td>Escitalopram, Citalopram</td>
</tr>
<tr>
<td></td>
<td>Nortryptiline</td>
<td>Fluoxetine, Sertraline</td>
</tr>
<tr>
<td></td>
<td>Mirtazapine</td>
<td>Imipramine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trazodone</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duloxetine, Venlafaxine</td>
</tr>
<tr>
<td>Anti-Epileptic Drugs</td>
<td>Valproic Acid (5-10%)</td>
<td>Wt loss: Felbamate, Topiramate, Zonisamide</td>
</tr>
<tr>
<td></td>
<td>Gabapentin (2.2 kg)</td>
<td>Wt neutral: Lamotrigine, Levetiracetam, phenytoin</td>
</tr>
<tr>
<td></td>
<td>Divalproex</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Carbamazepine (1.5 kg)</td>
<td></td>
</tr>
<tr>
<td>Anti-psychotics</td>
<td>Olanzapine (30% wt gain)</td>
<td>Aripiprazole</td>
</tr>
<tr>
<td></td>
<td>Quetiapine (16%)</td>
<td>Ziprasidone (7%)</td>
</tr>
<tr>
<td></td>
<td>Risperidone (14%)</td>
<td>Consider offset with metformin or topiramate (off-label)</td>
</tr>
<tr>
<td></td>
<td>Perphenazine (12%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clozapine (.9-9.5 kg)</td>
<td></td>
</tr>
</tbody>
</table>


Blackburn, George et al. Break Through Your Set Point. William Morrow (April 8, 2008)
## Medication Selection

<table>
<thead>
<tr>
<th>Disease</th>
<th>Avoid</th>
<th>Choose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids</td>
<td>Prednisone, etc. (4-8%)</td>
<td>NSAID, etanercept, etc.</td>
</tr>
<tr>
<td>Anti-Histamines</td>
<td>Sedating: Cyproheptadine Diphenhydramine</td>
<td>Non-sedating: Loratadine, Fexofenadine, Cetirizine</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Insulin (10 kg) Pioglitazone (3 kg), Rosiglitazone Sulfonylureas (10 kg)</td>
<td><strong>Metformin</strong> (-2.1 kg), <strong>GLP-1</strong>, <strong>DPP-4 SGLT-2 Inhibitors</strong>, acarbose, miglitol, pramlintide</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Beta-blockers (1.2 kg)</td>
<td>Ace-I , ARB, CCB</td>
</tr>
<tr>
<td>Contraception</td>
<td>Depo-medroxyprogesterone Acetate</td>
<td>Oral Contraceptive Pills (if not contraindicated), barrier methods, IUD, Vasectomy, Tubal...</td>
</tr>
</tbody>
</table>

Apovian 2015, Blackburn 2008
An **adjunct** to a reduced-calorie diet and increased physical activity for **chronic weight management** in adults with an initial body mass index (BMI) of:

- $\geq 30 \, \text{kg/m}^2$ (obese), or
- $\geq 27 \, \text{kg/m}^2$ (overweight) in the presence of at least one weight-related comorbidity (eg, hypertension, type 2 diabetes mellitus, or dyslipidemia)
Pharmacotherapy Improves the Odds of Losing 5-10% Body Weight

- Phentermine
- Phentermine / Topiramate ER
- Diethylpropion
- Orlistat
- Lorcaserin
- Bupropion / Naltrexone ER
- Liraglutide 3.0 mg

Results vary slightly between medications. This graph is for illustration purposes only.
Weight regained if treatment stopped

B Body Weight during Yr 1

C Body Weight during Yr 1 and 2

- Placebo (N=1499)
- Lorcanerin (N=1538)
- Placebo in yr 1 and 2 (N=684)
- Lorcanerin in yr 1, placebo in yr 2 (N=275)
- Lorcanerin in yr 1 and 2 (N=564)
Even after 3 years…
Intensive Lifestyle Intervention + Medication + Meal Replacements

- Medication Only
- Medication + Intensive Lifestyle Intervention
- Medication + Intensive Lifestyle Intervention + Meal Replacement

Wadden TA. Arch Intern Med. 2001; 161(2):218-227
Anti-Obesity Medications: Limitations

2% of adults with obesity receive pharmacotherapy

86% of adults with T2DM receive pharmacotherapy

Anti-Obesity Medications: Limitations

• Used short-term
  – Old drug labels encourage only short-term use.
  – Some state boards do not allow long-term use.
  – This is not consistent with the current state of medical knowledge¹

• Inadequate follow-up
  – Medications work as an adjunct to the lifestyle intervention²

Is Phentermine safe for Long-Term Use?

- **13,972 Adults Treated Long-Term**

```plaintext
Percent Change from Baseline Weight

6 months
- Short-Term (Referent): -6.3
- Short-Term Intermittent: -7.8
- Medium-Term Continuous: -9.6
- Medium-Term Intermittent: -8.5

12 months
- Short-Term (Referent): -4.1
- Short-Term Intermittent: -5.8
- Medium-Term Continuous: -7.7
- Medium-Term Intermittent: -8.3

24 months
- Short-Term (Referent): -3.0
- Short-Term Intermittent: -3.1
- Medium-Term Continuous: -3.5
- Medium-Term Intermittent: -5.5
- Long-Term Continuous: -10.7
```

Conclusion

“Recommendations to limit phentermine use to less than 3 months do not align with current concepts of pharmacological treatment for patients with obesity. Our results show that longer-term phentermine users experienced greater weight loss without apparent increases in cardiovascular risk.”
Why is keeping weight off so hard?
Body Mechanisms to Protect Body Weight

↑ Appetite

↑ Ghrelin
↓ Amylin
↓ PYY
↓ GLP-1
↓ CCK

↓ Weight Loss

↑ Skeletal Muscle Efficiency
↓ Resting Metabolic Rate
↓ Total Energy Expenditure

↓ Metabolism

References:
Fothergill et al. Obesity 2016
Surgical options for obesity treatment
Consensus Guidelines:

- BMI > 40
- BMI > 35 with 1 significant comorbidity when less invasive strategies for weight loss have failed and patient is at high risk for obesity related morbidity and mortality.
Long-term results

Mortality Reduction

- Swedish Obesity Study (SOS)
  - 29% reduction in death at average follow-up of 10.9 years

- NEJM: retrospective study of 7900 patients at 7.1 years
  - 40% reduction in mortality
    - 60% reduction in cancer death
    - 92% reduction in type 2 diabetes death
Comorbidities Improve

• Improves Comorbidities

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>% Improved</th>
<th>% Resolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>18</td>
<td>82</td>
</tr>
<tr>
<td>Hypertension</td>
<td>18</td>
<td>70</td>
</tr>
<tr>
<td>High Cholesterol</td>
<td>33</td>
<td>63</td>
</tr>
<tr>
<td>GERD</td>
<td>24</td>
<td>72</td>
</tr>
<tr>
<td>Sleep Apnea</td>
<td>19</td>
<td>74</td>
</tr>
</tbody>
</table>

• Improves Quality of Life

What does the future hold?

- Dietary Approaches
- Physical Activity Approaches
- Combination Pharmacotherapy
- New Pharmacotherapy
- Devices / Procedures
  - Balloons, drains, barriers, endoscopic gastroplasty
FDA Clears *Plenity* Hydrogel Capsules for Weight Management

Troy Brown, RN
April 16, 2019

The US Food and Drug Administration (FDA) has cleared Gelesis100 (*Plenity*, Gelesis) for weight management in adults with a body mass index (BMI) of 25 - 40 kg/m², when used together with diet and exercise, according to a company news release.
Combination Therapy

• Drug labels discourage combination therapy
  – Yet two of our drugs are combinations
    • phentermine / topiramate ER
    • bupropion SR / naltrexone
  – Combination treatments
    • One study achieved 31% weight loss with combination therapy [off-label].¹
    • Another showed additive weight loss with lorcaserin + phentermine [off-label].²

Take-home points

• **Successful treatment IS possible**
  – Consider further training in obesity medicine

• **Do a careful HISTORY**
  – Drivers of weight GAIN / Barriers to weight LOSS
  – Diet / weight history, comorbidities, medications

• **Develop an individualized treatment plan**
  – Structured Behavioral Intervention
    • Structured Food Plan
    • Structured Activity Plan
    • Frequency of interaction
    • 5-10% body weight loss is a good initial goal of treatment
  – Pharmacotherapy
    • Know indications, contraindications, interactions, stoppage rules etc.
    • Shoot for ~5% (or more) weight loss at 3 months
  – Surgical Referral
    • BMI ≥ 40, ≥ 35 with comorbidity, if above interventions not adequate