Update on Pharmacologic Strategies in the Management of Overweight and Obesity

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Objectives

• Review overweight, obesity, diagnosis & new guidelines (2013)
• Discuss contemporary management of obesity
• Provide an overview of currently available FDA approved short & long medications for obesity treatment
  – Focus on safety & efficacy
  – Off label medications will not be presented
Which of the following statements are true about obesity in the United States of America?

a. About 1 in 3 American adults are obese
b. Mexico and Great Britain are the only countries in the world with a higher percentage of obesity than the USA.
c. By 2015, about 75% of adult Americans will be overweight or obese
d. About 5% of American kids are overweight
e. a & c are correct
Obesity Epidemic

USA: 31%
Mexico: 24%
UK: 23%
Slovak Republic: 22%
Greece: 22%
Australia: 22%
New Zealand: 21%
Hungary: 19%
Czech Republic: 15%

Canada: 14%
Spain: 13%
Ireland: 13%
Germany: 13%
Portugal: 13%
Finland: 13%
Turkey: 12%
Belgium: 12%
Poland: 11%

Netherlands: 10%
Sweden: 10%
Denmark: 10%
France: 9%
Austria: 9%
Italy: 9%
Norway: 8%
Japan: 3%
Korea: 3%
• 66% of US adults are obese or overweight
  – 34% obese
  – 6% morbidly obese (6 X the rate since 1960s)

• 16% of children & adolescents are overweight/obese
  – 34% are at risk

• By 2015 75% of adults will be overweight or obese
  – 41% obese

www.cdc.gov
Obesity: A Chronic Disease in 2013

What is a disease?

– Disordered or incorrectly functioning organ, structure or system

– Result of genetic or developmental errors, infections, poisons, nutritional deficiency or imbalance, toxicity, unfavorable environment

– Manifests as illness, sickness or ailments

www.sante.public.lu
Question 2

Which of the following diseases are associated with obesity?

a. Hypertension
b. Dyslipidemia
c. Diabetes Mellitus type 2
d. Sleep Apnea
e. Polycystic ovary syndrome
f. All the above
Keep these in mind when conducting H&P

Medical Complications of Obesity

- Pulmonary disease
  - abnormal function
  - obstructive sleep apnea
  - hypoventilation syndrome
- Idiopathic intracranial hypertension
- Stroke
- Cataracts
- Coronary heart disease
- Diabetes
- Dyslipidemia
- Hypertension
- Severe pancreatitis
- Cancer
  - breast, uterus, cervix
  - colon, esophagus, pancreas
  - kidney, prostate
- Gynecologic abnormalities
  - abnormal menses
  - infertility
  - polycystic ovarian syndrome
- Osteoarthritis
- Skin
- Gout
- Phlebitis
  - venous stasis
- Nonalcoholic fatty liver disease
  - steatosis
  - steatohepatitis
  - cirrhosis
- Gall bladder disease

http://sites.psu.edu
Costs of Obesity
Trust for America’s Health and RWJ & CDC

Obesity in America 2010: 36%
Obesity in America 2030: 50%

Projected Obesity-Related Health Care Costs 2010 to 2030

Obesity Trends in the US: 1985 - 2010

1985, 2000, 2010

No Data, <10%, 10%–14%, 15%–19%, 20%–24%, 25%–29%, ≥30%

- Total Predicted Costs
- Total Predicted Costs with 1% BMI reduction
- Total Predicted Costs with 5% BMI reduction

2014 PCNA 20TH ANNUAL SYMPOSIUM | APRIL 10-12 | MARRIOTT ATLANTA
Anti-Obesity Drugs and Their Complex Pathways

“Differences in brain chemistry can affect the likelihood of weight gain”
– K. Streeter of NPR

www.npr.org
Approach to Obesity Management

**Historical Perspective**
- Lifestyle choice
- Character flaw
- Psychological disorder
- Medication fix

**Current Perspective**
- Complex disease
- Modern environmental changes
- Huge burden of associated illnesses
  - Cause of 60+ conditions
  - 12 types of cancer
- Negative impact on QoL
- Modest weight loss is significant
- Guidelines 2013
2013 AHA/ACC/TOS
Guideline for the Management of Overweight and Obesity in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society

_Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American Pharmacists Association, American Society for Nutrition, American Society for Preventive Cardiology, American Society of Hypertension, Association of Black Cardiologists, National Lipid Association, Preventive Cardiovascular Nurses Association, The Endocrine Society, and WomenHeart: The National Coalition for Women with Heart Disease_
What Guidelines Mean to You

The new cardiovascular prevention guidelines were written based on years of scientific research to develop the best approaches to preventing heart disease and stroke—the leading causes of death in the world. Here’s what you need to know about the guidelines, released Nov. 12 by the American Heart Association and American College of Cardiology:

IT ALL STARTS WITH AN ASSESSMENT OF YOUR RISKS PERFORMED BY YOUR HEALTHCARE PROVIDER

DISCUSSIONS WITH YOUR HEALTHCARE PROVIDER WILL HELP YOU UNDERSTAND YOUR RISKS AND OVERALL HEALTH

THOSE DISCUSSIONS DRIVE PERSONALIZED TREATMENT FOR EACH PATIENT.

The guidelines help healthcare providers provide the best treatment focused on four important areas:

**ASSESSMENT OF RISK**
(for heart disease, stroke and other cardiovascular diseases)

1. Calculators used to assess your personal risk set stage for discussions with healthcare provider
2. Risks for African-Americans specified for the first time
3. Stroke risks included for the first time

**OBESITY**

1. Team-based treatment
2. Weight-loss strategies based on body mass index
3. Diet, exercise still best bets

**CHOLESTEROL**

1. Overall health status and risks guide treatment
2. “Bad cholesterol number” no longer main factor guiding treatment
3. Decisions for drug treatment based on discussions with healthcare provider

**LIFESTYLE**

1. 40 minutes of exercise 3–4 days a week
2. Eat lots of fruit, veggies
3. Most Americans should reduce sodium intake

For more information, please visit Heart.org
Weight Classification

Overweight and Obesity Is Currently Defined Based Upon BMI

Overweight and obesity classifications
(BMI, kg/m²)

- Normal weight (18.5-24.9)
- Overweight (25.0-29.9)
- Class I obesity (30.0-34.9)
- Class II obesity (35.0-39.9)
- Class III obesity (≥ 40)

NHLBI website.[1]
BMI in Adults

**Advantages**

- Correlates with metabolic disease and fat mass
- Can be tracked over time
- Defines extent of overweight / obesity
- Easy to do
- Inexpensive

**Disadvantages**

- Does not acknowledge the role of fat cells / tissues, inflammation, from endocrine standpoint
- Does not consider muscle mass or breast tissue
- May not always correlate with metabolic disease
Prior to prescribing a comprehensive weight loss regimen including pharmacotherapy, the clinician should:

a. Perform and complete history and physical exam including assessing anthropometrics

b. Screen to rule out organic causes of overweight/obesity and make appropriate referrals for further work up

c. Assess comorbid conditions and determine weight loss contraindications (eg., pregnancy, eating disorders)

d. All of the above
Clinical Presentation

Take time to listen.....sensitive topic for many

• cc “Unable to lose weight, diets do not work, clothes are too tight”

• Less obvious complaints
  – exercise intolerance & fatigue, shortness of breath, rashes, insomnia, sexual dysfunction, pain (joint, abdominal)

• Comorbidities associated with obesity are common
  – easy to miss symptom association to obesity

Meires & Christie (2011) NP
Obesity Diagnosis & Plan

• Complete history, ROS and physical exam
  – Assessment of body type
  – Height, Weight, BMI, frame size
  – Waist circumference or waist-to-hip ratio
• Consider RFs, labs & differential diagnoses for obesity
• Explain diagnosis and treatment
• Consider indications, contraindications, interactions prior to adding a weight loss medication

Meires & Christie (2011) NP
Question 4

Goals of the weight loss protocol for adults includes:

a. Individualizing recommendations for lifestyle changes including nutrition, exercise, stress control and sleep prescriptions

b. Recommending a 500 calorie deficit below calculated need to result in 1 lb. of weight loss per week

c. Planning for the overall loss to achieve an ideal body weight

d. Prescribing pharmacotherapy for weight loss for up to 2 years

e. a & b

f. c & d

Jensen et al. 2013
Guideline Recommendations 2013

• Comprehensive Lifestyle Intervention
  Alone or with Adjunctive Therapies
  – Adding pharmacotherapy to comprehensive lifestyle intervention

• Weight Loss Maintenance

Jensen, et al. 2013
Lifestyle Intervention

- Screen for height / weight, BMI, determine category
- All weight loss patients should be offered education related to comprehensive lifestyle intervention
  - trained interventionist or nutrition professional (RD)
  - regardless of augmentation by medications or bariatric surgery
BMI, determine category

• **Pharmacotherapy**
  
  – history reveals unable to lose weight / sustain weight loss
  
  – previously participated in a comprehensive lifestyle intervention
  
  – at the time of initiation of lifestyle intervention if BMI ≥30 or
    ≥27 with comorbidity

• **Bariatric Surgery**
  
  – BMI ≥40 or BMI ≥35 with comorbidity

Jensen, et al. 2013
Guideline

Pharmacotherapy to Lifestyle Intervention

• Panel did not review evidence for pharmacotherapy for weight loss

• Medications should be FDA-approved

  – Clinicians should be knowledgeable about the product label

  – Clinicians should weigh the potential risks of the medication against the potential benefits of successful weight loss for the individual patient

Jensen, et al. 2013
Pharmacotherapy with Lifestyle Intervention

• Assess medication regimen
  – identify medications that may contribute to weight gain
    • propranolol, contraceptives, hormones, NSAIDS, anti-inflammatory drugs,
      corticosteroids, antidepressants, lithium, antipsychotics, antihistamines, MM,
      others
  – adjust medications if appropriate

• Obesity medication prescription
  – should lose at least 5% of initial body weight after 12 weeks on a maximal dose of the medication
  – reassess the risk-to-benefit ratio of that medication
  – DC drug side effects warrant, adverse effects, weight loss not sufficient, other reasons
A Collaborative Primary Care Team Approach to Manage Adult Obesity

PCP=MD, DO, NP, PA, PT

Assess Anthropometrics – RD/RN/PT
- Waist to hip ratio
- Waist circumference
- Height & Weight
- Calculate BMI
- Frame Size

Screen to Rule Out Organic Causes Make Appropriate Referrals – PCP
- Pituitary Dysfunction
- Thyroid disease
- Polycystic Ovary Disease
- Hypothyroidism Disorders
- Genetic Disorders

Assess Comorbid Conditions – PCP
- Hypertension
- Dyslipidemia
- CVD
- Diabetic
- Sleep Apnea
- GERD
- Osteoarthritis
- Depression
- Cancer
- Others
- Depression

Assess Health Risk-RN/PCP
- BMI
  - <25: Minimal
  - 25-47: Low
  - 27-50: Moderate
  - 50-54: High
  - 55-60: Very High
  - > 60: Extremely High
- Risk Adjusted Comorbidities (if one or more applies)
  - Low
  - Moderate
  - High
  - Very High
  - Extremely High

R/O Weight Loss Contraindications – PCP
- Pregnancy/Lactation
- Medical/Mental Conditions such as Eating disorders, psychosis, biplot disorder, severe depression

Assess Readiness for Weight Loss – RD/RN/PCP
- Is client ready?

Discuss Treatment Options – PCP

Implement Weight Loss Protocol – Goal is to Lose 5-10% Body Weight
- Individualized Lifestyle Changes including sleep recommendations
- 500 calorie deficit below calculated need to result in one pound weight loss/week
- Personalized Meal Plan – RD
- Self-Management Training – RD/PCP
- Exercise prescription – PCP
- Reinforce Physical Activity – RD/PCP

Implement Weight Maintenance Protocol
- Personalized Meal Plan – RD
- Self-Management Training – all clinicians
- Exercise prescription – PCP

Goal Weight Achieved?
- Yes
- Discuss Possible Adjunctive Therapy – PCP

Discuss Prevention of Further Weight Gain, Reevaluate Readiness at Next Visit

Adapted from: Medical Nutrition Therapy Across the Continuum of Care: Supplement 1. ©1997 The American Dietetic Association
Current FDA approved medications for treatment of adult obesity include all of the following except:

a. Sibutramine
b. Phentermine
c. Orlistat
d. Lorcaserin
e. Phentermine & Topiramate ER
<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Classification</th>
<th>Therapy Duration</th>
<th>Dose</th>
<th>Schedule</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine HCL</td>
<td>Fastin,</td>
<td>Sympathomimetic</td>
<td>Short term monotherapy; 3 months or less with concurrent diet and exercise</td>
<td>37.5 mg daily before or 1-2 hours after breakfast; or 18.75 mg 1-2 times daily May use a few times a week instead of daily dosing.</td>
<td>CIV</td>
<td>Limit use. Use lowest dose possible for shortest time. BMI ≥ 30 or ≥ 27 with risk factors. Not recommended for children the elderly, pregnant or nursing mothers. Avoid late evening dosing.</td>
</tr>
<tr>
<td></td>
<td>Adipex-P</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Phendimetrazine tartrate</td>
<td>Bontril PDM</td>
<td>Sympathomimetic</td>
<td>Short term monotherapy; 3 months or less with concurrent diet and exercise</td>
<td>35 mg 2-3 times daily; one hour before meals; may reduce to 17.5 mg per dose; maximum dose is 210 mg per day in three evenly divided doses. Slow release: 105 mg in am, 30-60 minutes before breakfast</td>
<td>CIII</td>
<td>Limit use. Use lowest dose possible for shortest time. Not recommended for children the elderly, pregnant or nursing mothers. Avoid late evening dosing or abrupt cessation after prolonged high doses. Abuse and dependence potential.</td>
</tr>
<tr>
<td>Benzphetamine HCL</td>
<td>Didrex</td>
<td>Sympathomimetic</td>
<td>Short term monotherapy; 2-4 weeks or less with concurrent diet and exercise</td>
<td>25-50 mg daily in mid-morning or mid- afternoon</td>
<td>CIII</td>
<td>Refer to physician for evaluation prior to prescribing. Limit use. Use lowest dose possible for shortest time. Not recommended in children, the elderly, pregnant (Category X) or nursing mothers. Abuse and dependence potential.</td>
</tr>
<tr>
<td>Orlistat</td>
<td>Xenical</td>
<td>Lipase inhibitor</td>
<td>Long term with concurrent diet and exercise prescriptions.</td>
<td>120 mg three times a day with 3 main meals. If meal is missed or has no fat, skip dose.</td>
<td>None</td>
<td>BMI ≥ 30 or ≥ 27 with risk factors. May decrease absorption of fat soluble vitamins. Significant GI side effects. Recent evidence/outcome data are available.</td>
</tr>
</tbody>
</table>

Table 2. Currently Available Medications for Adult Obesity Treatment in the United States
(Consult complete prescribing reference prior to use.)

Meires & Christie (2011) NP
Medications for treatment of obesity that have been withdrawn or abandoned include:

a. thyroid
b. “rainbow pills”
c. sibutramine
d. fenfluramine
e. all of the above
Withdrawn Antiobesity Medications

- **obesity medications – 1930s**
  - initial medications for obesity were amphetamines
    - methamphetamine & phenmetrazine; benzphetamine, and mazindol
  - serious adverse events, death, potential for abuse

- **fenfluramine & phentermine ("fen-phen") – 1990s**
  - weight loss but serious adverse effects
  - fenfluramine ( & D-fenfluramine) withdrawn in 1997
  - adverse cardiac, valvular, and pulmonary effects

“WD or Abandoned” Antiobesity Drugs

- Thyroid hormone
  - Hyperthyroidism, with its attendant sequelae
- Dinitrophenol
  - Cataracts and neuropathy
- Rainbow pills (a mixture of digitalis and diuretics)
  - Fatal arrhythmias and electrolyte derangements
- Aminorex
  - Pulmonary hypertension
- Phenylpropanolamine
  - Increased risk of myocardial infarction and stroke
- Sibutramine
  - CV event risk
Orlistat (Xenical)

- blocks the action of pancreatic lipase
  - reduces triglyceride digestion & absorption
  - dose 120 mg po TID w/ some fat for obesity and maintenance
  - peds – 12 to 16; adults same dose, Cat X pg; lactation unknown
  - avoid use in chronic malabsorption, cholestasis, kidney stones, eating disorders, organ transplant
  - improves lipid profiles in obese patients w/ low and high risk including DM2 - hypoglycemia (120mg TID)

- two major clinical trials showed sustained weight loss of 9-10% over 2 years, other trials showed less loss

- may reduce absorption of some fat-soluble vitamins (A, D, E, K), beta-carotene & some medications/supplementation recommended

- adverse effects include flatulence, fatty/oily stool, increased defecation, and fecal incontinence.

- rare but severe liver disease

Hamdy, O. 92014) Obesity tx & management. Medscape & Epocrates
Phentermine HCL

- a sympathomimetic amine, stimulants CNS, decreases appetite
  - increases the release and reuptake of norepinephrine and dopamine
  - effect occurs from satiety-center stimulation in hypothalamic / limbic brain areas
  - variable weight loss; some studies reports more loss with intermittent use
- indicated as a component of a comprehensive weight-reduction program
  - initial BMI of greater than 30 kg/m2 or between 27 and 30 kg/m2 w/ RF
- adults 16 yrs up, dose 15-37.5 mg daily for 3 months then DC
- contraindicated severe HTN, hyperthyroidism, glaucoma, severe CAD, MAOi, drug abuse history, or pregnancy / breastfeeding
- caution with renal impairment, HTN, elderly, DM avoid prolonged use and taper dose if patient on higher doses for prolonged time
- drug has been used for several decades in US (1959)

Indications and Usage

• **Serotonin 2C receptor agonist** indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults
  – BMI of 30 kg/m² or greater or 27 kg/m² or greater with at least one weight related comorbid condition such as hypertension, dyslipidemia, type 2 diabetes

Limitations of Use

• The **safety and efficacy** of co-administration with other products for weight loss have not been established

• The effect of on cardiovascular morbidity and mortality has not been established
Dosage and Administration

• 10 mg twice daily, discontinue if 5% weight loss is not achieved by week 12

Dosage forms and strengths

• 10 mg film-coated tablets

Contraindications

• pregnancy

Warnings and precautions

• Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like reactions
  – safety of co-administration with other serotonergic or antidopaminergic agents has not been established - immediate discontinuation / supportive treatment

• valvular heart disease - if signs or symptoms develop consider stopping the medication & evaluate for valve disease (may be asymptomatic)
Lorcaserin (Belviq)

Warnings and precautions

• cognitive impairment
  – may cause disturbances in attention or memory
  – use caution with hazardous machinery when starting treatment

• psychiatric disorders
  – euphoria and dissociation
  – do not exceed recommended dose of 10 mg twice daily
  – monitor for depression or suicidal thoughts and DC if s/s develop

• antidiabetic medications
  – weight loss may cause hypoglycemia
  – monitor blood glucose.
  – has not been studied in patients taking insulin

• priapism
  – seek emergency treatment if an erection lasts >4 hours; use with caution in patients predisposed to priapism
Lorcaserin (Belviq)

Adverse Reactions

- **greater than 5% in the non-diabetic** includes headache, dizziness, fatigue, nausea, dry mouth, and constipation
- **diabetic** patients are hypoglycemia, headache, back pain, cough, and fatigue.
- suspected adverse reactions
  - contact Eisai Inc. 1-888-274-2378 or FDA at 1-800-FDA-1088 or at [www.fda.gov/medwatch](http://www.fda.gov/medwatch)

Drug Interactions

- Serotonergic drugs SSRIs & SNRIs, MAOIs, triptans, bupropion, dextromethorphan
- St. John’s Wort use with extreme caution due to the risk of serotonin syndrome

Use in specific populations

- nursing mothers: discontinue drug or nursing
- pediatric use: safety and effectiveness not established, use not recommended

[www.belqiq.com](http://www.belqiq.com)
Medscape Reference

- Monitor for serotonin syndrome or NMS-like reactions
- Studies suggest possibility of regurgitant valvular heart disease (not likely); monitor if patient has congestive heart failure
- Advise patient to take caution when operating hazardous machinery
- Monitor for worsening of depression, suicidal thoughts or behavior, or any other unusual changes in mood or behavior
- May cause pulmonary hypertension (insufficient data)

From www.Medscape.com

- Monitor for hypoglycemia with type 2 diabetes mellitus; if hypoglycemia occurs while on therapy; adjust antidiabetic drug regimen
- Caution in men with predisposed conditions to priapism (e.g., sickle cell anemia, multiple myeloma, or leukemia) or anatomical deformation of the penis
- Caution with bradycardia or a history of heart block
- May cause decrease in white blood cell count and other hematological changes; consider periodic monitoring of CBC
- Moderately elevates prolactin levels
Abstract: Therapy of obese patents with cv disease

- Lorcaserin (Belviq)
  - 10mg BID for 1 yr, at least 5% weight loss in ~37% w/ diabetes and ~ 48% of those w/o diabetes
  - many of those remaining on drug maintained loss
  - improvement in lipids (NS)

Indications and usage

- **Qsymia** is a combination of phentermine, a sympathomimetic amine anorectic, and topiramate extended-release, an antiepileptic drug

- adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial BMI of 30 or greater or 27 or greater in the presence of at least 1 comorbidity

Limitations of Use:

- The effect of Qsymia on cardiovascular morbidity and mortality has not been established

- The **safety and effectiveness** of Qsymia in combination with other products intended for weight loss, including prescription and OTC drug and herbal preparations, have not been established
Dosage and Administration

• Take once daily in morning. Avoid evening dose to prevent insomnia

• **Recommended dose:** Qsymia 3.75 mg/23 mg (phentermine 3.75 mg/topiramate 23 mg extended-release) daily for 14 days; then increase to 7.5 mg/46 mg daily

• **Discontinue or escalate dose** (as described) if 3% weight loss is not achieved after 12 weeks on 7.5 mg/46 mg dose

• **Discontinue** Qsymia if 5% weight loss is not achieved after 12 weeks on maximum daily dose of 15 mg/92 mg
  
  — **Discontinue** 15 mg/92 mg dose gradually (as described) to prevent possible seizure

• **Do not exceed** 7.5 mg/46 mg dose for patients with moderate or severe renal impairment or patients with moderate hepatic impairment
Dosage Forms and Strengths

Capsules: (phentermine mg/topiramate mg ER)

- 3.75 mg/23 mg
- 7.5 mg/46 mg
- 11.25 mg/69 mg
- 15 mg/92 mg

Contraindications

- Pregnancy
- Glaucoma
- Hyperthyroidism
- During or within 14 days of taking monoamine oxidase inhibitors
- Known hypersensitivity or idiosyncrasy to sympathomimetic amines
Warnings and Precautions

- **Fetal Toxicity**: Obtain negative pregnancy test before treatment and monthly thereafter; use effective contraception.

- **Increase in Heart Rate**: Monitor heart rate in all especially those with cardiac or cerebrovascular disease

- **Suicidal Behavior and Ideation**: Monitor for depression / suicidal thoughts. DC if symptoms develop

- **Acute Myopia and Secondary Angle Closure Glaucoma**: Discontinue

- **Mood and Sleep Disorders**: Consider dose reduction or withdrawal for significant / persistent symptoms

- **Cognitive Impairment**: May cause disturbances in attention or memory. Caution patients about operating automobiles or hazardous machinery when starting treatment

- **Metabolic Acidosis**: Measure electrolytes before/during treatment

- **Elevated Creatinine**: Measure creatinine before/during treatment

- **Use of Antidiabetic Medications**: Weight loss may cause hypoglycemia, measure serum glucose before/during treatment
Adverse Reactions

- Most common adverse reactions (incidence greater than or equal to 5% and at a rate at least 1.5 times placebo) are: paraesthesia, dizziness, dysgeusia, insomnia, constipation, and dry mouth
  - To report SUSPECTED ADVERSE REACTIONS, contact VIVUS Inc., at 1-888-998-4887 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Drug Interactions

- Oral contraceptives: Altered exposure may cause irregular bleeding but not increased risk of pregnancy.
  - Advise patients not to discontinue oral contraceptives if spotting occurs
- CNS depressants including alcohol: Potentiate CNS depressant effects.
  - Avoid concomitant use of alcohol
- Non-potassium sparing diuretics: May potentiate hypokalemia.
  - Measure potassium before/during treatment

Use in Specific Populations

- Nursing Mothers: Discontinue drug or nursing
- Pediatric Use: Safety and effectiveness not established and use not recommended
Who needs Pharmacotherapy?

- Case 1 Paula, the accountant age 25
- Case 2 Pam, the RN age 39
- Case 3 Buddy, the southern man age 64
- Case 4 Donnie, retired age 70
Visit 1

- Paula is a healthy, 25 yo accountant who presents to the Primary Care clinic for an annual exam
- ROS, PMH & PSH - negative
- No meds or allergies to medications
- Lives alone, eats a balanced diet, does not smoke but enjoys a couple of glasses of wine after work each night and on the weekends
- Plays softball twice a week
- Paula’s family history is unknown (adopted)

- Paula’s History & PE is normal except for weight gain
- BMI is 29, up from 27 a year ago and her waist measures 38 inches
Case 1 - Paula

• Guideline -- best treatment plan
  – RD or nutritionist for review and diet recommendations as Paula is overweight
  – PCP Rx exercise program, sleep recommendations
  – Are medications appropriate for Paula?
    • Weight loss medication may be an option and should be discussed with Paula
    • What are the best medications based on H & P?
Case 1 - Paula

• Paula and the PCP decided medications were not necessary at this time
  – if unsuccessful with weight loss will reconsider them as option

• Monthly appointments X 3 were scheduled
  – clinic RN will monitor Paula’s progress with weight loss
    • record BMI, waist measurements and activity levels
    • share results with Paula & team
Case 1 - Paula

Visit 4

- At 3 months Paula’s BMI was 26 and she lost 3 inches from her waist line.
- Paula decreased calories (wine, junk food) added more fresh fruits, veggies & fiber to her diet.
- The exercise Rx was implemented.
- Paula downloaded a free mobile app to keep track of calories and activity levels.
  - She was jogging 3 miles a day in addition to weekend sports.

Example of a free app from Google.com
Comprehensive Lifestyle Intervention - Successful

• Rationale
  – the RD helped Paula adhere to a healthier lower calorie diet and determined a healthy weight for her
  – Paula was active and determined on her own to increase physical activity but the “Exercise Rx” gave her parameters
  – monthly follow up with RN facilitated progress
  – the smart phone application documented activity levels
  – Paula could use other applications to track calories, food groups
  – team will continue to help Paula maintain her health goals
Meet your Patient - Pam

Visit 1

A 39-year-old RN, Pam presents to the PCP for help with weight loss. She has difficulty losing weight and has gained a significant amount of weight in the last 12 months. Throughout her adolescence and early adulthood Pam tried numerous approaches with little success including Weight Watchers, Atkins diet, Grapefruit diet, and the Cabbage soup diet. She states she has been “yo-yo dieting for many years and wants to change her lifestyle”. Pam’s PMH and PSH is negative. She is on low dose oral contraceptives (no other meds). Pam denies the use of prescribed pharmacology for weight loss. She tried OTC Alli but didn’t work for her. She has NKDA.

Pam reports feeling depressed, tired, and is uncomfortable in her clothes since the weight gain. She denies chest pain, shortness of breath (SOB), palpitations, and edema.

Morenus, J. (2014) unpublished manuscript ANP2
Case 2 - Pam

FH: hypertension, obesity, stroke, coronary artery disease, heart failure, DM2, cardiomyopathy, cardiac arrhythmia, hypercholesterolemia, & hypothyroidism

O: VS - WNL T98.6 F oral, R 18, HR 83, and BP 114/80

Current weight is 197 pounds, height is 69 inches, **waist circumference is 35 inches**, hip circumference is 42 inches (0.83 – moderate risk)

BMI: 29.1

Exam: lungs are clear to auscultation; heart regular rhythm, rate, S1 S2, no murmurs, gallops, clicks, or rubs, no peripheral edema

A: overweight

P: fasting labs the following morning with a follow up visit in 1 week
Visit 2

Report lab findings, obtain second BMI 29.1, determine plan

- **Lipids:** total cholesterol 187 mg/dL, HDL cholesterol 80 mg/dL, LDL cholesterol 90 mg/dL, triglycerides 84 mg/dL.

- **Renal:** BUN 19 mg/dL, creatinine 0.70 mg/dL, sodium 137 mmol/L, potassium 4.2 mmol/L,

- **Liver:** alkaline phosphatase 47 U/L, ALT 11 U/L, AST 14 U/L,

- **FBS:** 90 mg/dL

- **TSH:** 1.81 mIU/L

- **Pregnancy test:** negative

- **Electrocardiogram:** normal sinus rhythm
Case 2 - Pam

Guidelines

• Pam’s health history, family history, and assessment findings increase her risk of cardiovascular disease, type 2 diabetes, metabolic syndrome, HTN, and other obesity related diseases

• Pam’s waist circumference and waist to hip ratio places her into a moderate disease risk classification
  – Indication of visceral fat or abdominal obesity

• Pam is overweight according to the 2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults
Treatment Plan was personalized for Pam

- lifestyle modification, dietary intervention, pharmacological treatment
  - recommended self-monitoring mobile-delivered lifestyle intervention application in achieving weight loss of Pam’s choice (personalized)
  - instructed by the RD to consume 1200 calories per day of healthy food choices and was prescribed physical activity - walking 5 times a week for 30 to 60 minutes by her PCP (Rxs given)
- prescribed a medication to help her lose weight
- Pam agreed to a follow up appointment monthly to monitor weight loss and to readjust weight loss treatment plan
What is the best pharmacologic choice for Pam?

a. Orlistat (Xenical)

b. Phentermine HCL (Fastin, Adipex-P)

c. Lorcaserin (Belviq)

d. Phentermine / Topirimate ER (Qsymia)

e. Phendimetrazine tartrate (Bontril DPM)
FDA approved pharmacotherapy as an adjunct to comprehensive lifestyle intervention

• Rationale
  – help Pam **adhere to a lower calorie diet** more consistently
  – help Pam achieve sufficient **weight loss** and health improvements
  – combined Pam’s treatment with **increased physical activity**

• Action
  – decrease **appetite** or **fat absorption**
  – help to **reinforce Pam’s new lifestyle change**
  – prescribed as an **adjunct** to lifestyle interventions
Case 2 – Pam

Pam and the PCP discussed her diagnosis of overweight and reviewed her RF profile

• lifestyle changes including revamping her diet based on recommendations by the RD

• given a prescription for sleep and for exercise

• all of the available FDA obesity medication options were offered along with a discussion of serious side effects

  – opted for short term medication & birth control to avoid pregnancy

  – phentermine HCL (Adipex-P) 37.5 mg / q. a.m. for 90 days

  – Pam will follow up in one month, sooner if needed
Nutrition Prescription

Family Medicine Center at Lem Turner
1225 Lila Avenue
Jacksonville, Fl 23308

Patient Name____________________          Date____________________

**Nutrition Prescription:**

WRITE A PRESCRIPTION PERSONALIZED TO YOUR PATIENT

Patient Signature __________________________
Nutritionist/RD __________________________
Exercise Prescription

Family Medicine Center at Lem Turner
1225 Lila Avenue
Jacksonville, Fl 23308

Patient Name_____________________ Date__________________

Exercise Prescription:

WRITE A PRESCRIPTION PERSONALIZED TO YOUR PATIENT

Patient Signature __________________________________________
PCP signature ___________________________________________
Case 2 - Pam

Listen to the patient...involve them in the plan

• determine what will work and when
  – Lifestyle modifications, pharmacotherapy if indicated

• discuss types of treatment
  – Medications, how they work, major side effects
  – Risks vs Benefits

• refer to interprofessional team members

• personalize prescriptions
  – written or typed
Visit 1

Buddy, a 64 yo “small town southern man” presents to his PCP with complaints of **fatigue and dizziness w/o syncope** for several weeks. He states that he is rarely ill and the dizziness and fatigue is interfering with his work at the local paper mill. More importantly, the symptoms were interfering with his golf game. For several years Buddy has been healthy with normal VS, waist circumference and labs.

Upon **exam** the PCP discovers that **Buddy gained 3 inches on his waist** and his BMI had moved from 25 to 30. Buddy is **obese**. His **random BS was elevated**. Buddy admitted that he was craving and eating lots of sweets at work and at night while watching TV even though his wife Bonnie was not happy about it. He also admitted the paper mill had given him a golf cart to drive instead of walking while working. The rest of Buddy’s physical exam was normal including his VS, pulse ox & BPs. Arrangements were made for Buddy to get fasting lab work done the next day.
Visit 2

• Buddy’s labs were WNL except for a **FBS of 120 mg/dl**. The PCP attributed his symptoms to elevated BS as no other cause was found.

• Buddy agreed to stop eating sweets and increase his exercise including walking more at work. He did not want “to become a diabetic”. He saw an RD and was given an exercise prescription by the PA. He was asked to follow up with the clinic RN for weekly fasting BS readings, weights and waist measurements. Bonnie insisted on going with Buddy to these appointments and offered her support by making sure he got healthy meals at home and at work. She instituted a walking program for both of them each night because Buddy liked his golf cart and didn’t want to give it up.
Visit 3

- At the 3 month follow up appointment Buddy had lost enough weight to have a healthy BMI again.
- His waist circumference was back down to baseline (36 inches).
- He no longer had dizziness or fatigue.
- His FBS were normal as well as a repeat Hgb a1C.
- To ensure continued success with his plan, Buddy sees the RN where he works monthly for weights, waist circumference measurements and random BS readings. The results are called to Buddy’s PCP.
Weight Loss Maintenance

• The pattern of weight loss in patients, like Buddy and Paula undergoing a lifestyle intervention is that maximum weight loss is achieved at 6 months, followed by plateau and gradual regain over time
  – also true for medication-assisted weight loss like Pam, although weight regain may be slower with continued medication use
  – it may take much longer for weight to plateau in bariatric surgery patients
Case 3 - Buddy

• What medication would be appropriate for Buddy if the comprehensive lifestyle intervention had not been successful?
Abstract: Long-term drug treatment for obesity / Systematic review

- When prescribed with lifestyle interventions obesity medications for long term use produce additional weight loss compared to placebo ranging from ~ 3% for orlistat and lorcaserin to ~ 9% for top dose of phentermine & topiramate ER at 1 year.

- All 3 medications demonstrated greater improvements in cardiometabolic risk factors

- No medication has yet to demonstrate reduced cardiovascular morbidity or mortality

- By discontinuing medication in those who do not respond with weight loss of at least 5%, clinicians can decrease exposure to risk and costs of treatment as there is little prospect for long term benefit

Visit 1

• Donnie age 70, has been healthy for a number of years. She practices yoga, walks 4 miles a day and eats a well balanced diet and has no chronic diseases.

• She presents to her PCP with increasing fatigue, a 14# weight gain, poor sleep and feeling sluggish.

• She states she isn’t has sharp as she was a few months ago. Her clothes are too tight and she wonders if she needs a diet pill.

• She states “I can’t afford a new wardrobe!”
**Case 4 - Donnie**

**ROS:** Donnie denies fever, chills, loss of blood, headache, nasal congestion, cough, chest pain, muscle aches or pains. She feels a little depressed mostly because she cant do what she used to (fatigue). But, she denies feeling sad or moody. Donnie says she can still do her ADLs and has no trouble managing her finances.

**Exam:** A&O x3. HEENT -, LCTA BL. HRRR S1 S2 no murmurs, gallops, or clicks. Abd - obese with good BS, no tenderness, extremities, good pulses BL, no edema. Her VS & MMSE is WNL.

The PCP ordered fasting labs and noted a **BMI of 31.**
Is Donnie a candidate for weight loss medication? Yes? No?
Obesity is likely related to excessive energy intake and decreased energy expenditure but other causes of obesity must be considered.
It turns out that Donnie was hypothyroid. She was started on low dose thyroid daily and is currently being followed monthly. Her fatigue has improved and she is slowly losing the weight she gained.
Obesity

- Scope of the problem is greater than a simple fix
- Pathophysiology complex
- Pharmacotherapy alone is not sufficient
- Comprehensive, personalized lifestyle changes are needed
- Requires expertise of a collaborative health care team
- Need to follow up
- Guidelines are useful

http://fasinfat.org/cost-containment
Weight loss strategies for treatment of obesity

Abstract: Obesity is one of the most serious and prevalent non-communicable disease of the 21st century. It is also a patient centered condition in which affected individuals seek treatment through a variety of commercial medical and surgical approaches. Considering obesity as a chronic disease state helps frame the concept of a three stepped intensification of care approach to weight management.

1. Counseling on lifestyle management / behavior change
2. Pharmacology as adjuncts – 2 new agents approved in 2012
3. Bariatric surgery for severe obesity
What we did today......

• Reviewed definition, incidence prevalence of obesity, costs, risk factors, comorbid conditions, pathophysiology

• Discussed new approaches to obesity management
  – Guidelines, BMI, diagnosis
  – Pharmacotherapy - 4 medications – safety & efficacy
  – Case presentations – pharmacotherapy / guidelines

• “Questions” throughout presentation

What we can do tomorrow......
Get some sun, eat veggies & stay hydrated
Rest...always get a good nights sleep
Exercise & hang out with friends

Photo from Karen Marley RN, BSN
No worries....A superhero can save the day!
Thank you!

- PCNA for this opportunity...I had fun!
- UNF Faculty
  - Drs. Catherine Christie & Katherine Robinson
  - presentation critique
- UNF CIRT team
  - David Wilson
- All of the UNF Graduate Students
  - Karen Marley – photos
  - Jessica Morenus – help with case presentations
Additional readings...

**Obesity** *Endocrinology*, Aug 26, 2013

**Safety of Antiobesity Drugs** *Therapeutic Advances in Drug Safety*, 2013-08-01


**New Obesity Guidelines: Authoritative 'Roadmap' to Treatment** *Medscape Medical News*, 2013-11-12


**New Obesity Drugs Provide 'Slim Pickings,' Say 2 Experts** *Medscape Medical News*, 2014-02-19

**The Obesity Epidemic: Addressing Weight Loss in Your Patients to Improve Health and Outcomes** *Medscape Education Diabetes & Endocrinology*, 2013-08-27

**An Unmet Need in Medical Training: Addressing Weight Bias** *Medscape Public Health*, 2014-02-03

**The Evolution of Obesity Therapies: New Applications for Existing Drugs** *Medscape Education Diabetes & Endocrinology*, 2010-06-17

**Obesity Treatment** *Endocrinology*, Dec 16, 2013
Adverse reactions to Lorcaserin (Belviq) in patients with diabetes include all but:

a. Hypoglycemia
b. Hyperglycemia
c. Headache
d. Fatigue
Adverse reactions to Lorcaserin (Belviq) in patients with diabetes include all but:

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Warnings / precautions for the antiobesity medication Phentermine & Topiramate (Qsymia) include:

a. Fetal Toxicity requiring the user to use effective contraception

b. Suicidal Behavior and Ideation

c. Acute Myopia and Secondary Angle Closure Glaucoma

d. Cognitive Impairment

e. All the above
Warnings / precautions for the antiobesity medication Phentermine & Topiramate (Qsymia) include:

a. Fetal Toxicity requiring the user to use effective contraception

b. Suicidal Behavior and Ideation

c. Acute Myopia and Secondary Angle Closure Glaucoma

d. Cognitive Impairment

e. All the above