Treatment of Severe Obesity. What tools are available?

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Duke Healthy Lifestyles Program
Objectives and Overview

• To describe the current epidemiologic prevalence of child and adolescent obesity and severe obesity in the US
• Behavioral/clinical approaches – tertiary care
• Innovations in Behavioral Treatment: Community partnerships, use of technology
• Diets
• Medications
• Surgery
• Devices
• Other considerations/Conclusions
Definition of Severe Pediatric Obesity

• BMI $\geq$ 120% of 95%ile for age and sex, OR
• BMI $\geq$ 35
• This accounts for all children and adolescents in Class II or III category of obesity.
Defining Obesity/Severe Obesity in Children
Why is severe obesity different?
Consequences

**Now**
- Mental health
- Teasing/bullying
- Low Quality of Life
- Asthma
- Obstructive sleep apnea
- Orthopedic problems
- Adverse cardiovascular and metabolic conditions
  - High blood pressure
  - Abnormal lipids
  - Insulin resistance

**Later**
- Continued obesity
- Type 2 Diabetes
- Adverse cardiovascular outcomes
  - Hypertension
  - Coronary artery disease
  - MI
  - Stroke
- Early mortality

Skinner et al. New England Journal of Medicine, 2017
National Health and Nutrition Examination Survey, 1999-2016

Cardiovascular Risk Factors and Excess Adiposity Among Overweight Children and Adolescents: The Bogalusa Heart Study
Freedman, David S. et al.
The Journal of Pediatrics, Volume 150, Issue 1, 12-17.e2
Increase risk of mortality
Why are we still struggling with this epidemic?
Obesity and Weight Bias

• Continued misconception:
  – Food intake – Energy expenditure = Net weight gain
Obesity and Weight Bias

• **Weight Bias**
  – June 2013 AMA recognized obesity as disease in adults.

• Whereas, The suggestion that obesity is not a disease but rather a consequence of a chosen lifestyle exemplified by overeating and/or inactivity is equivalent to suggesting that lung cancer is not a disease because it was brought about by individual choice to smoke cigarettes; (quote from the resolution).

• Negative imaging in news media.
Complexity of Obesity
Obesity as a Chronic Disease

- Children and teens who struggle with severe obesity will likely always struggle with weight.
- Ups and downs over the course of a lifetime.
- All about “managing” the disease to reduce long term health risk.
- Multiple interventions over course of lifetime will likely be needed.
Clinical Case: “Anna”

• Anna is a 9-year old Hispanic female with severe obesity, 135 percent of the 95th percentile (Class 2).
  - TG = 170, LDL 120, HDL 30; ALT 50, HbA1c 5.7
  - Getting teased at school, mom does not speak English and cannot talk with teacher

• Lives at home with her mother and 2 brothers. Mom works 3 jobs, dad lives in Mexico, kids attend public school.
Behavioral Interventions

• Multiple recommendations based on >20 years of clinical trial data
<table>
<thead>
<tr>
<th>Population</th>
<th>Children and adolescents 6 y and older</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation</strong></td>
<td>Screen for obesity; offer or refer children and adolescents with obesity to comprehensive, intensive behavioral interventions to promote improvements in weight status. Grade: B</td>
</tr>
<tr>
<td><strong>Risk Assessment</strong></td>
<td>All children and adolescents are at risk for obesity and should be screened; specific risk factors include parental obesity, poor nutrition, low levels of physical activity, inadequate sleep, sedentary behaviors, and low family income.</td>
</tr>
<tr>
<td><strong>Screening Tests</strong></td>
<td>BMI measurement, using height and weight, is the recommended screening test for obesity. Obesity is defined as an age- and sex-specific BMI in the 95th percentile or greater.</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>Comprehensive, intensive behavioral interventions of ≥26 contact hours resulted in weight loss. Effective interventions consisted of multiple components, including: sessions targeting both the parent and child (separately, together, or both); offering individual sessions (both family and group); providing information about healthy eating, safe exercising, and reading food labels; encouraging the use of stimulus control (e.g., limiting access to tempting foods and screen time), goal setting, self-monitoring, contingent rewards, and problem solving; and supervised physical activity sessions. Providers included primary care clinicians, exercise physiologists, physical therapists, dietitians, diet assistants, psychologists, and social workers, but the more intensive interventions usually involved referral outside the primary care office. Evidence regarding pharmacotherapy interventions was inadequate.</td>
</tr>
<tr>
<td><strong>Balance of Benefits and Harms</strong></td>
<td>The USPSTF concludes with moderate certainty that the net benefit of screening for obesity in children and adolescents 6 y and older and offering or referring them to comprehensive, intensive behavioral interventions to promote improvements in weight status is moderate.</td>
</tr>
<tr>
<td><strong>Other Relevant USPSTF Recommendations</strong></td>
<td>The USPSTF has made recommendations on screening for primary hypertension and lipid disorders in children and adolescents. These recommendations are available on the USPSTF website (<a href="https://www.uspreventiveservicestaskforce.org">https://www.uspreventiveservicestaskforce.org</a>).</td>
</tr>
</tbody>
</table>

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to https://www.uspreventiveservicestaskforce.org.
No POWER sites achieve ≥ 26 hours/6m

POWER: Projected enrollment
29 sites representing 20 states

Note: Enrollment in POWER currently ends on 12/31/14, however a 6-month extension will be proposed to the POWER Governance Board in January 2015.

Brooke Sweeney, MD – Kansas City, MO
Associate Director of Recruitment

★ = completed enrollment (n=23)
Duke Healthy Lifestyles Program
What other options exist for Anna?
Enhanced Behavioral Approaches/Community Collaborations

• To increase contact hours outside of clinic setting.
• To address a variety of the factors contributing to patients obesity
  – Cooking classes
  – Parenting classes
  – Access to organized physical activity
  – Grocery store tours...
Durham Parks and Recreation and Bull City Fit
A place Anna feels like she belongs
Freedom to move
To develop friendships
To discover new foods
Bull City Healthy and Fit Study Design

New Patients Referred to Duke Healthy Lifestyles Clinic → Research Assistant approaches at first visit → Parent consents/child assents to participate and completes baseline assessments → Intervention (n = 50): Usual clinical care plus Bull City Fit community programming (offered 6 days per week)

Randomization
N=100 will provide > 80% power to detect an effect of -0.14 on BMI z-score

Control (n = 47): Usual clinical care with community resource information from Durham Parks & Recreation

Baseline 1 mo. 2 mo. 3 mo. 4 mo. 5 mo. 6 mo.
T1 n = 97
T2 n = 56
T3 n = 68

Invited to Bull City Fit!

**Bull City Healthy and Fit Baseline**

**Child**
- Mean age: 9.1; 53% female
- Child race/ethnicity (primary)
  - Hispanic: 34%
  - Black/African-American: 51%
  - Other: 3%
  - White: 11%
- Mean BMI z-score: 2.28
  - 55% in Class II or III with “severe obesity”
- 12% with HbA1c $\geq$ 5.7%

**Parent**
- Mean age: 35.4; 87% female
  - 48% single parent
  - 43% born outside the USA
  - 26% mono-lingual Spanish-speaking
- Mean BMI: 34.6 kg/m²
- Total household income *per year*

## Bull City Healthy and Fit Primary Outcome: Treatment Hours

<table>
<thead>
<tr>
<th>Hours</th>
<th>Total n(%)</th>
<th>Control HL n(%)</th>
<th>Intervention HL + BCF n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>N = 97</td>
<td>N = 47</td>
<td>N = 50</td>
</tr>
<tr>
<td></td>
<td>8.2 (SD 11.6)</td>
<td>4.4 (SD 1.6, range 2-9)</td>
<td>11.7 (SD 15.3, range 2-67.8)</td>
</tr>
<tr>
<td>0-2</td>
<td>14 (14.4)</td>
<td>8 (17.0)</td>
<td>6 (12.0)</td>
</tr>
<tr>
<td>3-5</td>
<td>53 (54.6)</td>
<td>28 (59.6)</td>
<td>25 (50.0)</td>
</tr>
<tr>
<td>6-&lt;10</td>
<td>16 (16.5)</td>
<td>11 (23.4)</td>
<td>5 (10.0)</td>
</tr>
<tr>
<td>10&lt;26</td>
<td>8 (8.3)</td>
<td>0 (0.0)</td>
<td>8 (16.0)</td>
</tr>
<tr>
<td>26+</td>
<td>6 (6.2)</td>
<td>0 (0.0)</td>
<td>6 (12.0)</td>
</tr>
</tbody>
</table>

Bull City Healthy and Fit Secondary Outcomes: Quality of Life

- Significantly IMPROVED in the intervention vs. control at BOTH 3- and 6-months.
  - 3-months: total QOL, \textbf{+10.43 vs. +0.42} (95% CI -15.40 to -4.62, \( P < 0.001 \))
  - 6-months: total QOL, \textbf{+12.66 vs. +3.31} (95% CI -16.15 to -2.56, \( P = 0.008 \))

**Change in Quality of Life:**

**Intervention**

**Control**
No differences observed between intervention and control for:
- Child or parent BMI
- Blood pressure
- LDL

Significantly IMPROVED in intervention vs. control at 6-months (p=0.03)
Using Technology
TEXT-MI Study

<table>
<thead>
<tr>
<th></th>
<th>Total (n=100)</th>
<th>Control (n=53)</th>
<th>Intervention (n=47)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>9.5 (7-11)</td>
<td>9 (7-11)</td>
<td>10 (8-11)</td>
</tr>
<tr>
<td>Gender (%male)</td>
<td>39</td>
<td>42</td>
<td>36</td>
</tr>
<tr>
<td>Race (%Black)</td>
<td>48</td>
<td>43</td>
<td>53</td>
</tr>
<tr>
<td>Parental education (%HS or less)</td>
<td>46</td>
<td>49</td>
<td>43</td>
</tr>
<tr>
<td>REALM</td>
<td>65 (62-65)</td>
<td>65 (61-65)</td>
<td>65 (62-65)</td>
</tr>
<tr>
<td>Child BMI (kg/m²)</td>
<td>29.1 (24.7 – 32.8)</td>
<td>28.9 (23.3 – 32.7)</td>
<td>30.5 (25.8 – 34.0)</td>
</tr>
<tr>
<td>Mobile device (%smart phone, unlimited texts)</td>
<td>97, 99</td>
<td>94, 98</td>
<td>100, 100</td>
</tr>
</tbody>
</table>

TEXT-MI: Texting Motivational Interviewing to Improve Engagement

<table>
<thead>
<tr>
<th></th>
<th>Total (n=81)</th>
<th>No texting (n=42)</th>
<th>Texting (n=39)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI Z-score change (mean change)</td>
<td>+0.01 (p=0.97)</td>
<td>+0.02 units</td>
<td>0.00 units</td>
<td>p=0.14</td>
</tr>
<tr>
<td>Parent weight change</td>
<td>+0.35 (p=0.45)</td>
<td>+ 0.61 kg</td>
<td>+ 0.04 kg</td>
<td>p=0.25</td>
</tr>
<tr>
<td>3-min step test, beats per minute (BPM) change</td>
<td>-2.4 BPM (p=0.09)</td>
<td>-2 BPM</td>
<td>-3 BPM</td>
<td>p=0.83</td>
</tr>
<tr>
<td>Parent Global Self-Efficacy Scale</td>
<td>-0.1 (p=.22)</td>
<td>-0.4</td>
<td>0.0</td>
<td>p=.69</td>
</tr>
<tr>
<td>Number of HL clinic appts total (3 mo)</td>
<td>2.5</td>
<td>2.1</td>
<td>3.3</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

Diets?

- Dieting is a robust predictor of weight gain.
  - 2013 meta-analysis 40 studies
  - Finland study 2000 twins – 2-3x increased risk
- Project EAT dieting associated with:
  - unhealthy eating behaviors at time of dieting
  - higher BMI at 5 years
  - higher rate of eating disorders at 5 years
- Most diets produce short term weight loss only
- Some short term studies on low carb in children. Hard to maintain over time
- No real information on Mediterranean diet and children.

Lowe et al, Front Psychol, 2013
Pietilaineet et al, 2011.
Diets

• **Lifestyle-based eating plans show no harm. Focus on macronutrients, how to eat, when to eat, how to pair foods.**

• Some newer studies on timing of eating in children (time limited eating)

• Some hospitals will admit patients for ketogenic, or protein-sparing diet. Often to prep for surgery for complicating co-morbidity.
Medications?

• Review current med list
• Orlistat (FDA approved 12+)
  – Intestinal Lipase inhibitor
  – Side effects of incontinence and steatorrhea make use unrealistic
  – Only fair efficacy
    • 12 months of treatment showed small change in BMI of – 0.85 kg/m2 compared to control.
Off-label Medication for Children

• Metformin
  – FDA indication for T2D in adolescents.
  – Safety data profile reassuring down to age 10.
  – Meta-analysis shows modest short-term benefit (as adjunct to lifestyle therapy):
    – Tx for 6 months = BMI change -1.38kg/m2 (CI -1.93, -0.82)
    – 3.6% above lifestyle alone.
    – Starting BMI 33kg/m2, amounted to 8lb wt loss/6 months. (McDonagh MS, JAMA Peds, 2014)

• Topiramate
  – Anti-epileptic, FDA approved for adolescents with chronic migraine.
  – One retrospective chart review of 28 adolescents enrolled in pediatric weight management program showed 5% change in BMI at 6 months (Fox CK, Clin Pediatr, 2015).
## Medications for Adult Obesity

<table>
<thead>
<tr>
<th>Medication</th>
<th>Average weight loss</th>
<th>Mechanism of action</th>
<th>Potential side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td>5%</td>
<td>Adrenergic</td>
<td>Tachycardia, HTN</td>
</tr>
<tr>
<td>Phentermine/Topiramate (Qsymia)</td>
<td>10%</td>
<td>Adrenergic, CNS</td>
<td>Tachycardia, HTN, cognitive dysfunction</td>
</tr>
<tr>
<td>Buproprian/Naltrexone (Contrave)</td>
<td>4.5%</td>
<td>CNS, opioid antagonism</td>
<td>Worsening mood symptoms, worsening migraines, HTN</td>
</tr>
<tr>
<td>Lorcaserin (Belviq)</td>
<td>3.5%</td>
<td>Serotonergic (5HT$_{2c}$)</td>
<td>Headache</td>
</tr>
<tr>
<td>Liraglutide (Saxenda)</td>
<td>7%</td>
<td>GLP-1 agonist</td>
<td>Nausea</td>
</tr>
<tr>
<td>Orlistat</td>
<td>3%</td>
<td>Lipase Inhibitor</td>
<td>Steatorrhea, incontinence</td>
</tr>
</tbody>
</table>
Pharmacologic Agents

10 programs offer pharmacologic agents specific for weight control

<table>
<thead>
<tr>
<th>Pharmacologic agent</th>
<th># of Programs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>8</td>
</tr>
<tr>
<td>Orlistat</td>
<td>4</td>
</tr>
<tr>
<td>Topiramate</td>
<td>3</td>
</tr>
<tr>
<td>Phentermine</td>
<td>2</td>
</tr>
<tr>
<td>Bupropion</td>
<td>2</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>1</td>
</tr>
<tr>
<td>Exenatide</td>
<td>1</td>
</tr>
<tr>
<td>Topiramate+Phentermine (Qsymia)</td>
<td>1</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>1</td>
</tr>
<tr>
<td>Sandostatin</td>
<td>1</td>
</tr>
</tbody>
</table>
Weight Loss Surgery in Adolescents

• Obesity is a serious chronic disease
  – Affects the majority of body systems
  – Affects the health and quality of life of millions of children and adolescents
  – Obesity related co-morbid conditions being seen at younger ages.
• This leads to an imperative and acceptance of much more aggressive treatment options for patients at a younger age.
• Performing surgery during adolescence will likely have a much more profound affect on psychosocial trajectory of patient as well as prevention of associated chronic diseases and mortality.
Weight Loss Surgery?

- Adjustable Gastric Band (Lap Band)
  - 15K
  - 7.1%
  - -11.6kg/m²

- Roux-en-Y Gastric Bypass (RNY)
  - 24K
  - 9.3%
  - -16.6kg/m²

- Vertical Sleeve Gastrectomy
  - 19K
  - 4.5%
  - -14.1kg/m²
Bariatric Surgery

14 programs offer Bariatric Surgery for Severely Obese Youth

<table>
<thead>
<tr>
<th>Types</th>
<th># of Programs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric Sleeve</td>
<td>10</td>
</tr>
<tr>
<td>Roux-en-Y Gastric Bypass</td>
<td>6</td>
</tr>
<tr>
<td>Lap-Band System</td>
<td>4</td>
</tr>
</tbody>
</table>
AWLS at Duke History

• March 2010 – team goes to CME at Cincinnati Childrens
• Early 2012 Health System approves surgery for adolescents at Duke
• June 2013 – first surgery done on adolescent
• One patient had surgery per year for first 3 years (2013-2015)
• 3 patients had surgery in 2016
• 5 patients had surgery in 2017.
<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Procedure</th>
<th>Starting BMI</th>
<th>Δ BMI (kg/m2)</th>
<th>% EBW lost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>17</td>
<td>Bypass</td>
<td>62</td>
<td>-36 (30)</td>
<td>86 (3 yr) *</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>16</td>
<td>Bypass</td>
<td>42.6</td>
<td>-15.2</td>
<td>84 (1 yr)</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>19</td>
<td>Sleeve *</td>
<td>43.7</td>
<td>-7.3</td>
<td>39 (8 mo)</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>16</td>
<td>Sleeve</td>
<td>51.8</td>
<td>-12</td>
<td>51 (1 yr)</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>17</td>
<td>Sleeve</td>
<td>36</td>
<td>-10.3</td>
<td>95 (1 yr)</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>16</td>
<td>Sleeve</td>
<td>106</td>
<td>-9.5</td>
<td>16 (1 yr)</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>16</td>
<td>Sleeve</td>
<td>44.2</td>
<td>-4.3</td>
<td>20 (4 mo)</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>19</td>
<td>Sleeve</td>
<td>47.7</td>
<td>-13.3</td>
<td>53 (6 mo)</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>15</td>
<td>Sleeve</td>
<td>56.7</td>
<td>-8.9</td>
<td>28 (3 mo)</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>15</td>
<td>Sleeve</td>
<td>48.2</td>
<td>-6.7</td>
<td>30 (6 mo)</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>15</td>
<td>Sleeve</td>
<td>51.8</td>
<td>-7.9</td>
<td>32 (6 mo)</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>14</td>
<td>Sleeve</td>
<td>60.2</td>
<td>-4.8 (1mo)</td>
<td></td>
</tr>
</tbody>
</table>
AWLS Experience at Duke

- **62** patients have entered surgical track
- **12** patients have gone on to surgery
- **17** patients currently active in track
- **33** patients did not go on to surgery (changed mind, lost to follow up, had surgery elsewhere, one pregnancy, not covered by insurance plan)
Other approaches?
Parting Thoughts

• Redefine outcome measures and study design.

• Pharmaceuticals and medical device companies need to study effects and outcomes in children simultaneously or soon after adults.

• Move towards identifying characteristics of responders and non-responders and personalizing approach to treatment.
Address the Socioeconomics of Obesity

• Social determinants of health
• Health care disparities
• Trauma informed care
Advocacy Local and National

- Built environments
- Food Policy
- Payment for medical and dietary visits related to obesity care
Be a Role Model and Never Give Up!
In the families’ words...

https://vimeo.com/123779196