Education

Energy & vitality during perimenopause and beyond

Guest speaker

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Owner of @Uberhealth, University lecturer, speaker, mentor and practitioner for more than 28 years

vital.ly Pro

Agenda

Perimenopause & Menopause

Metabolism and mitochondria

Muscle mass and body fat

Nervous system, stress and HRV

Macronutrients and eating for exercise

Somatotypes and circadian rhythms

Putting it all together

National Institute of Health (NIH)

In 1985 the NIH published a report warning that ‘the historical lack of data/research focusing on women's health concerns has compromised the quality of health information and care available to women (USA)

- It took until 1993 for Congress to pass a bill requiring women to be included in clinical trials
- Prior to this, women had been excluded from studies of most drugs for ‘safety’ reasons
- To this day, some of the most underfunded diseases are the ones that primarily affect women (CFS, migraine, anorexia and endometriosis)
- Science often overlooks sex specific variable
- Australia still has no formal regulations that require women to be used in studies (as of 2022)

Menopause and perimenopause

Menopause

- Hormonal variations will cause changes that are as complex to study as puberty
- Fluctuations of perimenopause hormones are so variable that they affect all body systems
- Clinical trials are often too reductionistic to translate for individual women

Gaps in Menopause Knowledge

Sun Kyoung Yum, Tak Kim

Department of Obstetrics & Gynecology, Korea University Anam Hospital, Seoul, Korea

The average middle aged woman goes through a volatile period of endocrine fluctuations as she passes through menopause and the stages that precede and follow it. Ovarian hormones are steroid hormones. They readily cross the cell and nuclear membranes and influence transcription of numerous genes. Such influences are tissue specific and state specific. In short, changes in ovarian hormones mean that a women will experience changes in her entire body systems. When an individual woman's constitutional factors, pathologic states, medications, environmental exposures are taken into consideration, the integrated changes become too complex to predict. Inter-study sampling differences with the complexities in the backdrop may have led to conflicting conclusions in menopause research. This paper reviews some of the controversies in the care of menopausal women. **(J Menopausal Med 2014;20:47-51)**

How women are different

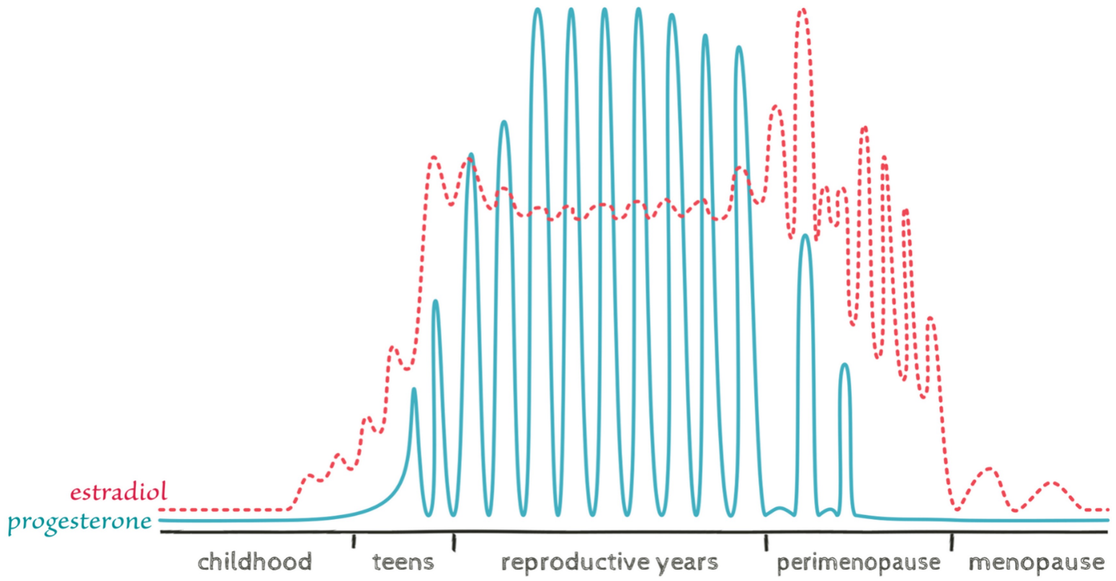
- Microbiome
- HPA axis
- Cardiovascular system
- Sleep architecture
- Insulin sensitivity
- Cellular detoxification
- Mitochondria
- Immune system
- Substrate utilisation with exercise
- Body composition and metabolism

30% of the human genome is behaving differently in men and women

The statistics

- Average life expectancy of women is 81
- Average age to hit menopause is 51/52
- Perimenopause can be 1-7 years on average
- 40% of life will be post menopause

Hormonal changes of perimenopause



Oestrogen and progesterone

E2 – Oestradiol/Estradiol

- Anabolic
- Supports structure and function of muscles
- Declines with age
- With loss = harder to maintain and make muscle
- Promotes insulin sensitivity
- Regulate hunger and satiety hormones
- Increases serotonin and prevents its breakdown
- Helps control cortisol levels
- Helps calcium absorption and its urinary loses

Progesterone

- Catabolic
- Anti-inflammatory
- Assist in bone density
- Supports grey matter in the brain and BDNF
- Helps with pain tolerance, calming and antianxiety
- Stabilises connective tissue

Recalibration of perimenopause and beyond

Possible metabolic consequences

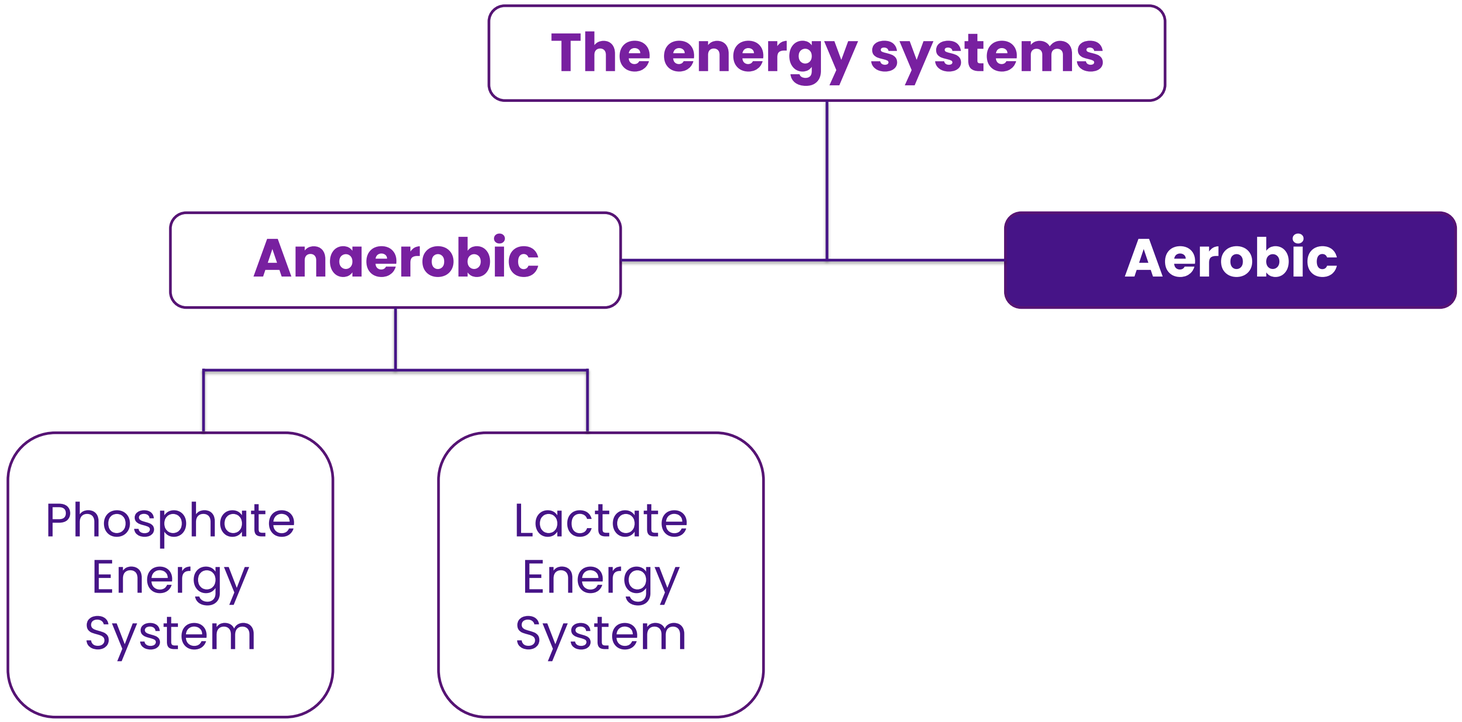
1. **Loss of progesterone:**
   Destabilisation of the HPA axis, sleep disturbance, increased androgen exposure

2. **High & fluctuating estrogen:**
   Histamine and mast cell activation, irritability and sleep disturbance, estrogen withdrawal

3. **Testosterone dominance:**
   Insulin resistance, weight gain, and shift from gynoid to android body shape

4. **A drop in oxytocin:**
   Anxiety, lower libido, sleep disturbance, increased appetite, insulin resistance

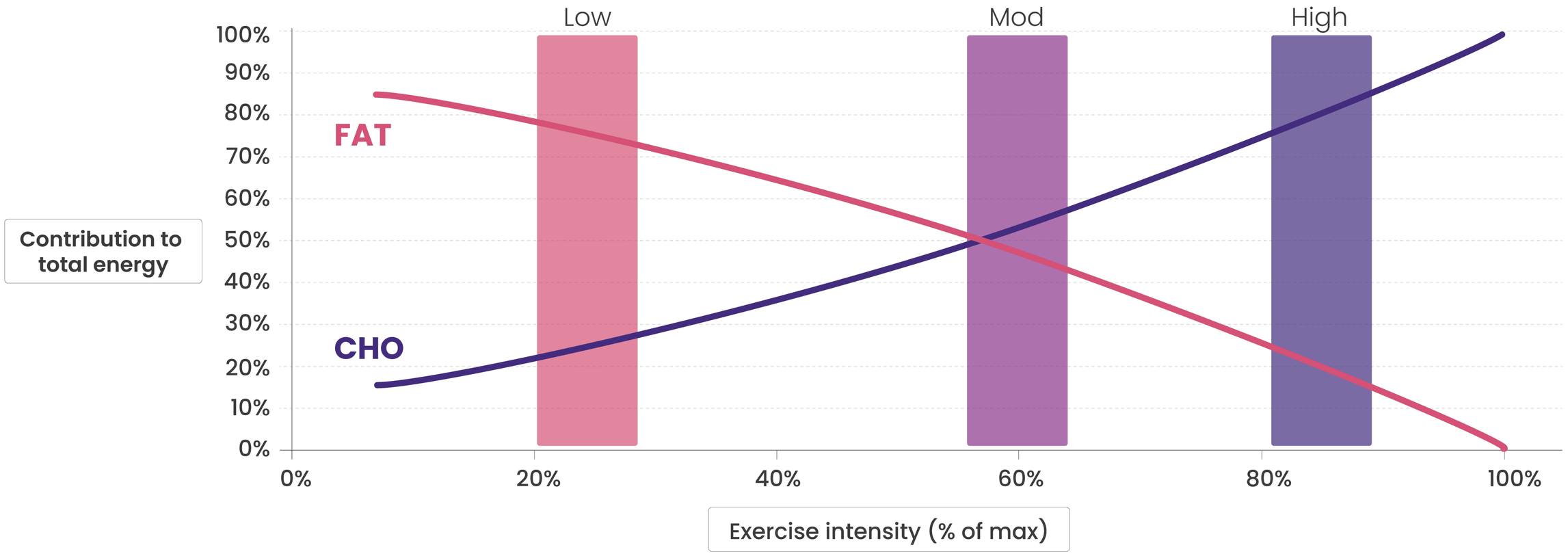
5. **Eventual shift to lower estrogen:**
   Temporary energy crisis


The energy systems
Anaerobic
Aerobic
Phosphate Energy System
Lactate Energy System

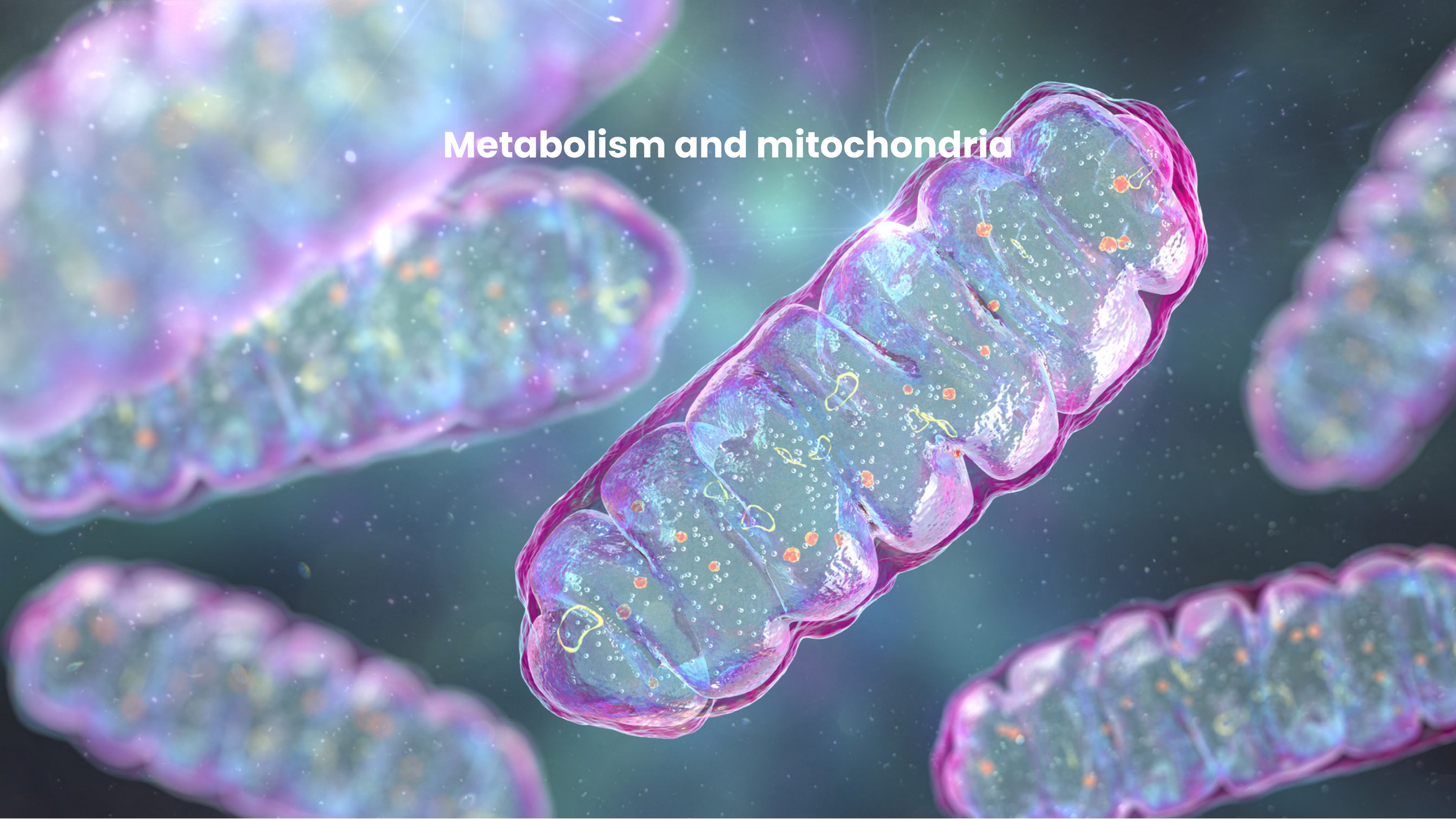
Energy for muscle contraction

	Aerobic	Lactate	Phosphate (ATP-PC)
Intensity of effort	Low intensity – up to 60% of max effort	High intensity 60-95% of max effort	**Very high intensity** 95-100% of max effort, explosive
Duration	At low intensity there is no limit	At 95% max lasts 30 seconds At 60% lasts about 30 minutes	10 seconds
Fuel	• Carbohydrates • Proteins • Fats	**Carbohydrate in the form of** • Muscle glycogen • Blood sugar	Phosphocreatine (PC)
Waste or by-product	Carbon dioxide and water	Lactic acid	No waste product
Recovery time	Time to replace fuel stores	It takes 20 minutes to 2 hours to break down the lactic acid	**Very quick** 50% - 30 seconds 100% - 2 minutes

Usage of carbohydrate and fat during exercise



Metabolism and mitochondria



Mitochondria

Supporting mitochondria

- Healthy insulin levels
- Oestrogen and progesterone
- Adequate melatonin production
- Healthy thyroid function
- Exercise/movement
- Intermittent fasting
- Circadian rhythm alignment
- Adequate sleep/rest

Damage to mitochondria

- Alcohol, smoking
- Pesticides, antibiotics
- Statins, paracetamol
- Lack of exercise, loss of muscle
- Vegetables oils (diet high in Omega 6)
- Overeating, high fructose corn syrup consumption

Issues of Energy Production

- Dysfunction in the mitochondria creates issues with aerobic respiration and a move to anaerobic pathways
- Increased fatigue and less fat being burned as fuel
- Stress and sleep deprivation cause oxidative damage to mitochondria
- High blood glucose increases production of ROS
- Increased ROS inhibits insulin signalling pathways and interferes with the oxidation of Acetyl CoA
- Increasing lipid and free fatty acid deposition in insulin target tissues
- Contributing to obesity, Type 2 diabetes and potentially PCOS

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ORIGINAL PAPER

WILEY Aging Cell

Metformin inhibits mitochondrial adaptations to aerobic exercise training in older adults

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Abstract

Metformin and exercise independently improve insulin sensitivity and decrease the risk of diabetes. Metformin was also recently proposed as a potential therapy to slow aging. However, recent evidence indicates that adding metformin to exercise antagonizes the exercise-induced improvement in insulin sensitivity and cardiorespiratory fitness. The purpose of this study was to test the hypothesis that metformin diminishes the improvement in insulin sensitivity and cardiorespiratory fitness after aerobic exercise training (AET) by inhibiting skeletal muscle mitochondrial respiration and protein synthesis in older adults (62 ± 1 years). In a double-blinded fashion, participants were randomized to placebo (n = 26) or metformin (n = 27) treatment during 12 weeks of AET. Independent of treatment, AET decreased fat mass, HbA1c, fasting plasma insulin, 24-hr ambulant mean glucose, and glycemic variability. However, metformin attenuated the increase in whole-body insulin sensitivity and VO_2max after AET. In the metformin group, there was no overall change in whole-body insulin sensitivity after AET due to positive and negative responders. Metformin also abrogated the exercise-mediated increase in skeletal muscle mitochondrial respiration. The change in whole-body insulin sensitivity was correlated to the change in mitochondrial respiration. Mitochondrial protein synthesis rates assessed during AET were not different between treatments. The influence of metformin on AET-induced improvements in physiological function was highly variable and associated with the effect of metformin on the mitochondria. These data suggest that prior to prescribing metformin to slow aging, additional studies are needed to understand the mechanisms that elicit positive and negative responses to metformin with and without exercise.

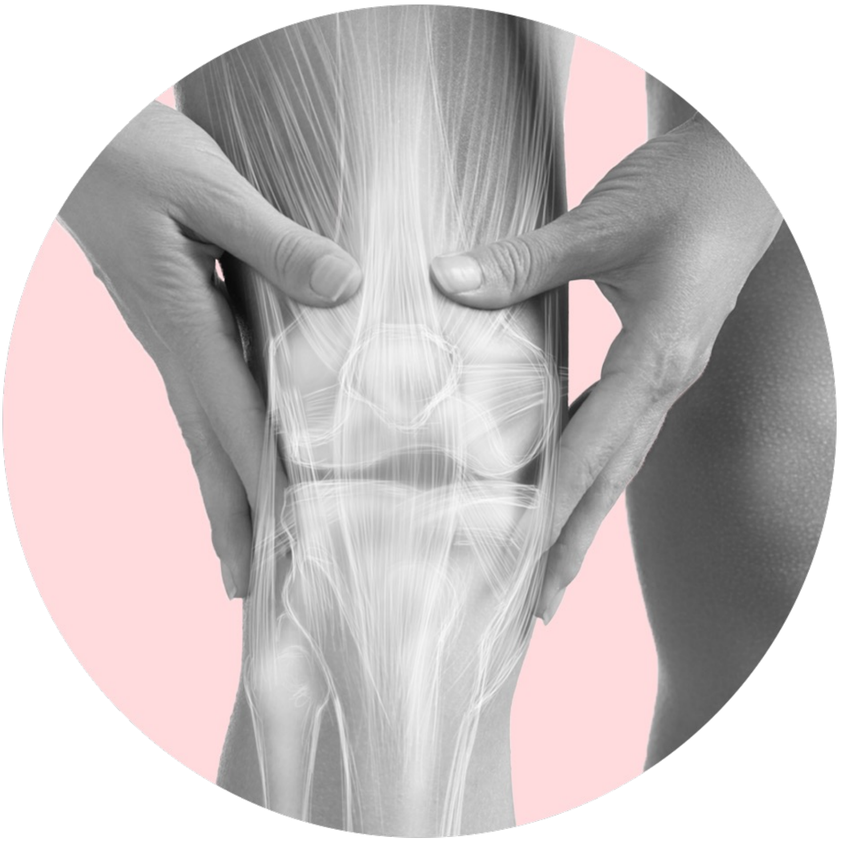
KEYWORDS
aging, healthspan, protein synthesis, proteostasis, telomere

Nutrients to Support Mitochondria and ATP

- **Coenzyme Q10** – cellular respiration, mitochondrial function, reduce ROS, antioxidant, membrane stabiliser
- **Curcumin** – reduce chronic and acute inflammation, cox 1 and 2 inhibitor
- **Magnesium and taurine**
- **Probiotics** – microbiome, gut, immune support
- **Carnitine** – Fatty acid metabolism within the mitochondria
- **B12** – energy production and red blood cells
- **Glutathione** – antioxidant and mitochondrial health
- **Alpha lipoic acid** – antioxidant, cell metabolism that leads to ATP production
- **Vitamin C** – antioxidant and biosynthesis of carnitine
- **Omega 3 fatty acids** -mitochondria membrane phospholipid component
- **Zinc** - inhibits mitochondrial ROS generation
- **Selenium** – antioxidant
- **Polyphenols**

Sarcopenia and mitochondria

- Loss of muscle means loss of mitochondria
- Maintain muscle mass = maintain mitochondrial numbers and function, slows the aging process
- Periodized aerobic training in a low carb state (1-2 times per week) can activate mitochondrial biogenesis pathways (Bartlett et al., 2015)
- Strength training 2-3 times week to maintain muscle
- Adequate protein intake to maintain muscle mass
- Exercise benefits glucose and lipid metabolism, skeletal muscle function and growth, maintain bone density and assists insulin sensitivity in adipose tissue



To counteract sarcopenia

- Resistance training is the most potent and cost-effective treatment to prevent sarcopenia
- Protein intake 1.6-2.0gm/kg/day or higher to maximally stimulate MPS
- Leucine at >4.5gm per day in conjunction with strength training
- Creatine, adequate vitamin D and Omega 3's

(Thomas, Erdman, Burke, 2016) (Phillips, 2012) (Mettler, Mitchell, Tipton, 2010)(Phillips, Van Loon, 2011)

nutrients

MDPI

Review

Nutritional Supplements to Support Resistance Exercise in Countering the Sarcopenia of Aging

James McKendry, Brad S. Currier, Changhyun Lim, Jonathan C. Mcleod, Aaron C.Q. Thomas and Stuart M. Phillips *

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check for updates

Abstract: Skeletal muscle plays an indispensable role in metabolic health and physical function. A decrease in muscle mass and function with advancing age exacerbates the likelihood of mobility impairments, disease development, and early mortality. Therefore, the development of non-pharmacological interventions to counteract sarcopenia warrant significant attention. Currently, resistance training provides the most effective, low cost means by which to prevent sarcopenia progression and improve multiple aspects of overall health. Importantly, the impact of resistance training on skeletal muscle mass may be augmented by specific dietary components (i.e., protein), feeding strategies (i.e., timing, per-meal doses of specific macronutrients) and nutritional supplements (e.g., creatine, vitamin-D, omega-3 polyunsaturated fatty acids etc.). The purpose of this review is to provide an up-to-date, evidence-based account of nutritional strategies to enhance resistance training-induced adaptations in an attempt to combat age-related muscle mass loss. In addition, we provide insight on how to incorporate the aforementioned nutritional strategies that may support the growth or maintenance of skeletal muscle and subsequently extend the healthspan of older individuals.

Keywords: aging; protein; diet; nutrition; exercise

Strength training

- Approximately 20% women engage in strength training 2+ times per week
- We start losing muscle around age 40 but it becomes more pronounced at peri-menopause
- Loss of hormones (especially oestrogen) accelerates your loss of muscle mass and bone density

Studies have shown lifting weights even 1 time per week to decrease risk of heart attack, stoke and CV risk

(Thomas, Erdman, Burke, 2016) (Phillips, 2012) (Mettler, Mitchell, Tipton, 2010)(Phillips, Van Loon, 2011)

Effect of weighted exercises on bone mineral density in post menopausal women. A systematic review

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Affiliations + expand

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Abstract

Purpose: Osteoporosis is both preventable and treatable with exercise playing an important role in osteogenesis. The purpose of this systematic review was to determine which specific exercise programs utilizing weights were effective in maintaining or increasing bone mineral density (BMD) in postmenopausal women.

Methods: A computerized search of the MEDLINE, CINAHL, EMBASE, PEDro, and Science Citation databases was conducted for the period 1990 through February 2005. The search was performed using English language-only keyword searches using MESH terms osteoporosis, postmenopausal, exercise, weight training, and bone mineral density. A total of 20 articles was critically evaluated for the quality of an intervention study using the criteria developed by MacDermid. An expert on the topic was asked to review the list of articles for omissions.

Results: The review revealed evidence to support the effectiveness of weight training exercises to increase BMD in postmenopausal women. The increases in BMD were site-specific and required high loading with a training intensity of 70% to 90% of 1 RM for 8 to 12 repetitions of 2 to 3 sets performed over one year duration.

Conclusion: Weighted exercises can help in maintaining BMD in postmenopausal women and increasing BMD of the spine and hip in women with osteopenia and osteoporosis. The exercise program must be incorporated into a lifestyle change and be lifelong due to the chronic nature of bone loss in older women.

Exercise

- Aerobic for cardiovascular health and mitochondrial biogenesis, reduces insulin resistance and elevates mood
- Strength/lifting heavy – maintain and build muscle, bone density, increase metabolism, reduces insulin resistance and improves body composition
- HIIT/sprint training – stimulate MPS, metabolic enhancement, increase cardiovascular health, decreases waist circumference and improves BMI
- Stabilising/Plyometric exercise (jump, skip, side to side) supports bone, muscle and connective tissue
- Walking, yoga, Pilates, stretching and core work increase flexibility, limit cortisol, improve posture and aid in injury prevention

@stacysims – Next Level book, website
@steph_gaudreau – website, podcast etc

Pre-exercise eating

- Fasted only 1-2 times per week (aerobic only)
- Small carbohydrate snack before (10-50g)
- Protein or BCAA’s can be an alternative (10-15g)
- Decreases cortisol and stress on the body
- Energy for exercise! Stronger, harder and recover better
- Supports immune system

Post exercise fuelling window

- 1-2 hours, optimum is 30ish minutes
- Glycogen replacement, glucose control
- Muscle recovery and synthesis (MPS)
- Catabolic to anabolic
- Decreases cortisol
- Supports microbiome
- Reduces risk of low energy availability (LEA)
- Supports immune system
- Eat a meal not a snack
- 3:1 or 2:1 ratio of Carb:protein

Macronutrients

Carbohydrates

- Rest days/light exercise: 2-2.5g/kg/day
- Exercise of 1-2 hours: 2.5-3g/kg/day
- Exercise of 2+ hours: 3-5g/kg/day
- Focus on intake pre- and post-exercise

Protein

- 1.6-2.2g/kg/day
- Higher amounts on strength days or weight loss
- Lower end on endurance or light exercise days
- 30-40grams with in 30-45 minutes post training

With every snack

Fat

- .75-1.25g/kg/day
- Depends on exercise volume and body fat goals

and body type

Heart rate variability (HRV) (doi.org/10.3389, www.elitehrv.com)

- The best-functioning hearts react to and recover from stressors quickly, causing heartbeat intervals to vary
- Progesterone has a calming effect on autonomic nervous system
- Vagal tone is a great indicator of how well we can relax after experiencing stress
- Its an interplay of sympathetic and parasympathetic NS
- Describes the variability in time between heart beats
- Higher HRV = more resilient to stress
- Lower HRV = less stress resilient, can be a sign of inflammation, fatigue, poor sleep, chronic pain etc.

Supporting HRV flexibility and the nervous system

- Breathing exercises
- 8 hours of sleep, rest and naps
- Hydration, less alcohol
- Healthy diet (leafy greens)
- Work life balance, gratitude
- Time in nature, yoga, stretching
- Meditation, weighted blanket
- Whoop band, Oura ring etc.
- Sunlight and outdoor exercise
- Breakfast, especially protein by 10am
- Vagal nerve tone (sing, hum, gargle, chewing gum)
- Herbs for the nervous system such as; Withania, Passionflower, Ziziphus, Lemon balm
- Zinc, B complex, magnesium, taurine and glycine

Nervines and adaptogens

- Skullcap
- Ziziphus
- Motherwort
- Passionflower
- Valerian
- Melissa

Target the HPA axis and help with energy, fatigue, inflammation, cortisol levels, anxiety and vasomotor symptoms

- Schisandra
- Withania
- Rhodiola
- Rehmannia
- Ginsengs
- Codonopsis
- Astragalus
- Mushrooms
- Licorice

Metabolic effects of menopause

Compared pre-, peri- and post-menopausal women and their body composition, fat distribution and metabolism both at rest and during exercise.

Perimenopause experiences

- vasomotor symptoms
- advanced changes in body comp
- increased risk of osteoporosis, CVD and metabolic syndrome
- accelerated loss of lean body mass and bone density

Perimenopause is the most opportune window for lifestyle intervention!

Menopause Is Associated With Postprandial Metabolism, Metabolic Health and Lifestyle: The ZOE PREDICT Study

18 Pages • Posted: 11 Mar 2022

Kate Bermingham
King's College London - Department of Twin Research and Genetic Epidemiology

Inbar Linenberg
Zoe Global Limited

More...

Abstract

Background: The menopause transition is associated with unfavourable alterations in health. However, postprandial metabolic changes and their mediating factors are poorly understood.

Methods: The PREDICT 1 UK cohort (n=1002; pre- n=366, peri- n=55, and post-menopausal females n=206) assessed phenotypic characteristics, anthropometric, diet and gut microbiome data, and fasting and postprandial (0-6h) cardiometabolic blood measurements, including continuous glucose monitoring (CGM) data. Differences between menopausal groups were assessed in the cohort and in an age-matched subgroup, adjusting for age, BMI, menopausal hormone therapy (MHT) use, and smoking status.

Findings: Post-menopausal females had higher fasting blood measures (glucose, HbA1c and inflammation (GlycA), 6, 5 and 4% respectively), sugar intakes (12%) and poorer sleep (12%) compared with pre-menopausal females ($p<0{\cdot}05$ for all). Postprandial metabolic responses for $glucose_{2hiauc}$ and $insulin_{2hiauc}$ were higher (42 and 4% respectively) and CGM measures (glycaemic variability and time in range) were unfavourable post- versus pre-menopause ($p<0{\cdot}05$ for all). In age-matched subgroups (n =150), postprandial glucose responses remained higher post-menopause ($peak_{0\text{-}2h}$ 4%). MHT was associated with favourable visceral fat, fasting (glucose and insulin) and postprandial ($triglyceride_{6hiauc}$) measures. Mediation analysis showed that associations between menopause and metabolic health indicators (visceral fat, $GlycA_{360mins}$ and glycemia ($peak_{0\text{-}2h}$)) were in part mediated by diet and gut bacterial species.

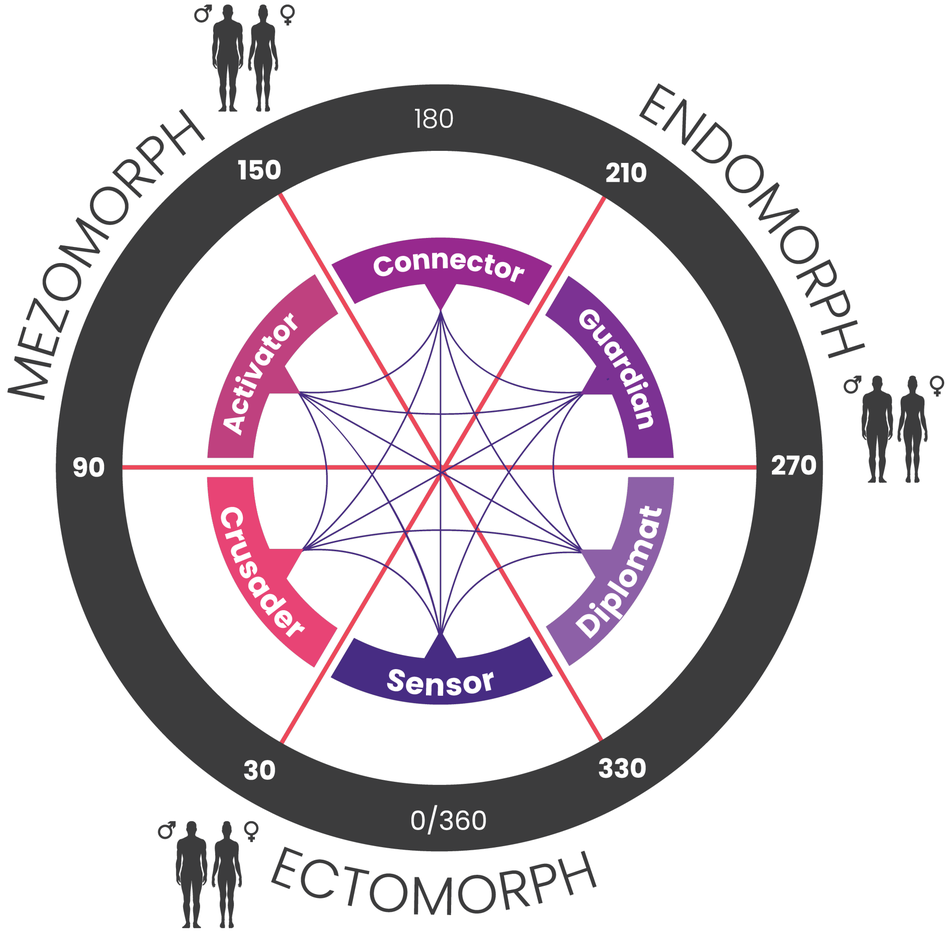
Interpretation: Findings from this large scale, in-depth nutrition metabolic study of menopause, support the importance of monitoring risk factors for type-2 diabetes and cardiovascular disease in mid-life to older women to reduce morbidity and mortality associated with oestrogen decline.

Reasons for weight gain

- Gut dysbiosis
- Chronic inflammation
- Thyroid issues
- Nervous system dysregulation
- Insulin resistance, fatty liver
- Medications
- Loss of muscle/sarcopenia
- Lack of exercise
- Mitochondrial dysfunction/loss

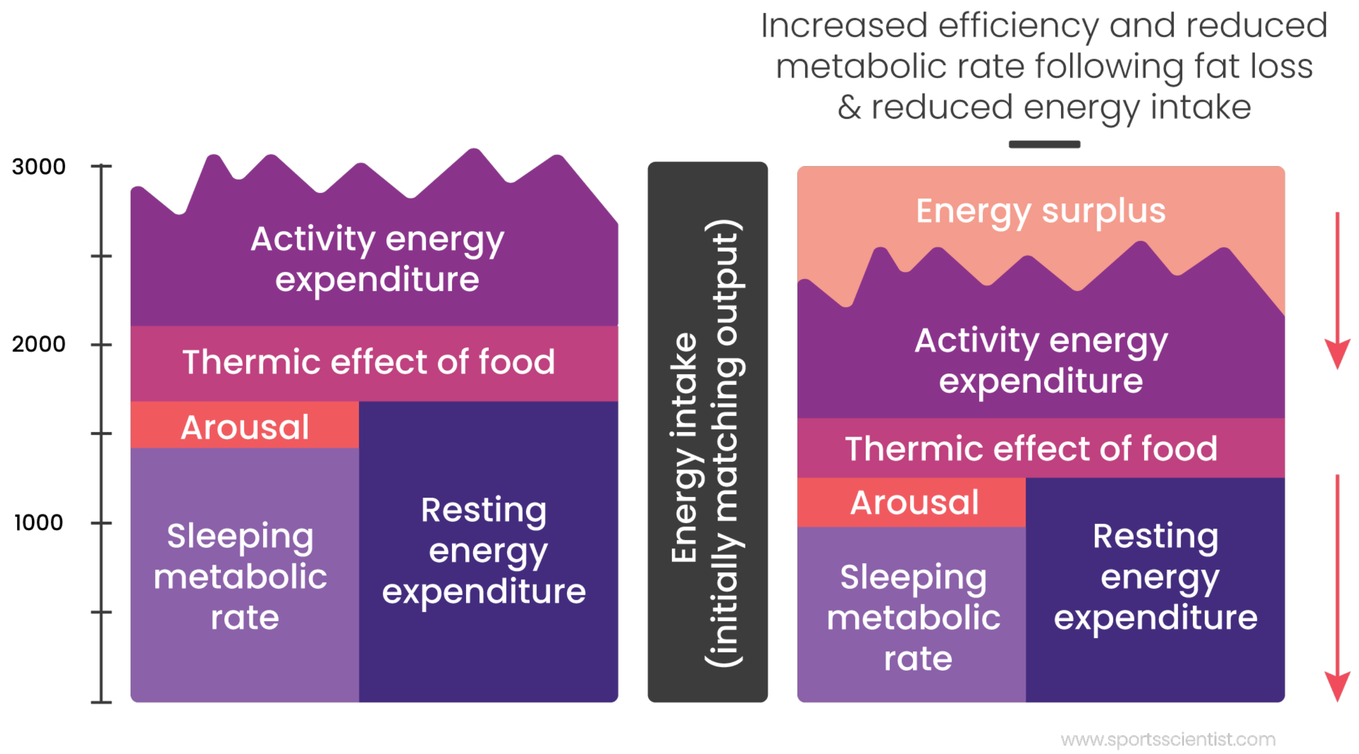
Parameters to measure

- Weight
- Body measurements (chest, waist, bum/hips)
- Lean body mass/muscle mass
- Body fat (19-32% considered healthy)
- DEXA, Bioimpedance or bodpod
- Get a baseline of your measurements just like we do with hormones
- Know your body type/somatotype (ph360.me)



Metabolism

- Thermic effect of food 10%
- Basal metabolic rate 70%
- Exercise and movement 20% (most variable)
- Set point theory



Adaptive Thermogenesis (AT)

- The metabolic alteration to minimise the degree of energy deficit created by continual energy restriction (CER)
- One study found a decrease in total daily energy expenditure (TDEE) by 6-18% due to AT (doi:10.1038/ijo.2010.184.)
- Decrease thyroid hormones (T3 and T4)
- Change in appetite regulating hormones (ghrelin/leptin)
- Potential increase in cortisol
- Do not under fuel!

Cortisol - The Stress Hormone

Intermittent dieting

(doi:10.3390/sports7010022)

- Intermittent energy restriction
- Used to decrease fat mass while sparing fat free mass/muscle
- A break in calorie restriction will attenuate some of the adaptive responses to long term calorie restriction
- One study found alternate day fasting only decreased total daily energy expenditure (TDEE) by 1%
- 2/7 or 14/28 days

Open Access | Published: 17 August 2017

Clinical Studies and Practice

Intermittent energy restriction improves weight loss efficiency in obese men: the MATADOR study

N M Byrne, A Sainsbury, N A King, A P Hills & R E Wood

International Journal of Obesity **42**, 129–138 (2018) | Cite this article

76k Accesses | **560** Altmetric | Metrics

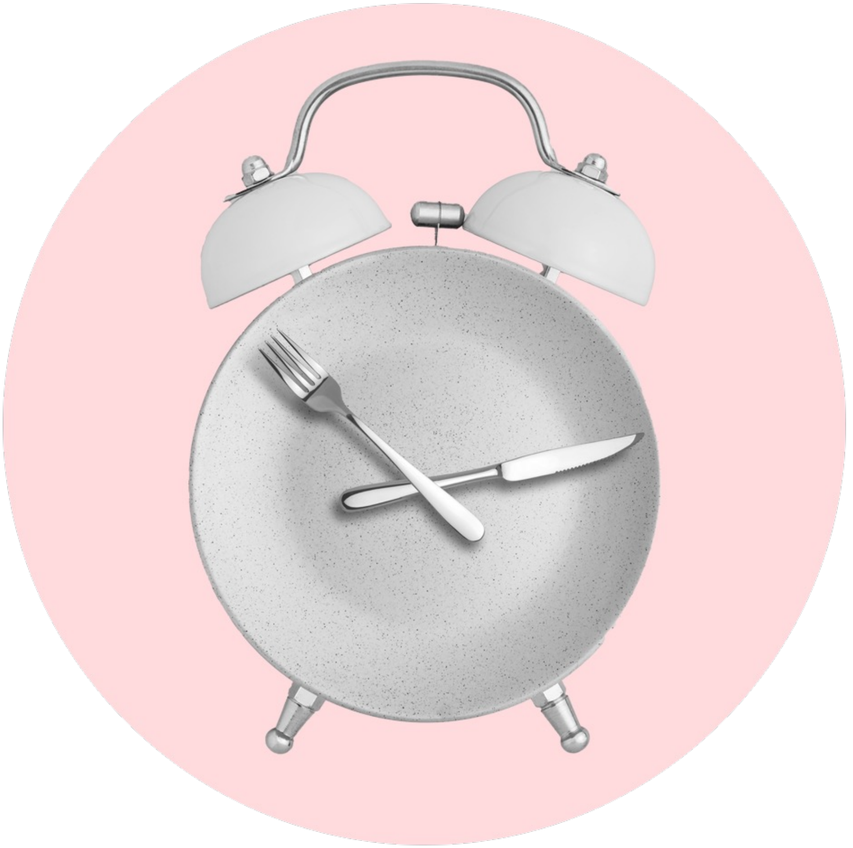
Abstract

Background/Objectives:

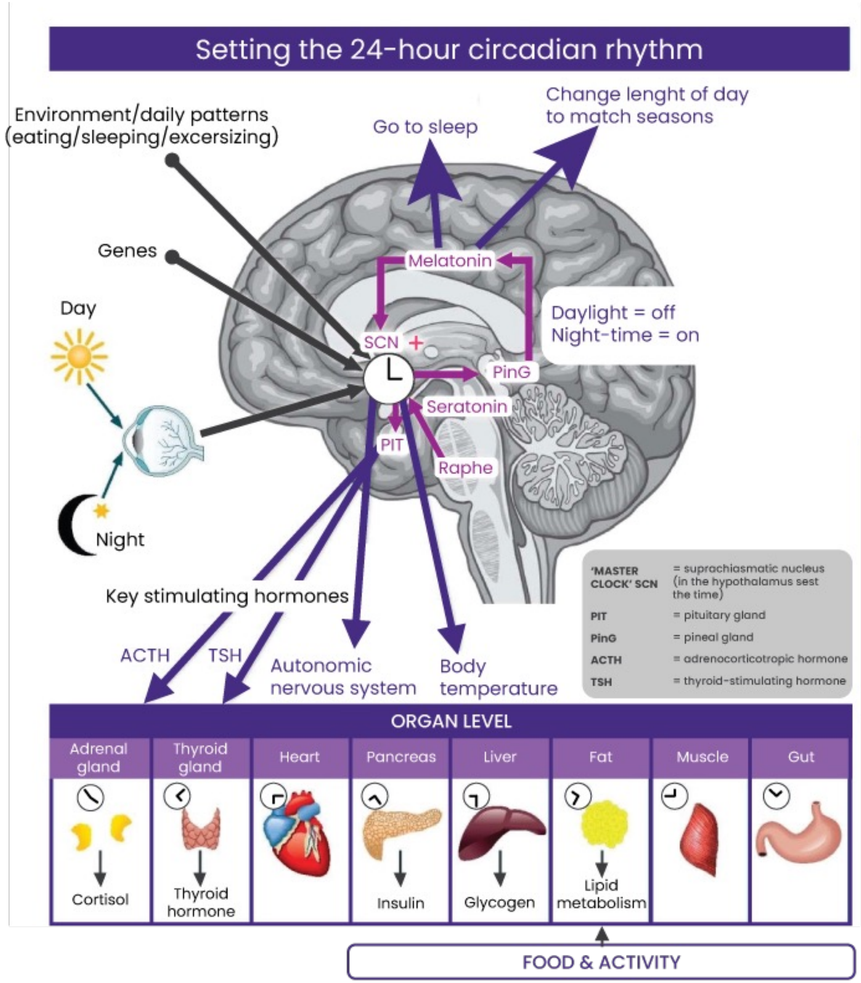
The MATADOR (Minimising Adaptive Thermogenesis And Deactivating Obesity Rebound) study examined whether intermittent energy restriction (ER) improved weight loss efficiency compared with continuous ER and, if so, whether intermittent ER attenuated compensatory responses associated with ER.

How to apply IF or cyclical dieting

- Find what works for you
  14/10, 12/12 eating window
- Alternate day fasting (ADF)
  (0-500 calories on fast days)
- Fasting mimicking diet (FMD)
  (5 days low calorie)
- 5/2 (two days of 500-700 calories)
- Cyclical dieting (1-2 weeks)



Altered eating and sleeping patterns



Circadian misalignment

- Decreases leptin and increases ghrelin levels
- Increases glucose and insulin levels
- Disrupts the cortisol rhythm
- Thus, affecting endocrine and adipose tissue metabolism

Day

Muscle
Fatty acid uptake
Glycolitic metabolism

Fat
Lipogenesis
Adiponectin production

Liver
Glycogen synthesis
Cholestrol synthesis
Bile acid synthesis

Pancreas
Insulin secretion

Night

Muscle
Oxidative metabolism

Fat
Lipid catabolism
Leptin secretion

Liver
Gluconeogenesis
Glycogenolysis
Mitochondrial biogenesis

Pancreas
Glucagon secretion

Greater caloric intake at breakfast *versus* dinner

- Weight loss
- Improves fasting glucose levels
- Insulin sensitivity
- Healthy blood lipid profiles

High Caloric Intake at Breakfast vs. Dinner Differentially Influences Weight Loss of Overweight and Obese Women

Daniela Jakubowicz,[1] *Maayan Barnea*,[2] *Julio Wainstein*,[1] *Oren Froy*[2]

Objective: Few studies examined the association between time-of-day of nutrient intake and the metabolic syndrome. Our goal was to compare a weight loss diet with high caloric intake during breakfast to an isocaloric diet with high caloric intake at dinner.

Design and Methods: Overweight and obese women (BMI 32.4 ± 1.8 kg/m^2) with metabolic syndrome were randomized into two isocaloric (~1400 kcal) weight loss groups, a breakfast (BF) (700 kcal breakfast, 500 kcal lunch, 200 kcal dinner) or a dinner (D) group (200 kcal breakfast, 500 kcal lunch, 700 kcal dinner) for 12 weeks.

Results: The BF group showed greater weight loss and waist circumference reduction. Although fasting glucose, insulin, and ghrelin were reduced in both groups, fasting glucose, insulin, and HOMA-IR decreased significantly to a greater extent in the BF group. Mean triglyceride levels decreased by 33.6% in the BF group, but increased by 14.6% in the D group. Oral glucose tolerance test led to a greater decrease of glucose and insulin in the BF group. In response to meal challenges, the overall daily glucose, insulin, ghrelin, and mean hunger scores were significantly lower, whereas mean satiety scores were significantly higher in the BF group.

Conclusions: High-calorie breakfast with reduced intake at dinner is beneficial and might be a useful alternative for the management of obesity and metabolic syndrome.

Obesity (2013) **00**, 000–000. doi:10.1002/oby.20460

Lack of sleep

- Harder to lose body fat
- Decreases fat oxidation and increases carbohydrate dependence
- Inhibit muscle gains from exercise
- Increase hunger and cravings for sugar and starchy carbohydrates
- Increases inflammation and BP
- Decreases heart rate variability (HRV)

Roles of Circadian Rhythmicity and Sleep in Human Glucose Regulation*

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I. Introduction
II. Characteristics and Causal Mechanisms of 24-h Rhythms of Glucose Regulation in Normal Young Subjects
  A. 24-h variations in glucose tolerance
  B. Causal mechanisms
III. Alterations of 24-h Rhythms of Glucose Regulation in Normal Aging
  A. Daytime variations in glucose tolerance
  B. Nighttime variations in glucose tolerance
  C. Respective roles of sleep and time of day
  D. Significance and clinical implications
IV. Diurnal Variations of Glucose Regulation in Obesity
  A. Daytime variations in glucose tolerance
  B. Nighttime variations in glucose tolerance
  C. Significance and clinical implications
V. Alterations in 24-h Rhythmicity of Glucose Regulation in Non-Insulin-Dependent Diabetes Mellitus (NIDDM)
  A. Alterations in daytime variations in glucose tolerance
  B. Alterations in nighttime variations in glucose levels during fasting
  C. Significance and clinical implications
VI. Alterations in 24-h Rhythmicity of Glucose Regulation in Insulin-Dependent Diabetes Mellitus (IDDM)
  A. Alterations in daytime variations in glucose tolerance
  B. Alterations in nighttime variations in glucose tolerance
  C. Significance and clinical implications
VII. Conclusions

I. Introduction

IN NORMAL man, plasma glucose homeostasis results from a tightly controlled balance between glucose delivery (from the liver in the postabsorptive state and from the gut in the postprandial state) and glucose utilization. Insulin plays a key role in this process by inhibiting hepatic glucose production and by stimulating glucose uptake by insulin-sensitive tissues (mainly skeletal muscle and adipose tissue).

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Human insulin secretion is a complex oscillatory process, including rapid pulses recurring every 10 to 15 min superimposed on slower oscillations with periods in the range of 90–120 min (1, 2). The so-called counterregulatory hormones, mainly glucagon, catecholamines, cortisol, and GH, are able to increase blood glucose concentrations by stimulating hepatic glucose production and/or inhibiting tissue glucose uptake. The daily secretion of cortisol and GH follows a complex pattern of temporal organization that reflects the control of their pulsatile release by the interaction of circadian rhythmicity (*i.e.*, an endogenous oscillatory signal with a near 24-h period generated in the suprachiasmatic nuclei of the hypothalamus) and the sleep or wake state. Cortisol secretion is markedly modulated by circadian rhythmicity while the majority of the daily GH output occurs after the onset of sleep. In the present review, the term "diurnal" will be used to designate temporal variations recurring regularly at a time interval of 24 h, regardless of their underlying causal mechanisms.

Human sleep is generally consolidated in a single 7- to 9-h period, whereas fragmentation of the sleep period in several bouts is the rule in other mammals. An important metabolic consequence of this organization of sleep and wake states is that an extended period of total fast must be maintained on a daily basis, generally during the overnight period. The consolidation of the sleep period is probably responsible for the fact that the wake-sleep and sleep-wake transitions in man are associated with physiological changes that are usually more marked than those observed in animals. Man is also unique in his capacity to ignore circadian signals and to maintain wakefulness despite an increased pressure to go to sleep. Voluntary sleep curtailment, rapid travel across time zones (*i.e.*, "jet lag"), and shift work rotations are highly prevalent conditions in modern society, and their hormonal and metabolic implications have only begun to be recognized (3).

While the roles of sleep and circadian rhythmicity in the modulation of endocrine function have been most investigated for hormonal secretions that are directly dependent on the hypothalamo-pituitary axes, it is also well established that the characteristics of normal glucose regulation vary across the 24-h cycle (4). Abnormalities in the diurnal variation of glucose tolerance have been recently demonstrated in aging, obesity, and diabetes. These findings, which form the topic of the present review, may have significant clinical

Sleep hygiene

- 7.5-8 hours
- Circadian alignment
- No/low alcohol and caffeine
- Magnesium bisglycinate
- Digestive herbs/Vata tea
- Sleep herbs
- Melatonin rich foods or supplement
- Bed before 10 (Ayurvedic clock)
- Bath before bed
- Cool room, dark, white noise
- No blue light/screens

What to consider

- Exercise – cardio, weights, HIIT, strength training
- Eating before and after training
- Address hormones and insulin resistance
- Cyclical/intermittent dieting
- Eating by 10am even if doing IF (cortisol)
- 3 meals no snacks
- Optimum protein and leucine intake
- Protein threshold theory – eat protein first
- Larger meals at breakfast/lunch, smaller at dinner
- Know your calorie and macro needs

More ideas

- Stress reduction/cortisol control
- Track your heart rate variability
- Nature therapy/forest bathing
- Learn your somatotype
- Supplements/herbs to assist in weight loss, adrenals, nervous system and mitochondrial health
- Analyse cravings, deficiencies and habits
- Change up your exercise (SAID/specific adaptation to imposed demands)
- Cold thermogenesis/showers/bathing/less clothing

Thank you

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