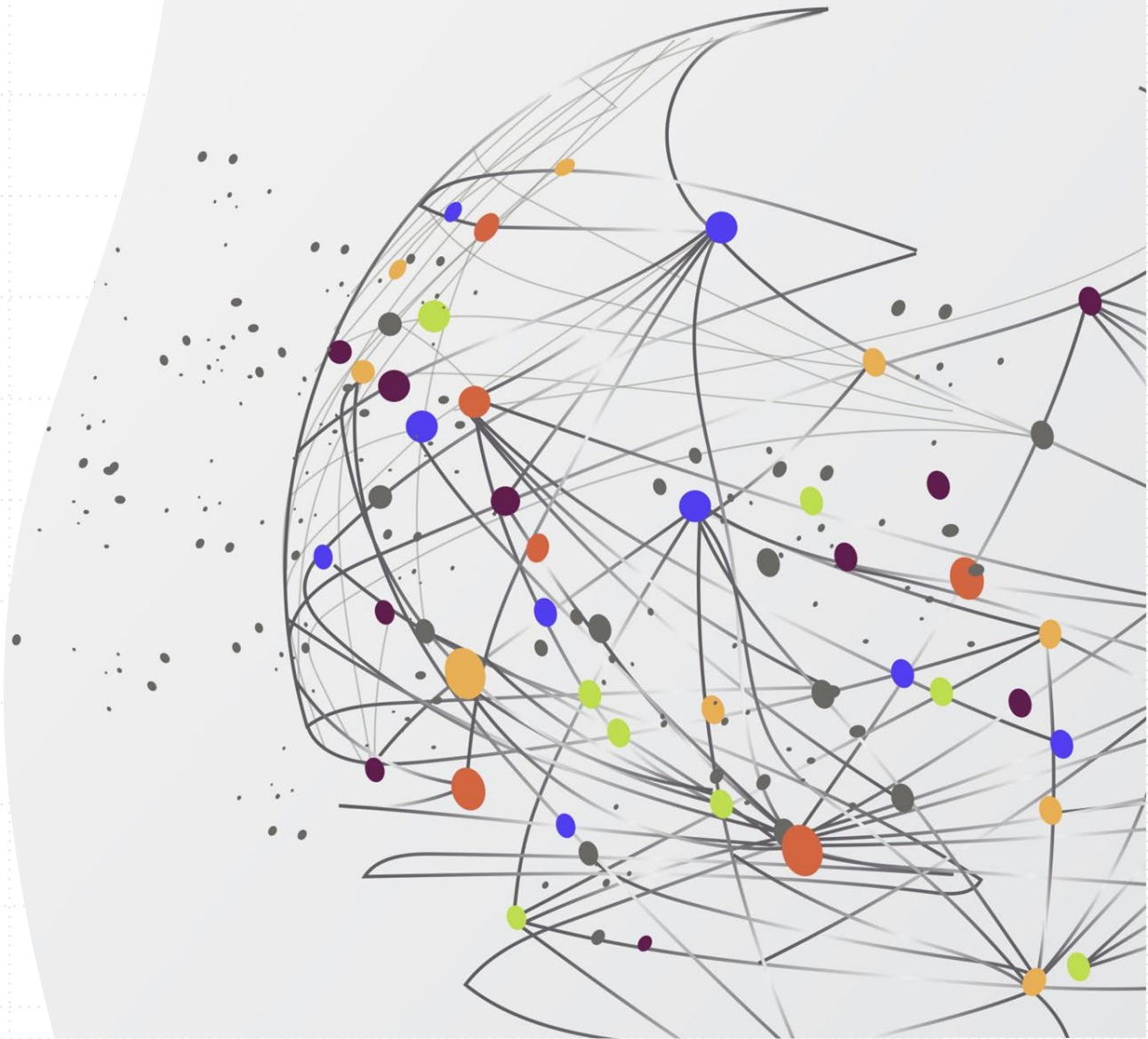
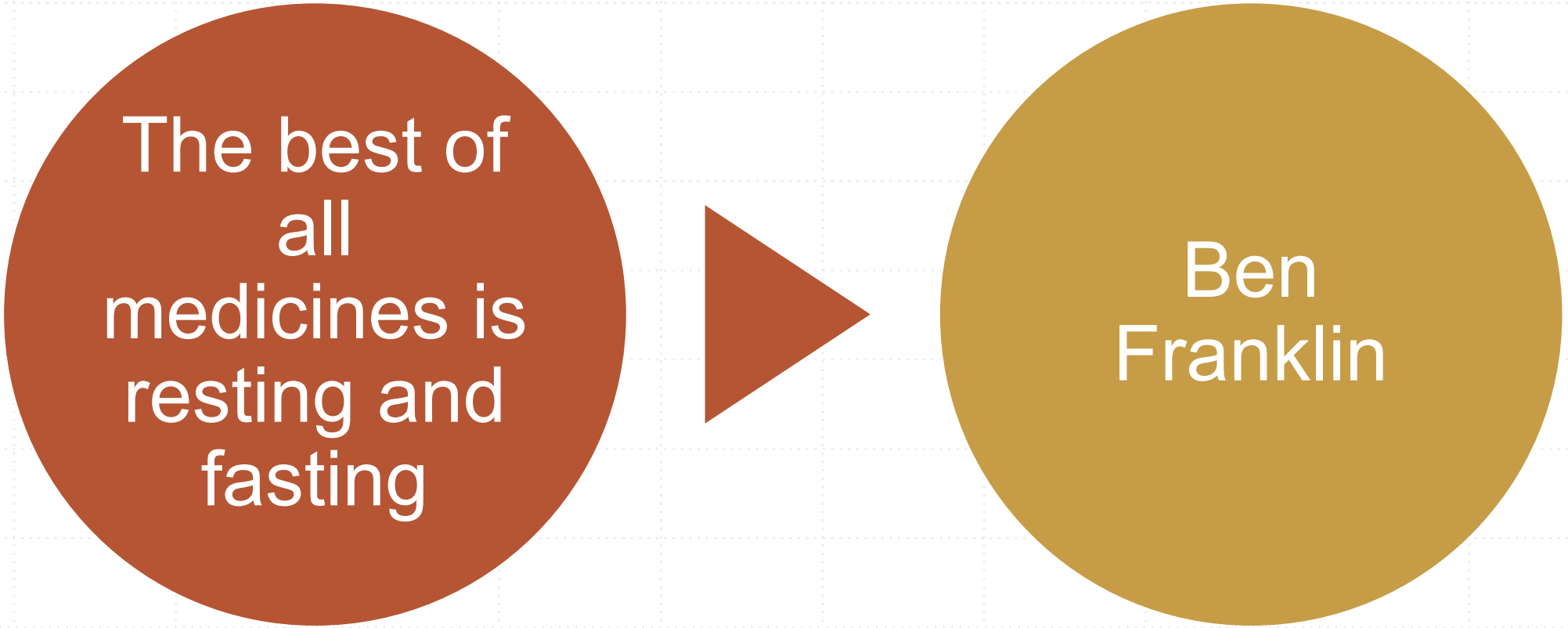
Metabolic Health, Fasting & Gender Differences

Cynthia Thurlow, NP



Quote


The best of all medicines is resting and fasting
Ben Franklin

Public Health Crisis

1 billion worldwide are obese

According to WHO, rates have tripled since 1975

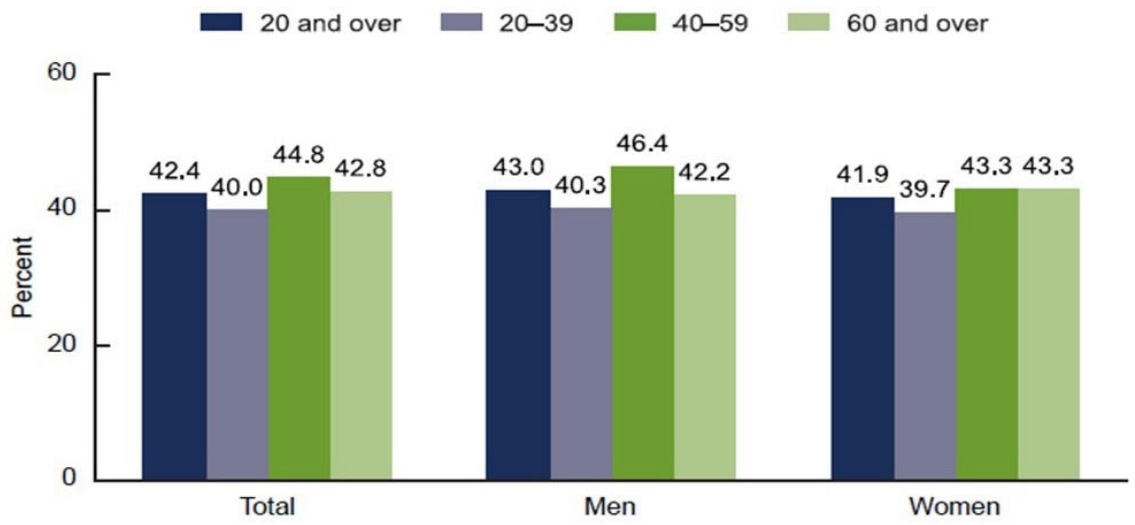
42% of Americans are obese, exacerbated by the pandemic, and has increased by 26% since 2008

A survey by the American Psychological Association: Pandemic averaged 30lbs of weight gain with a median of 15lbs, 10% gained more than 50lbs; changes in sleep and ETOH consumption also contributed

https://www.apa.org/news/press/releases/2021/03/one-year-pandemic-stress
CDC: Behavioral Risk Factors Surveillance System (BRFSS)

Metabolic Health Status in US

- 37.9% of men; 41.1% of women in the US are obese, twice as many as 3 decades ago
- 20% of children are overweight, three times as many as 3 decades ago
- In 2020, 16 states had adult obesity rates >35%
- 1/3 US are pre-diabetic
- **130 million Americans are insulin resistant or diabetic**
- 25% of US adults have NAFLD
- High blood sugar is linked to 8 out of top 10 leading causes of death
- Systemic and social inequalities: family income below the poverty line; highest prevalence (13.7-14.4%); less education/higher prevalence



NOTES: Estimates for adults ages 20 and over were age adjusted by the direct method to the 2000 U.S. Census population using the age groups 20–39, 40–59, and 60 and over. Crude estimates are 42.5% for total, 43.0% for men, and 42.1% for women. Access data table for Figure 1 External link (PDF, 97.2 KB) .
SOURCE: National Center for Health Statistics, National Health and Nutrition Examination Survey, 2017–2018.

Metabolic Health Markers

- Gender: Profound impact on metabolism
- Global prevalence men>women (Type 2 DM) (Munguia-Mongana)
- HDL <40 in men/<50 in women
- Triglycerides >150gm.dl
- Fasting glucose >100gm/dl, insulin >5gm/d0
- HTN >130/85
- Waist circumference >45 in men/>35 in women

https://pubmed.ncbi.nlm.nih.gov/27490920/

How have we gotten off course?

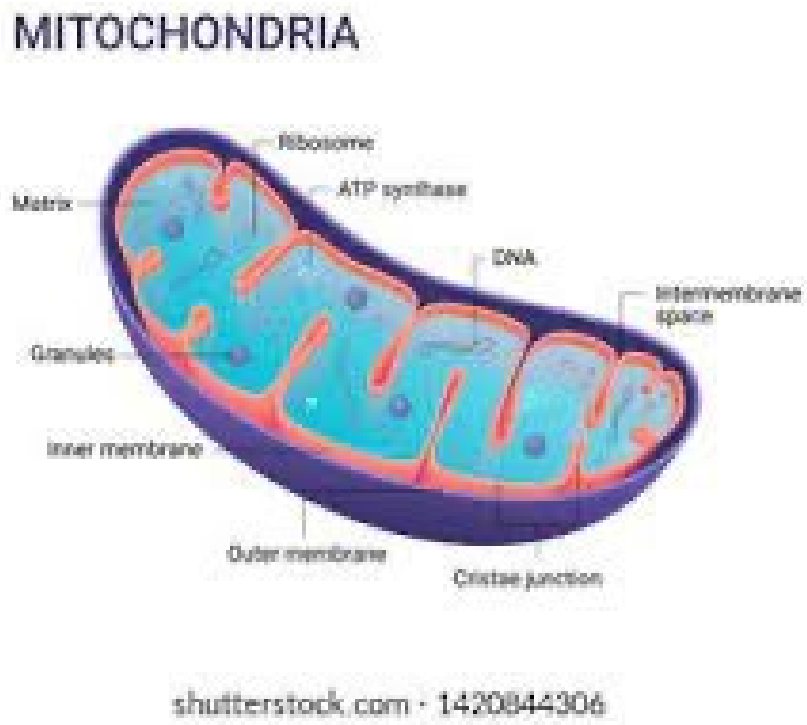
- Rise of the processed food industry $1 trillion dollar per year with $450 billion in profit
- Portion distortion: 23% more calories consumed now vs 1970
- Sedentary lifestyles: 1:4 Americans spends >8hrs/day sitting
- Meal Frequency: snacks/mini-meals
- Consumption of highly processed foods, including seed oils, sugar, soy
- Lack of prioritization for nutrition research dollars by the federal government

What is ONE strategy that can profoundly impact all of these?

- Intermittent Fasting

Why Fasting is Invaluable for Metabolic Health

- Fat oxidation: aka burns fat
- Brown vs white fat: role of metabolically rich/mitochondrial dense beige fat
- Promotes gut health: role of gut microbiome balance, aligns with circadian biology and internal clocks, role of the migrating motor complex (MMC) aka housekeeper of the small intestine propelling food residue and enterocytes forward; stimulates c-AMP an energy molecule used by gut bacteria that comprise the gut lining; role in serotonin production
- Promotes metabolic health: sustained energy, balanced hormones, less blood sugar dysregulation, less cravings, improved lipolysis
- Enhances mitochondrial function: produce 90% of the energy our bodies need to thrive; increases sirtuins, which are proteins that regulate fat and glucose metabolism, fight chronic inflammation, boost energy levels, increase alertness and repair damaged genetic material in cells



https://www.nature.com/articles/nrgastro.2012.57

Why Fasting is Invaluable for Metabolic Health (2)

- Role of NAD: provide gas for sirtuins; NAD declines with age, but can be improved with fasting and can lead to more energy and anti-aging benefits
- Role of AMPK: can help build new mitochondria through this enzyme; it is the body's master regulator of energy metabolism and promotes fat burning
- Autophagy : promotes mitochondrial health, prevents neurodegenerative disorders, reduces inflammation, strengthens immunity, protects against cancer
- Boosts Brain Health: BDNF, BHB, GH, clears beta amyloid plaques
- Increases immunity
- Reduces inflammation, slows aging

Impact of Insulin

- **A humble hormone from the pancreas** (Dr. Ben Bikman)
- Meal frequency can impact fat storage; if insulin remains high, you can develop IR and metabolic inflexibility
- 2018 study: fasting reverses IR and permitted pts to wean off of insulin and reduce their weight circumference and lose weight
- Another study: participants who fasted saw 3-6% reduction in their blood sugar, and a 20-31% decline in insulin levels. This suggested that fasting is equally as effective as traditional caloric restriction at accelerating weight loss, protect heart health and prevent Type 2 DM

How does fasting benefit hormones?

Fasting glucose: levels in plasma reflect the interplay between basal whole body glucose disposal and endogenous glucose production

Large cross-sectional study with 1188 indivduals, prevalence of impaired fasting glucose was higher in men than women (17 vs 13%)

Cohort of 8000 Swedish men and women evaluated for insulin action via OGTT, prevalence of impaired fasting glucose and diabetes was 2-fold higher in men compared to women

Based on large cross-sectional trails: men might be more prone to IR

Higher glucose uptake in female skeletal muscle when stimulated by physiologic insulin concentrations

Kuhl et al. Characteristics of subjects with early abnormalities of glucose tolerance in the Stockholm Diabetes Prevention Program; the impact of sex and Type 2 diabetes heredity. Diabetologia (2005) 48(1): 35-40
Munguia-Miranda et al, Impaired fasting glucose detection in blood donors population. Rev Med Inst Mex Seguro Sco (2009) 47 (1): 17-24

Quote

Being a woman is a terribly difficult task, since it consists principally in dealing with men

- Joseph Conrad

Gender Differences…it isn’t all equal

The Facts

Research : potential complexities of controlling for a woman's menstrual cycle serve as a deterrent for the inclusion of females in experimental design for both animal and human studies (gender inequality)

1977-1993 women of reproductive age were required to be excluded from Phase 1 clinical trials bc of concerns about potential teratogenic effects

Since then, there has been increasing emphasis on the inclusion of women in clinical trials as well as statistical analyses that specifically evaluate possible sex differences

Most studies: lab animals, men, obese menopausal women

Institute of Medicine Committee on Understanding the Biology of Sex and Gender Differences. Exploring the biological contributions to human health: does sex matter? Ed. Wizemann et al, National Academy, 2001

The lack of research on women….

- Is Troubling

Physical differences

- **Bone**
- **Skeletal muscle**
- Vasculature
- Liver
- Immune system
- Brain

Puberty

- Females gain more body fat vs males gain more lean muscle
- Females: peripherally & hips; males: waist
- Importance of estradiol
- Menarche: body fat of 17% and 22% for regular menstrual cycles

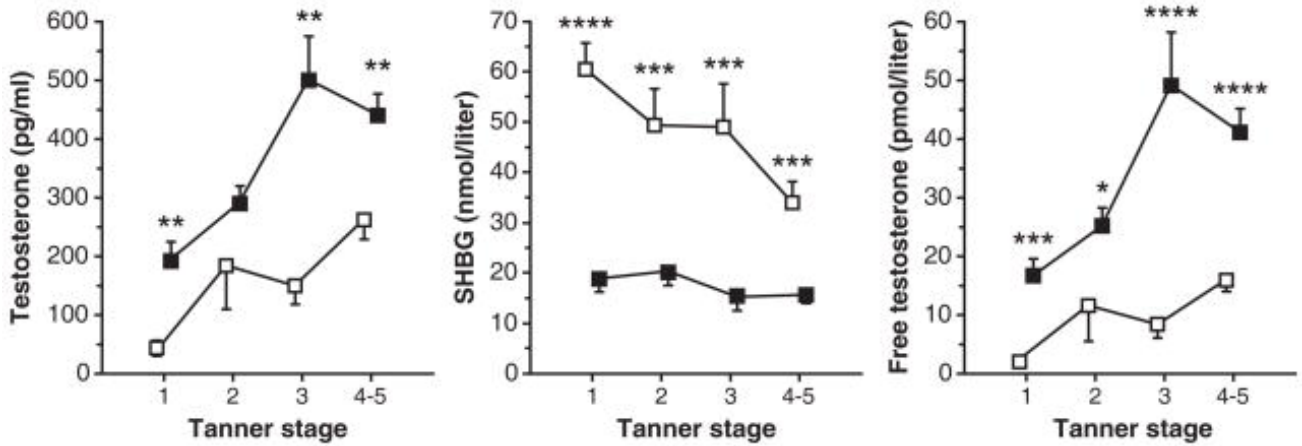


Figure 2

Total testosterone, SHBG, and free testosterone concentrations in obese (BMI-for-age percentile ≥ 95; solid squares) and normal-weight girls (BMI-for-age percentile < 85; open squares) grouped by Tanner stage. Data are shown as mean ± SEM. Differences were assessed with Wilcoxon rank sum tests: *, P < 0.05; **, P ≤ 0.01; ***, P ≤ 0.001; ****, P ≤ 0.0001 before Bonferroni correction. Conversion from conventional to SI units: total testosterone × 3.47 (nanomoles per liter). Data from McCartney *et al.* 2007(used with permission).

Adami, F., Benedet, J., Takahashi, L.A.R. *et al.* Association between pubertal development stages and body adiposity in children and adolescents. *Health Qual Life Outcomes* **18,** 93 (2020). https://doi.org/10.1186/s12955-020-01342-y

Men

- More muscle mass with higher output; higher capacity for anerobic metabolism
- More bone mass
- Lower body fat
- Related to impact of steroid hormones on muscle and bone growth (testosterone, IGF-1)

Women

- Skeletal muscle is a quantitatively important site for insulin stimulated glucose clearance; differences in muscle fibers that allow for greater nutritive flow
- Distinct gender dimorphisms in the intrinsic properties of skeletal muscle; gender has a stronger influence on gene expression than age and training status (Roth)
- Higher body fat deposition in women: impacts circulating adipokines, which impact metabolism in skeletal muscle by receptor binding
- Women 2/3 skeletal muscle mass of men; twice the adipose tissue than men
- 80% of osteoporosis in females
- Multifactorial: exercise, genetics, diet, contributions of testosterone and estrogen re: bone metabolism; decline in estrogen production is one of the key factors that predisposes menopausal women to the development of osteoporosis (Wizeman et al, 2001)

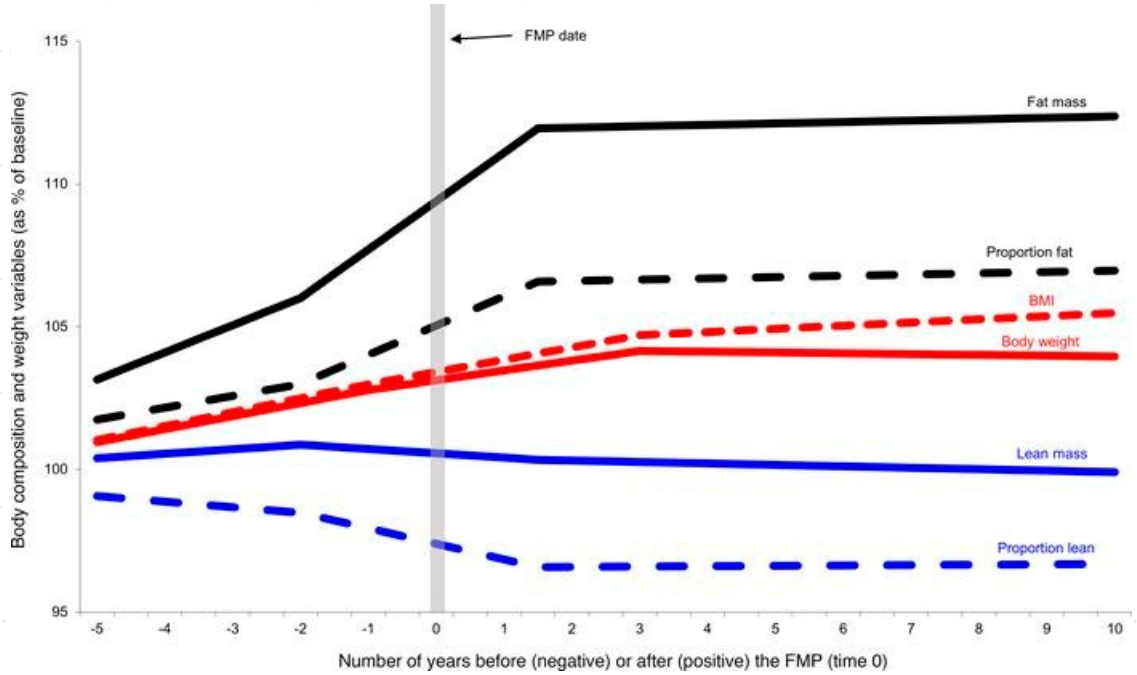
Menopause/andropause

- Men: decreased strength/energy, weight gain, sore muscles, low libido, insomnia
- 2006 HIM study: nearly 40% of US males >45yo had low T (13 million men)
- Causes: insulin resistance, estrogen mimicking chemicals

- Women: average age in US 51yo
- Weight gain, hot flashes, low libido, muscle loss, insomnia
- Exacerbated by insulin resistance/loss of insulin sensitivity , loss of estradiol, testosterone, progesterone

Body composition women

- Study of Women's Health Across the Nation (SWAN) cohort, over 3000 participants
- Rate of fat doubled at menopausal transition; lean mass declined; gains and losses continued until 2 years after the menopausal transition
- Net impact on the HPO (hypothalamic pituitary ovarian axis)
- Fat mass doubles 1-1.7%/yr, leading to 6% total gains in fat mass
- Or 1.6kg
- Role of estradiol and FSH, which help regulate energy balance
- FSH: role in beige fat, increased thermogenesis and activation of brown fat adipocytes
- Leptin levels (women) play a role in fat oxidation in skeletal muscle
- Role of adiponectin=insulin sensitivity



https://insight.jci.org/articles/view/124865

Fasting for Men and Women

Differences based on life stages: cycling, peak fertility vs non-cycling

Differences based on lifestyle factors: sleep quality, stress mgmt., exercise, anti-inflammatory nutrition, including low carb/keto

Cycling Women

- Role of Infradian rhythm (28-day cycle)
- Stages: follicular, ovulatory, luteal
- Fluctuations in energy, temperature, metabolism, glucose/insulin sensitivity, cortisol, sleep quality
- Differentiators: peak fertile years vs perimenopause (5-10 years preceding menopause)
- Five phases of perimenopause
- Perimenopause: sleep, stress, nutrition, exercise

Men and Menopausal women

Less hormonal flux, less issues with fasting

Men tend to lose body fat more easily

Menopausal women: focus in on sleep quality, stress mgmt., nutrition and exercise

Who should not fast

- Pregnant or breastfeeding women
- Hx of disordered relationship with food (binge eating, anorexia, bulimia)
- BMI < 18
- Children, teens
- Frail/elderly
- Recently hospitalized
- Best practice: always discuss the appropriateness of fasting with your healthcare team

Best practices for starting IF

- Stop snacking
- Start with a 12-13hr fast (dinner-breakfast)
- Reduce carbohydrate intake (ideally less than 50-75gm)
- Consume plain coffee, bitter teas, water and electrolytes
- Aim for 30-40gm of protein with each meal in your feeding window
- Add in healthy fats (if appropriate): ribeye vs filet; salmon vs cod
- Non-starchy veggies

Signs that fasting is not working for you

- Poor quality sleep
- Low energy
- Fatigue
- Poor cognition/brain fog
- Weight gain/truncal obesity
- Loss of menstrual cycle (barometer for women!)