Managing Metabolic Syndrome and Obesity

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Speaker Disclosure Statement

Dr. Tim Gieseke has no relevant financial relationships with commercial interests to disclose.
Objectives

- Classification of obesity & potential complications
- Metabolic syndrome role in obesity complications.
- Management options:
  - Assessment tools
  - Interventions for health improvement.
  - Partnering with community and web based resources

Culture Change: Obesity

- The new “Normal”
- Average Weight gain ~ 30# over last 40 years
- Plate & portion sizes have increased
- Disproportionately affects women
- Closely linked with 7 of the top leading causes of death
- Mortality similar to lifetime cigarette smoking
- Parents may outlive children
- All of our tissues become “Fatter”
- Toxic “Metabolic Changes” are common
“Toxic” Metabolic Abnormalities

- Insulin resistance
- Adipocyte cytokines
- Atherogenic Lipid changes
- White Adipocytes expansion of gut mesentery and gut obesity, rather then healthy more metabolically active Brown adipocytes.
- BP (multiple mechanisms)
- Sympathetic nervous system activity.
- Endothelial dysfunction (reduced vaso-dilation)
- Pro-inflammatory (> CRP)
- Pro-thrombotic state

Co-morbid Complications

- Type 2 DM
- CAD, HBP, HFpEF (Diastolic CHF), A. Fib
- Obstructive Sleep Apnea, Pulmonary HTN
- CKD, Kidney stones, Incontinence
- Stroke & Dementia
- Pulmonary Embolus & DVT
- Fatty liver, Steatosis, & Cirrhosis
- DJD (Back, Hips, Knees), Deconditioning, Falls, Fractures, & Frailty
Co-Morbid Complications

- Cancers:
  - Esophageal (Barret’s Esophagus), Breast, Ovary, Cervical, Colon, Liver, Bile, Kidney, Thyroid, & Leukemia
- Mental illnesses:
  - Depression, Anxiety Disorders, PTSD, Adjust D.O’s
- Infections
  - Influenza, Post-op skin & soft tissue
- Health Stigma:
  - Education, Employment, Health Care
- > Health Care costs, # Sick days, & 3x > Disabled pensioner.

Obesity & Reduced Hospice Use (AIM Feb 7, 2017)

- Retrospective cohort of 5,677 community dwelling Medicare fee for service beneficiaries who died 1998-2012.
- The greater the BMI
  - < likely to enroll in hospice
  - < duration on hospice
  - < likely to have in-home death
- If morbidly obese, 15% < enrollment, 4.3 days < duration, & 6.3% < in-home death
- Potential Reasons:
  - Dying trajectory less obvious
  - More difficult to open cases and sustain care at home
Some Pathways through Which Excess Adiposity Leads to Major Risk Factors and Common Chronic Diseases.

- > Fast food access
- > Soft drinks
- < Physical activity in our occupations
- > Leisure time filled w/ sedentary activities
  - TV, computers, smart phones, spectators, etc.
- > Food Portions at meals / Snacks / Deserts
- > Medications associated with weight gain
- < Sleep
Glucose >100 or Drug Rx for **Pre-DM or D.M.**

- Low HDL Cholesterol
  - < 40 mg/dl in Men
  - < 50 mg/dl in Women

- High Triglycerides > 150 mg/dl or Drug Rx

- Abdominal obesity (Waist circumference)
  - > 102 cm (40 inches) for men*
  - > 88 cm (35 inches) for women*

- HBP > 130/85 or Drug Rx for HBP

* Asian patients: > 90 cm men, > 80 cm women. European men > 94 cm (37 inches).
• Differ by requirements for:
  – Insulin resistance or fasting hyperinsulinemia in top 25% quartile
  – Presence of co-morbidities commonly associated with insulin resistance & obesity
  – BMI > 30
  – > Waist hip ratio
    • 0.9 for Men
    • 0.85 for Women
Prevalence of NCEP ATP III metabolic syndrome among subjects in the NHANES III survey, by age


Prevalence of NCEP ATP III metabolic syndrome among subjects in the NHANES III survey by race/ethnicity and sex

Classification of overweight and obesity by BMI, waist circumference, and associated disease risk

<table>
<thead>
<tr>
<th>BMI kg/m²</th>
<th>Obesity class</th>
<th>Disease risk relative to normal weight and waist circumference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>≤18.5</td>
<td>↓</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5 to 24.9</td>
<td>↓</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0 to 29.9</td>
<td>Increased</td>
</tr>
<tr>
<td>Obese</td>
<td>30.0 to 34.9</td>
<td>Very high</td>
</tr>
<tr>
<td>Extremely obese</td>
<td>≥40</td>
<td>Extremely high</td>
</tr>
</tbody>
</table>

*BMI of ≥ 30 kg/m² is consistent with overweight/obesity.*

**Increased risk of chronic disease also exists in persons of normal weight.**


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Body mass index and the risk of disease

- **Type 2 diabetes:** Increased risk.
- **Hypertension:** Increased risk.
- **Cholesterol:** Increased risk.
- **Cerebrovascular disease:** Increased risk.

**Increasing body mass index (BMI, kg/m²), even within the normal range of BMI (18.5 to 24.9), is associated with an increased risk of type 2 diabetes, hypertension, coronary disease, and cerebrovascular disease.**

### Clinical and laboratory data for the evaluation of overweight patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Units or Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height, in or cm</td>
<td></td>
</tr>
<tr>
<td>Weight, lb or kg</td>
<td></td>
</tr>
<tr>
<td>Body mass index (BMI), kg/m²</td>
<td></td>
</tr>
<tr>
<td>Waist circumference, in or cm</td>
<td></td>
</tr>
<tr>
<td>Blood pressure: SBP/DBP, mmHg</td>
<td></td>
</tr>
<tr>
<td>Fasting serum triglyceride, mg/dl, or mmol/l</td>
<td></td>
</tr>
<tr>
<td>Serum HDL cholesterol, mg/dl, or mmol/l</td>
<td></td>
</tr>
<tr>
<td>Fasting blood glucose, mg/dl</td>
<td></td>
</tr>
<tr>
<td>(or glycosylated hemoglobin [A1C], %)</td>
<td></td>
</tr>
<tr>
<td>Are there symptoms of sleep apnea?</td>
<td></td>
</tr>
<tr>
<td>Are there medication(s) that increase body weight?</td>
<td></td>
</tr>
<tr>
<td>Is there regular physical activity?</td>
<td></td>
</tr>
<tr>
<td>Are there other lifestyle factors?</td>
<td></td>
</tr>
</tbody>
</table>

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high-density lipoprotein.
Medications associated with weight gain

- Glucocorticoids (prednisone)
- Diabetes medications (insulin, sulfonylureas, thiazolidinediones, metformin)
- First-generation antipsychotics (thioridazine)
- Second-generation antipsychotics (risperidone, olanzapine, clozapine, quetiapine)
- Neurologic and mood stabilizing agents (carbamazepine, gabapentin, lithium, valproate)
- Antihistamines (especially cyproheptadine)
- Antidepressants (paroxetine, citalopram, amitriptyline, nortriptyline, imipramine, mirtazapine)
- Hormonal agents (especially progesterone, eg, medroxyprogesterone)
- Beta-blockers (especially propranolol)
- Alpha-blockers (especially terazosin)

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Categoricalization of anti-depressants, anti-convulsants, and anti-psychotic drugs by their effects on body weight

<table>
<thead>
<tr>
<th>Positive weight loss</th>
<th>Neutral/weight neutral</th>
<th>Positive weight gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td>Sodium valproate</td>
<td>Fluoxetine</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>Fluoxetine</td>
<td>Nortriptyline</td>
</tr>
<tr>
<td>Lisdexamfetamine</td>
<td>Fluoxetine</td>
<td>Lisdexamfetamine</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>Fluoxetine</td>
<td>Amphetamine</td>
</tr>
<tr>
<td>Dextroamphetamine</td>
<td>Fluoxetine</td>
<td>Dextroamphetamine</td>
</tr>
</tbody>
</table>

Basic Therapeutic Interventions

- Portion control is key issue (plate size).
- Emphasize foods less calorically dense that quench hunger
  - Vegetables, Salads, Fruits (Apple slices), Mixed non-salted nuts.
  - Diets: Mediterranean, DASH, “Healthy Diet for All”
  - Commercial Programs: Weight Watchers & Jenny Craig
- Graded exercise program complements diet efforts, but alone are ineffective
- Behavioral therapy & counseling
- Treatment of co-morbidities per guidelines
- Cigarette Cessation (2x > risk mortality if obese)
- Drug Therapy
- Bariatric surgery

### Table 1. Recommended Components of a High-Intensity Comprehensive Lifestyle Intervention to Achieve and Maintain a 5-to-10% Reduction in Body Weight.

<table>
<thead>
<tr>
<th>Component</th>
<th>Weight Loss</th>
<th>Weight-Loss Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counseling</td>
<td>≥14 in-person counseling sessions (individual or group) with a trained interventionist during a 6-mo period; recommendations for similarly structured, comprehensive Web-based interventions, as well as evidence-based commercial programs</td>
<td>Monthly or more frequent in-person or telephone sessions for ≥1 yr with a trained interventionist</td>
</tr>
<tr>
<td>Diet</td>
<td>Low-calorie diet (typically 1200–1500 kcal per day for women and 1500–1800 kcal per day for men), with macronutrient composition based on patient's preferences and health status</td>
<td>Reduced-calorie diet, consistent with reduced body weight, with macronutrient composition based on patient's preferences and health status</td>
</tr>
<tr>
<td>Physical activity</td>
<td>≥150 min per week of aerobic activity (e.g., brisk walking)</td>
<td>200–300 min per week of aerobic activity (e.g., brisk walking)</td>
</tr>
<tr>
<td>Behavioral therapy</td>
<td>Daily monitoring of food intake and physical activity, facilitated by paper diaries or smartphone applications; weekly monitoring of weight; structured curriculum of behavioral change (e.g., DPP), including goal setting, problem solving, and stimulus control; regular feedback and support from a trained interventionist</td>
<td>Occasional or frequent monitoring of food intake and physical activity, as needed; weekly-to-daily monitoring of weight; curriculum of behavioral change, including problem solving, cognitive restructuring, and relapse prevention; regular feedback from a trained interventionist</td>
</tr>
</tbody>
</table>

Data are from the Guidelines (2013) for the Management of Overweight and Obesity in Adults, reported by Jensen et al. The guidelines concluded that a variety of dietary approaches that differ widely in macronutrient composition, including ad libitum approaches (in which a lower calorie intake is achieved by restriction or elimination of particular food groups or by the provision of prescribed foods), can lead to weight loss provided they induce an adequate energy deficit. The guidelines recommended that practitioners, in selecting a weight-loss diet, consider its potential contribution to the management of obesity-related coexisting disorders (e.g., type 2 diabetes and hypertension). The guidelines did not address the possible benefits of strength training, in addition to aerobic activity. DPP denotes Diabetes Prevention Program.
Medications Approved by the Food and Drug Administration for Long-Term Weight Management.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Main Mechanisms of Action</th>
<th>Dose</th>
<th>Study Duration</th>
<th>Mean Weight Loss</th>
<th>Common Side Effects</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat11</td>
<td>Pancreatic and gastric lipase inhibitors, resulting in fat malabsorption</td>
<td>120 mg before meals (three times a day)</td>
<td>52</td>
<td>Drug: 3.8 (8.2); placebo: 3.8 (3.4); P=0.0.6</td>
<td>GI upset, cramps, increased flatulence, fecal incontinence</td>
<td>Pregnancy, chronic malabsorption syndrome, cholelithiasis</td>
</tr>
<tr>
<td>Lorcaserin12</td>
<td>Selective 5-HT4 receptor agonist</td>
<td>10 mg twice a day</td>
<td>52</td>
<td>Drug: 3.8 (5.4); placebo: 2.3 (2.2); P=0.32</td>
<td>In patients without diabetes, headache, dizziness, fatigue, nausea, stomachache, dry mouth, constipation, diarrhea, back pain, leg cramps</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>Liraglutide8</td>
<td>GLP-1 receptor agonist</td>
<td>Starting dose: 0.6 mg given subcutaneously; then increased weekly to 0.9 mg at t(0)</td>
<td>56</td>
<td>Drug: 4.4 (38); placebo: 2.8 (2.8); P=0.33</td>
<td>Nausea, vomiting, constipation, hyperglycemia, diarrhea, headache, fatigue, diarrhea, dry mouth, increased appetite, increased pain, increased systolic blood pressure</td>
<td>Pregnancy, preexisting or family history of medullary thyroid cancer or multiple endocrine neoplasia type 2c</td>
</tr>
<tr>
<td>Phentermine-topiramate9</td>
<td>Phentermine atarctic (phentermine, topiramate)</td>
<td>Starting dose: 3.75 mg t(0); 7.5 mg q(0)</td>
<td>56</td>
<td>Drug: 0.8 (2.6); placebo: 0.5 (2.2); P=0.31</td>
<td>Insomnia, dry mouth, constipation, paraesthesia, dizziness, angioedema</td>
<td>Pregnancy, hypertension, pheochromocytoma, hyperthyroidism, hyperparathyroidism, hypothyroidism, psychosis</td>
</tr>
<tr>
<td>Naltrexone-loxapine10</td>
<td>Opioid antagonist (naltrexone), dopamine and norepinephrine reuptake inhibitor (loxapine)</td>
<td>Starting dose: 8 mg followed by 8 mg at 12- and 24-hour intervals</td>
<td>56</td>
<td>Drug: 4.4 (4.4); placebo: 1.1 (2.2); P=0.01</td>
<td>Nausea, constipation, headache, vomiting, diarrhea, insomnia, dry mouth, dizziness</td>
<td>Uncontrolled hypertension, severe diarrhea, anemia, increased risk of infection, drug dependency, allergic reactions, decreases in platelet count, increases in blood pressure, weight loss, weight loss greater than 20% of body weight in weight loss studies, weight loss greater than 10% of body weight in weight loss studies</td>
</tr>
</tbody>
</table>

* For each medication, weight loss data are from a period phase 3 trial submitted to the FDA for drug approval.11-10 CNS indicates central nervous system, CAM gamma-amino butyric acid, GLP-1 glucagon-like peptide 1, SHT serotonin, 5-hydroxytryptamine 2C and NADH monooxygenase inhibitors, 8 Data on placebo-subtracted weight loss (P=0.01) are from a meta-analysis of studies.11
Weight Loss at 1 Year with High-Intensity Lifestyle Interventions or Pharmacotherapy Combined with Low-to-Moderate-Intensity Lifestyle Counseling.

- Look AHEAD
- DEEP
- Teixeira, et al.
- Metformin
- Orlistat
- Lorcaserin
- Liraglutide
- Phentermine-topiramate
- Naltrexone-bupropion

Surgical Interventions for Obesity

- Laparoscopic Adjustable Gastric Banding (LAGB)
  - Least invasive, safest, & reversible
  - High re-op rate and reduced long term efficacy so seldom done now (< 6% of obesity procedures in 2013)
- Roux-en-Y
  - Creates upper gastric pouch connected to Jejunum with 95% of food bypassing stomach and duodenum
  - ~ 25% wt. loss at 1 year
- Vertical-sleeve Gastrectomy
  - Removes 70% of stomach w/acceleration of gastric emptying
  - ~ 30% wt. loss at 1 year
Benefits & Risks of Surgery

- Remission rates for Diabetes at 3 years
  - 5% for intensive medical therapy (IMT)
  - 24% for IMT combined with vertical-sleeve gastrectomy
  - 38% for IMT combined with Roux-en-Y gastric bypass
- Mortality: 0.1, 0.2, & 0.3% for Lap Band, Vertical-sleeve, and Roux-en-Y
- Serious Periop ADEs: 1, 5, & 5% respectively
- Long term efficacy likely for: Vertical-Sleeve and Roux-en-Y.
- NEJM Feb 2017, @ 5 years, gastric bypass vs. IMT for DM w/BMI (27-43) had much > improvement in DM, lipid, Wt., and QOL measures.

Team Approach (KJ Page, T Clark Presentation & Case Studies)

- Engage your Team:
  - Physicians, Nurses, CNAs
  - Admissions Coordinator
  - Dietary
  - Facilities engineer
  - MDS Coordinator – Effective Care Conferences
  - Clinical Psychologist
  - Activities / Community Developer
  - Rehabilitation Team
- Partner with centers of expertise
  - Center for Well Being
  - Hospital Bariatric Programs
  - Community Weight Loss Programs
  - Internet Behavioral Health programs targeted for overweight persons
  - Healthy Eating Active Living Community Health Initiative in Sonoma County (HEAL)
Obesity & Metabolic Syndrome are common, but wellness is possible.

5-10% weight loss is possible with intensive medical therapy (IMT) programs.
- < risk for diabetes, HBP, CVD & other complications of obesity.

Long term drugs are an option for high risk patients & promote > weight loss than IMT alone.

Surgery should be consider for those who remain seriously obese
- BMI > 40 or
- > 35 with complications (DM, HBP, CAD)

Treat complications per guidelines.

Cigarette cessation (double risk of dying)

Clinical evaluation and assessment tools for care planning
- Identify weight promoting meds

Provide behavioral health and counseling.

Partner with local centers of expertise.