DPC SUMMIT

Menopause & Metabolism

A Perfect Storm

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AAFP1.CNF.IO

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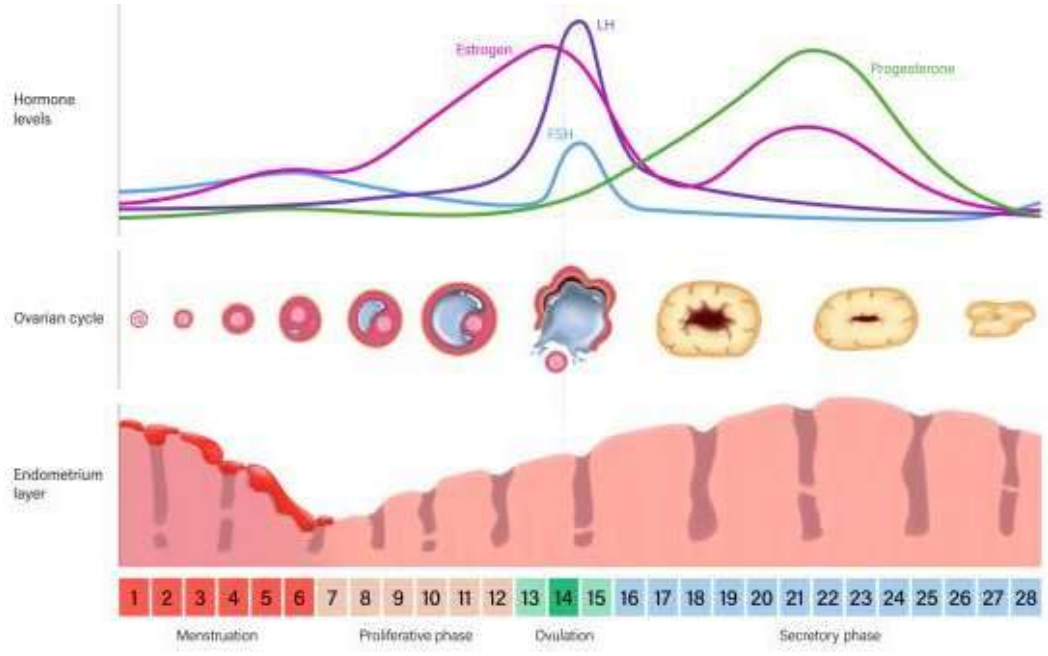
Learning Objectives

1. Identify common systemic symptoms of perimenopause and menopause.
2. Determine the effect of menopause transition on markers of metabolic health.
3. Consider risk mitigation and treatment strategies including medication and lifestyle modifications.

Menopause – What is it?

- Menopause is defined by menstrual cycles
- Average age is 51 years old
- Early-onset – 40-45 years
- Premature ovarian Failure - <40 years old
- Perimenopause
  - Symptoms 7-10 years prior to menopause



Ovarian Reserve

Decline in ovarian follicles

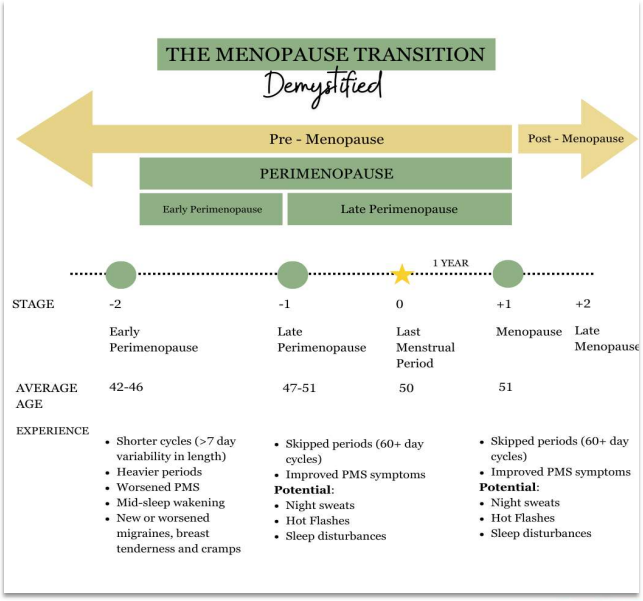
- People born female start with 1-2 million eggs
  - By age 30, we have 10%
  - By age 40, we have 4%
- Menopause <1000 eggs
- Late menopause > 55 y.o. correlates to longer lifespan
- Accelerated decline of ovarian reserve
  - Tobacco use, history of endometriosis, chemical exposures

Anti-Mullerian Hormone (AMH) by Age

	Low (ng/mL)	Slightly Low (ng/mL)	Normal (ng/mL)	Slightly High (ng/mL)	High (ng/mL)
18 – 25	< 1.02	1.02 – < 1.20	1.2 – < 5.0	5.0 – 10.0	> 10
26 – 30	< 0.69	0.69 – < 1.20	1.2 – < 5.0	5.0 – 10.0	> 10
31 – 35	< 0.36	0.36 – < 1.20	1.2 – < 5.0	5.0 – 10.0	> 10
36 – 40	< 0.18	0.18 – < 1.20	1.2 – < 5.0	N/A	>= 5
41+	< 0.01	0.01 – < 1.20	1.2 – < 3.0	N/A	>= 3

Ovarian Reserve

- STRAW staging
  - Stages of Reproductive Aging Workshop
- Loss of ovarian reserve triggers negative feedback to the brain
- Increase in FSH
- Decrease in AMH
- Continued decline in estrogen



Perimenopause symptoms

- Vasomotor symptoms (hot flashes)
- Interrupted sleep
- Gynecologic
  - Abnormal Uterine Bleeding (AUB)
- Genitourinary syndrome of menopause
  - Urinary tract infections
  - Pain with sex
- Cardiac
  - Palpitations
- Mental health
  - Anxiety, Depression, ADHD-like symptoms with volatile hormones
  - Cognitive decline
    - Decrease in verbal memory
- Musculoskeletal syndrome of menopause
  - Joint aches
  - Body composition changes
    - Decrease lean body mass
    - Increase visceral fat from 8% to 23%
    - Low bone density

Perimenopause symptoms (Lesser known)

- Cold flushes
- Dry eyes
- Brittle nails
- Heartburn
- Dizziness
- Altered sense of smell
- Tinnitus
- Burning mouth
- Skin crawling and itchy skin

Body Composition Changes

- Increase in visceral fat
  - Post-menopausal women have 5x higher risk of developing abdominal obesity than premenopausal
  - Increase risk of metabolic syndrome, dementia and breast cancer
  - Burn less fat
  - Insulin resistance
  - DHEA decreases
- Osteosarcopenia
  - Loss of bone density
  - Loss of muscle mass
  - Metabolism slows down

Menopause and Metabolic Health

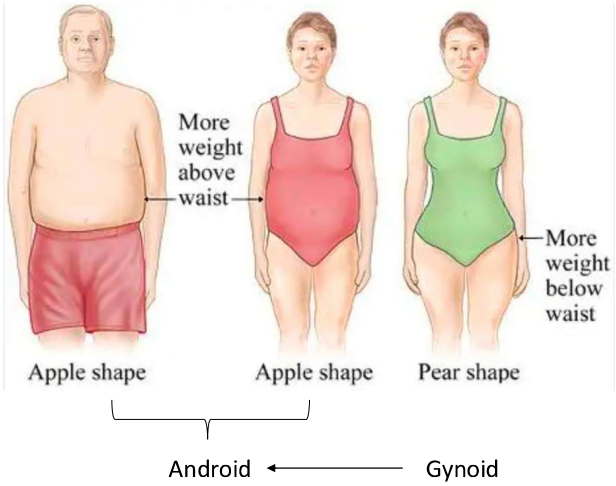
- Woman see a significant increase in cardiovascular disease after their menopause transition
  - 2.6 x risk in postmenopausal women
- Metabolic changes of Menopause
  - Lipids - Increase in total cholesterol, LDL, triglycerides and decrease in HDL
  - Glucose– Insulin resistance and risk of diabetes
  - Adipose deposition – Increase in visceral abdominal fat
  - Hypertension
- Disruptions in sleep worsen these changes

Metabolic Syndrome – ATIII definition

- Triglycerides >150 mg/dL
- HDL Cholesterol
  - Men <40 mg/dL
  - Women <50 mg/dL
- Fasting glucose >110 mg/dL
- Central Obesity Waist Circumference
  - Men >102 cm
  - Women >88 cm
- Blood Pressure >130/85 mm Hg

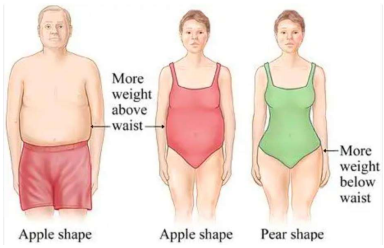
Body Composition

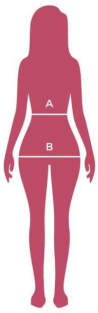
- Apple Shape = Android
  - Increase visceral fat
- Pear Shape = Gynoid



Body Composition

- Waist Hip Ratio (WHR)
  - AHA recognizes WHR as a positive predictor of CAD in patients with and without obesity
  - The Obesity Society recognizes WHR as markers of increased cardiometabolic risk





Waist Hip Ratio

$$WHR = \frac{\text{Waist Circumference (A)}}{\text{Hip Circumference (B)}}$$

A healthy WHR is:

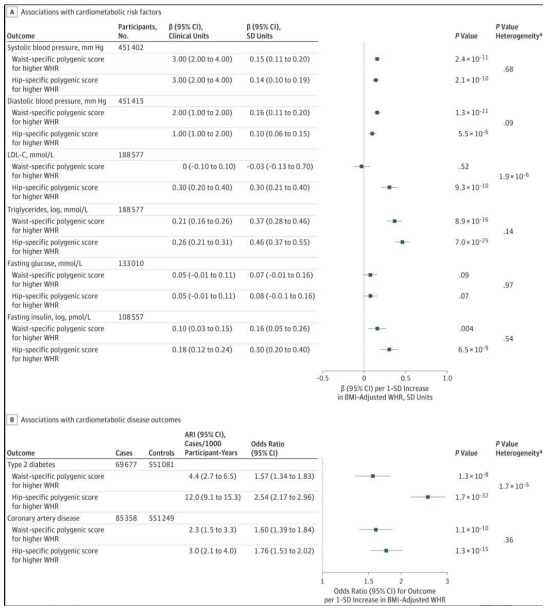
0.9 or less in men

0.85 or less for women

**Waist circumference is measured at the narrowest part of the waist and hip circumference is measured at the widest part of the hips.

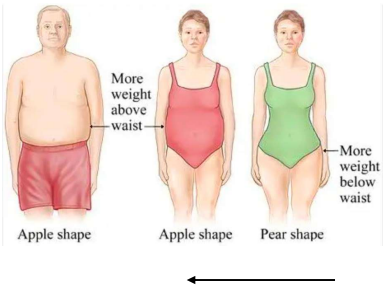
Body Composition

- Waist Hip Ratio
  - AHA recognizes WHR as a positive predictor of CAD in patients with and without obesity
  - The Obesity Society recognizes WHR as markers of increased cardiometabolic risk
  - JAMA study showing increase risk on most cardiometabolic risk factors



WHR and Estrogen

- Inverse relationship between WHR and estrogen
  - Estrogen promotes a gynoid fat distribution (lower WHR)
  - Favors subcutaneous fat in hips and thighs
  - Mediated through estrogen receptor signaling in adipose tissue
- After Menopause
  - Declining estrogen levels lead to a redistribution of fat from peripheral to central depots, resulting in an increased WHR
    - Estrogen upregulates antilipolytic alpha2A adrenergic receptors in subcutaneous adipocytes
  - Hormone therapy attenuates this shift



Musculoskeletal Syndrome of Menopause

- Increase in visceral fat added to decrease in muscle mass
- Estrogen deficiency
  - Impaired muscle protein synthesis
  - Increased muscle apoptosis
  - Reduced satellite cell proliferation
  - Heightened inflammatory signaling
  - END RESULT - Muscle atrophy and reduced muscle quality
- Estimated 10% muscle loss

Summary of Weight shift in Menopause

- Shift of adipose tissue from Gynoid to Android
- Increase WHR
- Increase risk of Metabolic Syndrome
  - Increase TGL
  - Decrease in LDL
  - Increase glucose
  - Increase visceral adipose tissue

- Could GLP-RA agonists help?

GLP-RA agonists and Menopause

- Estrogen deficiency leads to impaired GLP-RA secretion
- Should you treat with estrogen or GLP-RA? Or Both?
  - Ovariectomized rats lead to increased DPP-IV activity in plasma and WAT
  - Treated with 17B estradiol or liraglutide for 21 days
  - Estrogen blocked the DPP-IV in WAT and plasma
  - Liraglutide blocked DPP-IV in WAT ONLY
  - FAT MASS – Estradiol and Liraglutide EQUAL
  - **Liraglutide increased pro-inflammatory cytokines and inflammatory cells in WAT**

GLP-RA agonists
- Increased insulin secretion from pancreas
- Decreased gluconeogenesis and secretion
- Slow gastric emptying
- Decrease hunger

STEADY Health at Fulcrum Health

- STEADY Health
  - Sociality
  - Thoughts & Cognition
  - Emotions
  - Activity
  - Diet
  - Youthfulness

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Emotional Health
- Stay social
- Preserve your sleep
  - Get at least 7 hours
  - Moderate-High Intensity Exercise
  - Increase slow-wave sleep = NREM
    - Improve muscle repair
    - Improve glucose metabolism
    - Supress cortisol
    - Improve fatty acid oxidation
  - Decrease alcohol consumption
  - Get up and get out

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Activity

- Zone 2 Exercise
  - 30-45 minutes with weighted vest
- SIT vs. HIIT
- Resistance training
  - Lift heavy
  - 20% women train twice weekly
- Hand grip strength
- Prevention of osteopenia
- Prevention of sarcopenia

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Nutrition

- Hair loss
  - Iron rich foods
  - Consider testosterone's role
- Skin elasticity
  - 30% decline after menopause
  - Reduction of glycosaminoglycans and ceramides impairing water retention
  - Sunscreen!
  - Collagen

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Youthfulness

- Primary source is food
- Content
  - Avoid inflammatory foods
  - Limit alcohol
  - Increase anti-inflammatory foods
  - Protein – 1 g/lb of lean body mass
  - Carbs – Net carbs versus total carbs
  - Fat – Saturated fat versus unsaturated fats
  - Fiber – 25-30 g
- Timing
  - Intermittent Fasting

Supplements

Some Evidence

- Succinate based vitamins
- Creatine
  - Muscle growth
  - Cognition
- Taurine
- Sleep
  - Magnesium
  - Tart Cherry Juice
- Collagen
  - Skin, Intervertebral discs, Carotid intima
- Gut Health
  - Fiber
  - Probiotics
- Omega 3 FA

Potentially Problematic

- Phytoestrogens
  - Soy, Isoflavones, Wild Yam, Black Cohosh
- Dong Quai
- Evening primrose oil
- Ashwaganda
- Vitamin E

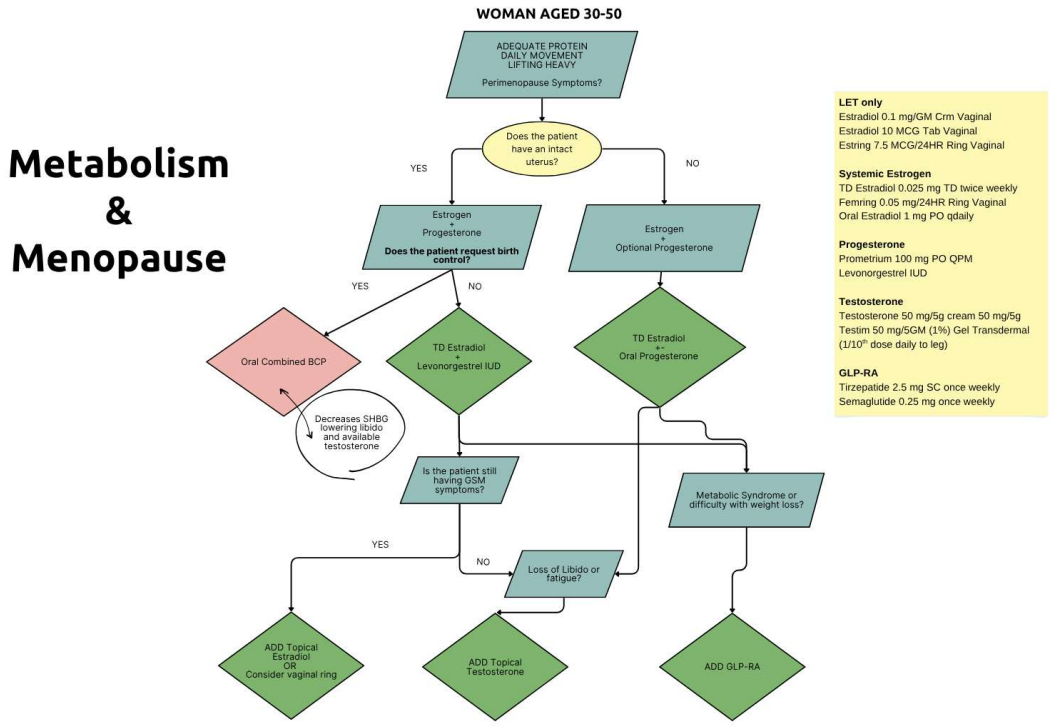
The Menopause Society
Non-hormonal options for Menopause Care

Hormone Replacement Therapy (HRT)

- Systemic HRT
  - Estradiol
    - Transdermal vs. oral vs. Vaginal Ring
  - Micronized progesterone
- Local Estrogen Therapy (LET)
  - Does not increase systemic hormone levels
  - Topical vs. Vaginal Ring
- Testosterone
- Non-hormonal options

Where to start

- Does the patient have an intact uterus?
- Does the patient want birth control?
- Family or personal history of blood clots/stroke?
- Family or personal history history of medullary thyroid cancer? Breast cancer? Any cancer?



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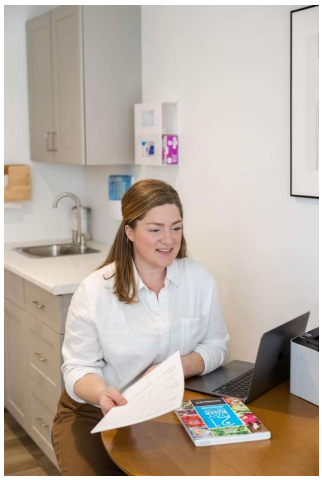
Clinical Resources

- The Menopause Society
  - https://menopause.org/
- Stacy Sims, PhD
  - https://www.drstacysims.com/



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Social Q&A for Menopause & Metabolism Health

QUESTIONS?

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