Medical Treatment of Metabolic Syndrome from a HAES® Perspective

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Background

- Rice University
- Baylor College of Medicine
- Georgetown University- Providence Hospital Family Medicine Residency
- Carl Moore Health Center
- Northwest Health Center
- Vida Family Medicine

Agenda

- What is metabolic syndrome?
- Commonly prescribed medications for metabolic syndrome and how they might impact your work with your client
- Collaboration with your client's physician
- Helping your client advocate for themselves in a flawed system

What is metabolic syndrome?

- Caused by a combination of genetic, psychological, socioeconomic, and behavioral factors
- Most commonly-accepted definition from National Cholesterol Education Program Adult Treatment Panel III (NCEP ATPIII) 2005
 - Guidelines based on identifying risk factors and best practices for treatment of individuals to reduce cardiovascular morbidity and mortality
- 3 or more of the following conditions
 - Abdominal obesity (waist >102cm men, >88cm women, in Asian patients >90cm men or >80cm women)
 - Insulin resistance/hyperglycemia (fasting glucose >100mg/dL)
 - Hypertension (>/= 130/85)
 - Hypertriglyceridemia (fasting TGs >/= 150mg/dL)
 - Low HDL cholesterol (<40 mg/dL men, <50mg/dL women)

Symptoms of Metabolic Syndrome

- Increased appetite
- Fatigue
- Weight gain
- Increased frequency of urination
- Increased thirst
- Headaches (associated with high blood pressure)
- May have no symptoms at all

Why is treating metabolic syndrome important?

- Major cause of morbidity and mortality in the US
- HTN/HLD-> coronary artery disease/heart disease (#1 cause of death in USA in 2021), stroke (#5)
- Insulin resistance -> prediabetes -> T2DM (#8)
- Fatty liver disease -> cirrhosis (#9)
- Increased risk of death from COVID-19 due to altered expression of ACE2 receptor increased in HTN, T2DM, adipose tissue (#2)
- Increased risk of certain cancers- colon, uterine, breast, melanoma (#3)

Why is medical treatment of metabolic syndrome important?

- Health disparities- SES, weight stigma, BIPOC
- Impact on fertility (male and female) and lactation
- Many of the resulting complications are completely preventable with proper treatment
- Earlier treatment is often less invasive and more effective, and prevents development of complications

First line treatment: Lifestyle modification

- Balanced diet
- Regular physical activity
- Stress management
- Adequate sleep
- Quit smoking

"Weight Loss" is not a treatment plan



It's not about weight

Top News

Adults With Genetically Predicted High BMI May Have Lower Risk For CVD Than Those Whose Obesity Is Tied To More Environmental Factors

Healio (4/6, Monostra) reports, "Adults with a genetically predicted high BMI may have a lower risk for cardiovascular disease" (CVD) "than those whose obesity is linked more to environmental factors," researchers concluded in findings published online in the journal eClinicalMedicine. The study of "midlife and late-life adult twins" revealed that "obesity was associated with an increased risk for CVD across the entire range of polygenic scores from BMI," whereas "midlife adults with a genetically predicted low BMI had the highest CVD risk."

MedPage Today (4/6, Phend) reports, "The analysis included 15,786 Swedish twins born before 1959 who had BMI measured at ages 40-64 and 5,488 with BMI measured at age 65 or later (3,286 were in both groups)," while "CVD was determined from prospective data in linked nationwide healthcare and cause of death registries through 2016, for a follow-up averaging 18 years."

Blood Pressure Lowering Medications

Commonly Prescribed Medications	Side effects
ACE inhibitors (Lisinopril, etc) \$	Cough. Not safe in pregnancy.
Angiotensin receptor blockers (Losartan, etc) \$	Not safe in pregnancy.
Calcium channel blockers (Amlodipine, Nifedipine, etc) \$	Swelling, flushing
Diuretics (Hydrochlorothiazide, Spironolactone, etc) \$	Increased urination, dehydration
Beta blockers (Metoprolol, Labetolol, etc) \$	Lightheadedness, dizziness.

Lipid Lowering Medications

Commonly Prescribed Medications	Side effects
Statins (Lipitor, Crestor, etc) \$	Muscle pain, increased LFTs. Not safe in pregnancy
Ezetimibe \$	Muscle pain, increased LFTs, not safe in pregnancy.
Fibrates \$	Increased LFTs, lowered HDL
Omega 3 Fatty Acids \$-\$\$	Nausea, fishy taste, abnormal bleeding

Metformin \$

- Decreases gluconeogenesis in the liver
- Decreases intestinal absorption of glucose
- Increases insulin sensitivity in the muscle/peripheral tissues
- Decreases fatty acid synthesis in liver
- Reduces risk of progression to T2DM
- Improves ovulation and pregnancy rates but not live birth rates
- May improve glandular tissue growth and milk supply in patients experiencing insufficient lactation- anecdotal, under investigation
- Improves satiety/reduces excessive hunger- not an appetite suppressant!
- Side effects: Diarrhea/GI upset, lactic acidosis (with underlying risk factors), Vitamin B12 deficiency

Regulation of Obesity, Appetite, and Weight Loss by Metformin

CNS Effects: · Suppression of orexigenic hypothalamic AgRP neurons via AMPK suppression · Increase in hypothalamic leptin sensitivity · Increased production of incretins and vagal signaling via NTS (GLP-1, PYY) · Appetite suppression via post-prandial **Hepatic Effects:** elevation in lactate production · Decrease in hepatic glucose production and reduced systemic insulin requirement Aging Effects: · Reduction in sarcopenic obesity? Gut Microbiome Effects: · Reversal of aging-related metabolic Alteration of gut microbiota (Bacteroides/ derangement Firmicutes ratio) Metformin \$ · Alteration in Lactobacillus sp. and hepatic glucose production **GI Effects:** · Increase in Ackermansia sp. Nausea (central vs. GLP-1 mediated) · Increase in the production of SCFA · Alteration in bile absorption and secondary gut hormone signaling · Diarrhea and bloating due to altered enterocyte metabolism Dysgeusia

"Weight Loss" Medications

- Orlistat \$\$
 - Inhibits pancreatic lipase-> increased fecal fat excretion
 - Side effects: diarrhea, kidney stones/kidney injury, malabsorption of fat-soluble vitamins
- Phentermine \$
 - Stimulant- increases norepinephrine, suppresses appetite
 - Not approved for use >12wks
 - Not appropriate if CV disease, hyoerthyroidism
 - Side effects: inc BP, HR, dry mouth, constipation, nervousness
- Qsymia (topiramate + phentermine) \$\$
 - Neurologic effects on appetite (decr neuropeptide Y)
 - Side effects: Taste disturbance, mental health/cognitive side effects
 - Must taper off- inc risk of seizure
- Contrave (bupropion + naltrexone)\$\$
 - Dopamine reuptake inhibitor + opioid receptor antagonist
 - Decreases appetite
 - Helps reduce EtOH intake
 - Side effects: Decreases seizure threshold, CV disease considerations

GLP-1 Receptor Agonists: How they work

- Semaglutide (Ozempic, Wegovy) \$\$\$
 - Weekly SC or daily PO, more effective for glycemic control and weight loss
- Liraglutide (Saxenda) \$\$\$Daily SC
- Stimulate glucose-dependent insulin secretion
- Inhibits glucagon release
- Slows gastric emptying
- Suppresses hunger cues at the level of the brain

GLP-1 Receptor Agonists- Side Effects

- Nausea/Vomiting
- Constipation
- Diarrhea
- Decreased appetite
- Effect on neurotransmitters- reduced cravings for EtOH, improved depression/anxiety Sx- early data
- Rare: pancreatitis, thyroid cancer

Tirzepatide (Mounjaro) \$\$\$

- GLP-1 Receptor Agonist and GIP Receptor Agonist
- GIP stimulates insulin secretion, suppresses glucagon secretion during hyperglycemia and stimulates secretion during euglycemia and hypoglycemia, increases fatty acid and glucose uptake by fat tissue
- More weight loss, more powerful "turn off" of cravings compared to GLP-1 receptor agonists
- ONLY FDA APPROVED FOR TYPE 2 DIABETES but is being used off-label for weight loss. May be approved for weight loss in the future.

Collaborating with your client's physician

- Share your assessment of your client's eating behaviors and your recommendations
- Forward consult notes with your contact information
- Request lab results/office visit notes

Patient Advocacy

- Schedule yourself appropriately
- Make a list of concerns to be addressed
- Share all relevant history
- Ask which tests are being ordered and why
- Ask for results to be explained in full
- If a medication is being recommended- ask why and what the medication will do
- Ask about possible side effects
- Ask about medication cost
- Ask about alternatives- non-medication approaches or other medications

My Approach

- Assess symptoms
- Assess lifestyle factors (sleep, stress, nutrition, activity level, substances)
- A1C, Lipid Panel, CMP, Vitamin D, +/- TSH + free T4, CBC and fasting insulin level
- Calculate HOMA-IR
- Calculate 10yr ASCVD risk score
- Collaborate with dietitian/therapist re: behaviors
- Discuss risks and benefits of medications- shared decision making

Questions?

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