Weight Management as Women Age

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Statistics

• 2008: Medical costs linked to obesity were estimated to be $147 billion.
• 2012: Estimated cost of diagnosed diabetes was $245 billion, including $176 billion in direct medical costs and $69 billion in decreased productivity.
• In the United States, nearly two-thirds of women aged 40 to 59 years and about three-fourths of women 60 years and older are overweight (BMI > 25 kg/m²). Furthermore, almost half of the women in these age groups are obese (BMI ≥ 30 kg/m²).

Objectives

1. Describe the epidemiology and contributing factors to weight gain as women age.
2. Determine factors relating to consequences of obesity.
3. Relate the principles for dietary and pharmacologic management and practical tips for the advanced nurse practitioner.

Objective #1: Describe the epidemiology and contributing factors to weight gain as women age.

Slowing metabolism and contributing factors

- Hormonal changes
- Decreased activity
- Medications
- Chronic disease
- Physiological responses to stress

Hormonal Changes

- Obesity is more prevalent in women
  - Estrogen:
    - Has a relationship with adipose tissue (AT)
    - Increases gluteofemoral subcutaneous (SC) AT mass;
    - Decreases central AT mass in women of reproductive age
    - This has a protective cardiometabolic effect
    - After menopause (loss of estrogen):
      - Increases total AT mass and decreases lean body mass
      - Little net effect on body weight but partially reverses protective AT distribution (think “belly fat”)
Hormonal Changes

- **Estrogen (cont.):**
  - Higher levels in follicular and peri-ovulatory phases decrease eating
  - Possibly has an impact on the satiating potency of the gastrointestinal hormone cholecystokinin in the pre-ovulatory phase

- **Progestins:**
  - Higher levels in luteal phase associated with eating but no causal relationship established
  - May increase binge eating and eating stimulated by negative emotional states during the luteal phase

- **Progestins (cont.):**
  - Progestin-only contraception may slightly increase body weight and adiposity, but little evidence to support

- **Other hormones:**
  - Genetic defects in brain α-melanocyte-stimulating hormone-melanocortin receptor (melanocortin 4 receptor, MC4R) signaling lead to a syndrome of overeating and obesity in women and female animals
  - Syndrome appears around puberty in mice with genetic deletions of MC4R, suggesting a role of ovarian hormones

Decreased Activity

- Aging → Decreased lean body mass → Decreased resting metabolic rate
- Half of women aged 50 to 64 years old report regular physical activity
- If caloric intake isn’t reduced or physical activity increased, weight gain occurs
- High physical activity associated with lower risk of metabolic syndrome

Medications

- **Insulin:**
  - Despite weight gain side effect, providers encouraged to use for glycemic control.

- **Contraception:**
  - Mean weight gain at 6 and 12 months was less than 4.4 lbs.

- **Anti-psychotics (i.e. clozapine, risperidone, etc.):**
  - Weight gain is a common side effect due to blocking of serotonin receptors → increased appetite
  - Consider metformin if initiating 2nd generation anti-psychotic agents (i.e. olanzapine or clozapine)

Chronic Disease

- Menopausal transition → increase in and redistribution of adipose tissues → decreased energy expenditure
- Impairment in insulin secretion/sensitivity → DMII
- "Fit but fat?": active/obese women with risk factors for coronary heart disease (CHD) and cardiovascular disease (CVD) did not have increased rates of CHD or MI, and had decreased risk for stroke.
- Active/obese women are at increased risk for asthma, arthritis, and depression.

Physiological Responses to Stress

- Age, body fat percentage, waist/hip ratio, and leptinemia positively association with anxiety & depression
- Overweight postmenopausal women more likely to have insulin sensitivity and mental health issues compared to overweight premenopausal women.
- A woman with abdominal obesity and leptin resistance is more likely to have mental health issues.
- Stress & glucocorticoids → increased consumption of fat & sugar
Lifestyle Factors
- Decreased activity
- Caloric intake
- Eating habits
- Stress
- Sleep habits

Caloric Intake
- Does the type of diet matter?
- Lower calorie intake → weight loss
- Calorie deficit of 500 to 750 kcal daily for women (total daily caloric intake of 1200 – 1500 kcal/day) → average weight loss of 0.5 to 0.75 kg/week

Eating Habits & Stress
- Obese women have higher cortisol levels than normal weight women.
- Obese women had sustained evening cortisol elevation → sleep disruption risk
- Hypothalamic-pituitary-adrenal (HPA) axis needs to be considered

Sleep Habits
- Vasomotor symptoms of menopause → sleep disruption
- Mood disorders
- Obstruction sleep apnea
- Sleep deprivation → daytime fatigue and decreased physical activity
- Women with less than 5 hours of sleep daily gained more weight than those with 7+ hours of sleep

External Factors
- **Food Quality:**
  - Genetically modified organisms (GMOs)
  - Processed foods
- **Food Convenience:**
  - So long to the hunters/gatherers
  - Food access is abundant

**Objective #2:**
Determine factors relating to consequences of obesity.
Chronic Disease
- Metabolic syndrome
- DMII
- Hyperlipidemia
- PCOS
- Musculoskeletal discomfort
- Cancer
- Sleep apnea
- Other

Metabolic Syndrome
• Definition (need 3/5 of the following):
  • A large waistline
  • A high triglyceride level
  • A low HDL cholesterol level
  • High blood pressure
  • High fasting blood sugar
• Central obesity after menopause associated with dysglycemia, dyslipidemia, hypertension, and cardiovascular disease
• Cardiovascular disease is the leading cause of death in postmenopausal women

Diabetes Mellitus (Type II) (T2DM)
• Frequency and prevalence of diabetes has increased in the US adult population from 21.2 million (10.3%) in 2003-2004 to 30.2 million (13.2%) in 2013-2014.
• Abdominal obesity needs to be evaluated.
• BMI is not always a risk factor.
• T2DM risk increases if waist circumference is not modified despite improved BMI.

Hyperlipidemia
• In women, abdominal obesity is a major driver of hepatic large VLDL particle secretion.
• Postmenopausal status was characterized by increased small VLDL particle size.

Polycystic Ovarian Syndrome (PCOS)
• Both obese and lean women with PCOS have some degree of insulin resistance.
• All women with PCOS require evaluation for the risk of metabolic syndrome (MetS) and its components, T2DM, hypertension, hyperlipidemia, and the possible risk of clinical events, including acute myocardial infarction and stroke.
• Obese women with PCOS are at increased risk for MetS with impaired glucose tolerance and T2DM.

PCOS (cont.)
• Weight loss is the primary therapy in PCOS.
• Reduction in weight of as little as 5% can restore regular menses and improve response to ovulation-inducing and fertility medications.
• Metformin in premenopausal PCOS women has been associated with a reduction in features of MetS.
Musculoskeletal Discomfort

- Increased strain on joints → decreased physical activity
- Rheumatoid Arthritis (RA): obesity decreases odds of achieving remission and negatively impacts disease activity.

Cancer

- Obesity increases risk of certain cancers including breast and uterine.
- Risk of death from all cancers combined was 62% higher in women with a BMI > 40 compared with normal weight women.
- Women with MetS had 2-fold increase in endometrial CA if waist circumference included in the definition of MetS.
- Women with hyperglycemia, HTN, and dyslipidemia combined had nearly 2-fold increase of risk of endometrial cancer.

Cancer (cont.)

- Women who were overweight and obese had an increased invasive breast cancer risk vs. women of normal weight.
- BMI > 35.0 strongly associated with risk for estrogen receptor-positive and progesterone receptor-positive breast cancers but NOT estrogen receptor-negative cancers.
- Larger tumors, advanced disease, positive lymph nodes, regional and/or distant stage, and deaths after breast cancer also associated with obesity.

Sleep Apnea

- As many as 70% of obstructive sleep apnea (OSA) patients are obese.
- Some studies show that OSA may reinforce obesity.
- Basal metabolic rate (BMR) significantly decreased after CPAP.
- Weight gain can occur after CPAP therapy (mechanism unclear).
- Higher leptin levels, lower ghrelin levels, and higher eating behaviors associated with weight gain.
- Risk factors for increased BMI after CPAP: younger age, female, lower baseline BMI, non-smoker, decrease in plasma cortisol, and increased caloric intake.

Other

- Vasomotor symptoms of menopause often worse in obese women
- Obesity can cause fertility issues, spontaneous pregnancy loss in early gestation, and congenital anomalies.
- Increased risk of cesarean delivery
- Difficulty breastfeeding
- Wound complications
- Venous thromboembolism

Objective #3:
Relate the principles for dietary and pharmacologic management and practical tips for the advanced nurse practitioner.
Dietary Management

• Whole foods
• Food Pyramid evaluation: Is it best for preventing obesity?
• Low-carbohydrate diet
• The influence of sugar
• Nutritional supplementation

Whole Foods

• Positive correlation between amount of processed foods in households and obesity prevalence.
• Consumption of processed foods is associated with increased risk of diet-related non-communicable diseases.
• Plant-based diets decreased diabetes risk.

Government Guidelines

• Still incorporates processed foods
• Recommends limits on “added” sugar
• Grains and dairy becoming more controversial
• Exercise recommended

Government Guidelines: Recommendations vs. Reality

Average Whole and Refined Grain Intakes in Ounce-Equivalents per Day by Age-Sex Groups, Compared to Ranges of Recommended Daily Intake for Whole Grains and Limits for Refined Grains

Low Carb vs. Low Fat Diet

• Low-fat diets can improve low-density lipoprotein cholesterol levels (LDL)
• Low-carbohydrate diets can improve triglycerides and high-density lipoprotein (HDL) cholesterol levels.
• Differences are small based on research.
• Calorie-restriction remains the key to preventing obesity.
• Mediterranean Diet: moderate fat intake, plant-based foods, whole grains, nuts, and legumes → weight loss and decreased cardiovascular risk.
The Influence of Sugar

Average Intakes of Added Sugars as a Percent of Calories per Day by Age-Sex Group, in Comparison to the Dietary Guidelines Maximum Limit of Less Than 10 Percent of Calories

Nutritional Supplementation

• Green Tea Extract
• Inositol
• B-vitamin injections
• Vitamin D
• Probiotics
• Chromium
• Caffeine
• Ephedrine

Lifestyle Management

• Physical Activity
  -Health.gov: 150 minutes (2 hours and 30 minutes) to 300 minutes (5 hours) a week of moderate-intensity, or 75 minutes (1 hour and 15 minutes) to 150 minutes (2 hours and 30 minutes) a week of vigorous-intensity aerobic physical activity.
  -Adults should also do muscle-strengthening activities of moderate or greater intensity and that involve all major muscle groups on 2 or more days a week.
  -American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Obesity Society recommend 150 to 175 minutes of physical activity (brisk walking or similar aerobic exercise) per week for weight loss.

Sleep (CDC Recommendations)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Recommended Hours of Sleep Per Day</th>
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<tbody>
<tr>
<td>Newborn</td>
<td>14–17 hours (National Sleep Foundation)</td>
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<tr>
<td>Infants</td>
<td>12–16 hours per 24 hours (including naps)</td>
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<tr>
<td>Toddler</td>
<td>11–14 hours per 24 hours</td>
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<tr>
<td>Preschool</td>
<td>10–13 hours per 24 hours</td>
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<tr>
<td>School Age</td>
<td>9–12 hours per 24 hours</td>
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<tr>
<td>Teen</td>
<td>8–10 hours per 24 hours</td>
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<tr>
<td>Adult</td>
<td>7 or more hours per night</td>
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Sleep

• Insufficient amount of sleep associated with obesity.
• Weight gain can occur due to decreased dietary restraint.
• Fat and carbohydrate cravings increase with sleep deprivation.
• Ghrelin elevation and leptin reduction.

Pharmacological Management

• Drugs used in obesity management:
  -phentermine
  -naltrexone/bupropion hydrochloride
  -orlistat
  -metformin
  -phentermines
  -diethylpropion
  -lorcaserin
  -liraglutide
How the Drugs (Current and Under Development) Work

• Act peripherally to impair dietary fat absorption
• Act centrally to decrease food intake
• Facilitate energy expenditure

Other Pharmacologic Considerations

• Thyroid medication
• Hormone replacement
• Off-label uses of certain medications

Approved Anti-Obesity Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of Action</th>
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<tr>
<td>Phentermine</td>
<td>Non-selective stimulator of synaptic noradrenaline, dopamine, and serotonin release. Appetite suppressant. Approved by FDA in 1959 for short-term (&lt; 12 weeks) weight management along with caloric restriction and lifestyle modification. Most commonly prescribed weight loss drug in US. Studies show significant weight reduction and lowering of total and low-density lipoprotein cholesterol levels. Most common side effects: dry mouth and insomnia. Serious side effects: tachycardia, palpitations, and hypertension.</td>
</tr>
<tr>
<td>Orlistat</td>
<td>Gastrointestinal lipase inhibitor approved by FDA in 1999. By inactivating lipase, less dietary fat is absorbed. In studies, weight loss occurred with in subjects using this drug along with with caloric restriction. Orlistat also improved blood pressure, insulin resistance, and serum lipid levels. Common side effects: diarrhea, bloating, flatulence, abdominal pain. Risk of acute kidney injury in those with metabolic conditions (i.e. diabetes) due to oxalate deposition.</td>
</tr>
<tr>
<td>Phentermine and Topiramate</td>
<td>Phentermine: NE transporter inhibitor; Appetite suppression mediated by activation of POMC neurons in the arcuate nucleus. Topiramate: GABA agonist; Appetite suppression may be due to modulation of voltage-gated ion channels, increased activity at GABA-A receptors and/or inhibition of AMPA/kainite glutamate receptors.</td>
</tr>
<tr>
<td>Naltrexone and Bupropion</td>
<td>Naltrexone: Opioid receptor antagonist; Prevents β-endorphin-mediated negative feedback on α-MSH release. Bupropion: DA and NE transporter inhibitor; Stimulates hypothalamic POMC neurons that release α-MSH resulting in decreased food intake and increased energy expenditure.</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>Selective 5-HT2C agonist; Promotes satiety.</td>
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<tr>
<td>Liraglutide</td>
<td>GLP-1 agonist; Decreases appetite.</td>
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Challenges of Anti-Obesity Medications

-The majority of drugs launched for the treatment of obesity over the last two decades have been withdrawn due to safety issues associated with increased risk of cardiovascular and psychiatric complications.
**Lorcaserin**
- Approved by FDA in 2012
- Selective 5-HT<sub>2C</sub> agonist
- Causes feelings of satiety
- Approved for subjects with BMI > 30 with at least one weight-related co-morbidity
- Common side effects: headaches, dizziness, fatigue, nausea, dry mouth, constipation, back pain, cough, and fatigue
- Serious side effect: serotonin syndrome

**Phentermine/topiramate**
- Topiramate is an anticonvulsant.
- Anecdotal reports of weight loss in epileptic patients (mechanism of action unclear)
- Not used as a monotherapy due to neuropsychiatric and cognitive side effects (i.e. memory impairment, language difficulties, and mood changes)
- Assess for depression and suicidal ideation
- Common side effects: paresthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth

**Naltrexone/bupropion**
- Naltrexone: non-selective opioid receptor antagonist used to treat opioid and alcohol dependence.
- Bupropion: inhibits dopamine and norepinephrine transporters; used to treat depression and nicotine addiction.
- Combo approved for adults with BMI > 30 or BMI > 27 with obesity-related co-morbidities
- Compared to placebo, improvements in cardiometabolic risk markers, weight-related quality of life, and control of eating in subjects on this medication.
- Common side-effects: nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, and diarrhea.
- Black Box Warning: increased risk of suicidal behavior and ideation

**Liraglutide**
- Long-acting GLP-1 analog approved for treatment of DM2
- Approved by FDA in 2014 for chronic weight management in obese and overweight adults with at least one weight-related co-morbidity.
- Subjects treated with Liraglutide showed greater weight loss than placebo along with reduced cardiometabolic risk factors, and lower blood sugar.
- Common side effects: nausea, hypoglycemia, diarrhea, constipation, vomiting, headache, decreased appetite, dyspepsia, fatigue, dizziness, abdominal pain, and increased lipase activity.
- Serious side effects: acute pancreatitis, chest pain, and bronchitis.
- Do not use in patients with thyroid tumors.

**Metformin**
- Can help lower BMI in women with PCOS along with lifestyle modification.
- Can also improve menstruation in this population.
- More studies needed for this drug as it relates to weight loss.

**Thyroid Medication**
- Not indicated as a weight loss drug but appropriate assessment of the thyroid needs to occur in the obese population.
- Optimization of thyroid function can lead to successful weight loss.
- T4, T3, and T4/T3 combos
Hormone Replacement Therapy (HRT)

- Not indicated for weight management.
- Women often report favorable body composition while on HRT.
- HRT can promote lean body mass, insulin resistance, lipid levels, and decrease central adiposity.

Other Strategies

- Behavioral Therapy: geared toward identifying barriers to change, problem solving, strategizing, and reinforcement.
  - Group or individual
  - Manage psychological issues to promote greater success with weight loss.

Tips for the Advanced Practice Nurse

- Complete assessment including personal/lifestyle contributors
- Knowledge assessment
- Food diary counseling and review
- Medication review
- Know when to refer
- Support

Case Studies

- Blaming the political climate (yes, it has happens...A LOT!)
- "I eat well."
- "It must be my thyroid.

Questions?