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Nutritional Medicine Institute

1

4:00 - 4:45pm

Menopause and Longevity: Translating Biological Ageing into Clinical Practice



Dr. Denise Furness, PhD

PRE-SUMMIT EVENT

Sponsored by pure encapsulations

2



Menopause & Longevity:

Translating Biological Ageing into Clinical Practice

Dr Denise Furness, PhD BSc(Hons) RNutr
CSO and Founder, Your Genes and Nutrition
Sunshine Coast, Australia

3

Affiliations & declaration of interest

Affiliations

- Founder and practitioner — Your Genes & Nutrition
- Founder and Chief Scientific Officer — Academy for Precision Health
- Board member — Endeavour College of Natural Health
- Faculty member — Australasian College of Nutritional and Environmental Medicine (ACNEM)

Declaration of interest

- Paid advisor/KOL to Pure Encapsulations and receiving an honorarium for this presentation.
- Presentation content developed independently; Pure Encapsulations has had no involvement in its development.
- No other relevant conflicts of interest to declare.

4

Learning Objectives:

- **Explain the relationship between menopause timing and biological ageing**, including the impact of early and surgical menopause on ageing trajectories.
- **Describe key biological pathways influenced by hormonal changes**, including inflammation, metabolic health, and cognition.
- **Understand individual variability in response to hormone therapy**, including considerations of hormone metabolism and personalised prescribing.
- **Recognise the role of functional testing** in supporting a personalised, precision health approach.
- **Apply a systems-based approach to peri- and post-menopause management**, integrating lifestyle, nutritional, and hormonal factors.

5



6

We arrive at Menopause with different reserves, risks & resources

- **Reserves:** muscle, bone, nutritional status and physical capacity.
- **Risks:** genetic susceptibilities, health history, adipose tissue and accumulated exposures.
- **Resources:** habits, support, time and access to care.

The menopause transition interacts with a lifetime of influences.

7



Symptoms in perimenopause & menopause

8

Symptoms in perimenopause & menopause

- The Australian Longitudinal Study on Women's Health (ALSWH) is an ongoing study tracking the health and well-being of Australian women since 1996.
  - 58,000 women representing different generations.
- Reports women experience menopausal symptoms with varying degrees of severity.
  - ~20-30% of women experience severe symptoms that significantly impact their daily lives.
  - ~50-60%, experience moderate symptoms that may cause some discomfort but are generally manageable without intensive medical intervention.

9

Factors Influencing Individual Symptom Variability

- ALSWH identified lifestyle, socioeconomic status, body mass index (BMI), smoking status, and physical activity levels impact symptoms.
  - E.g women with higher BMI or those who smoke tend to report more severe vasomotor symptoms like hot flashes and night sweats.
- Other factors include genetics, epigenetics, alcohol, relationships (work, family, social support), psychological factors (depression, anxiety and health anxiety, and general health (chronic conditions, surgeries).

10

Menopause. 2022 Oct 1;29(10):1124-1129. doi: 10.1097/GME.0000000000002033.
Epub 2022 Aug 23.

Perception of higher frequency of daily hot flas
50-year-old women today: a study of trends ov
time during 48 years in the Population Study of
Women in Gothenburg, Sweden

Kerstin Rödström [1], Lilian Weman, Valter Sundh, Cecilia Björkelund

Abstract

Objective: The aim of this study was to examine if there are any differences in the pre
hot flashes in 50-year-old women in a longitudinal perspective (from 1968 to 2017).

Methods: Cohort comparisons of four population-based samples of 50-year-old wom
1918, 1930 (earlier-born cohorts), 1954, and 1966 (later-born cohorts) from the Prospe
Population Study of Women in Gothenburg examined in 1968-1969, 1980-1981, 2004-
2016-2017. Questions about frequency of hot flashes have been formulated in the sam
throughout all follow-up examinations. Changes between four generations of 50-year
were studied.

Results: In the unadjusted model, we found an increased prevalence of daily hot flash
old women born in 1954 and 1966 compared with 50-year-old women born in 1918 a
ratio, 1.74; 95% confidence interval, 1.37-2.22). When considering potential predictors
flashes (smoking, perceived level of high stress, BMI, waist-to-hip ratio, hormone thera
hormonal contraceptives) in the adjusted model, there was a notable difference; odds
from 1.74 to 1.92 (95% confidence interval, 1.46-2.52). Smoking frequency was substan
the later-born cohorts, 39% compared with 17%.

Conclusions: In this prospective longitudinal study of 50-year-old women, we found r
high odds of reporting daily hot flashes in the later-born women compared with earlie
controlling for potential predictors, there was still an obvious difference, which cannot
our study. These findings have not earlier been described, and there is a need for furth
population studies investigating the prevalence of hot flashes over time. Moreover, ad
research is required exploring the underlying mechanism of hot flashes, as well as stud
into account potential risk factors in the environment and societal development over t
impacts of endocrine-disrupting chemicals changes in lifestyle, environmental, and die
well as working conditions.

-Compared four cohorts of 50-yr old women

-Earlier-born cohorts (1918, 1930) and later-born cohorts (1954, 1966)

-Found ~2 x daily hot flashes in the later-born women compared with earlier-born.

-Controlling for potential predictors, there was still a difference, which cannot be explained in our study.

-Additional research is required exploring endocrine-disrupting chemicals changes in lifestyle, environmental, and dietary factors, as well as working conditions.

11

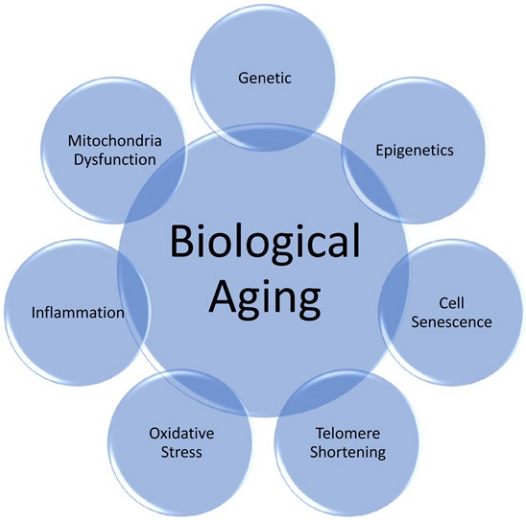


Biological Age & Menopause

12

Hormonal Shifts & Ageing

- The decline in estrogen and progesterone has been shown to influence multiple ageing pathways.
- Impacts metabolic health, vascular health, inflammation, and brain function.
- Earlier menopause is linked with accelerated biological ageing.



13

Menopause as a whole-body transition

Skeletal muscle	Mitochondria	Brain	Bone	Metabolic health	Inflammation
↓ mass & strength	↓ ATP capacity	↓ glucose use	↑ bone resorption	↑ visceral fat	↑ IL-6, TNF-α
⬇	⬇	⬇	⬇	⬇	⬇
Sarcopenia & frailty	Fatigue, low capacity	Cognitive decline	Osteoporosis, fracture	Insulin resistance	Accelerated ageing

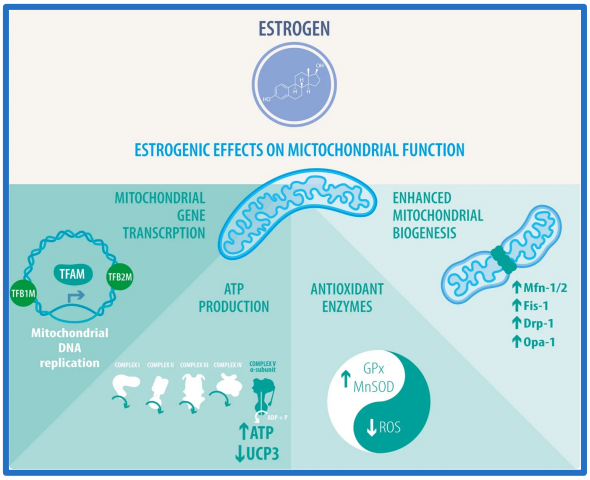
The goal is not symptom management — it is healthy ageing.

14

What does estrogen have to do with mitochondria?

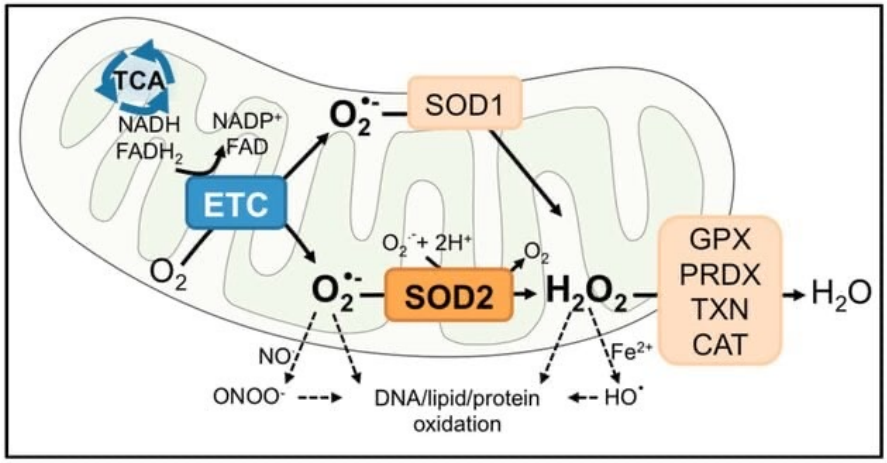
Estrogen signalling influences:

- Mitochondrial energy production & ATP
- Mitochondrial biogenesis
- Glucose & lipid metabolism
- Redox balance & antioxidant defence



15

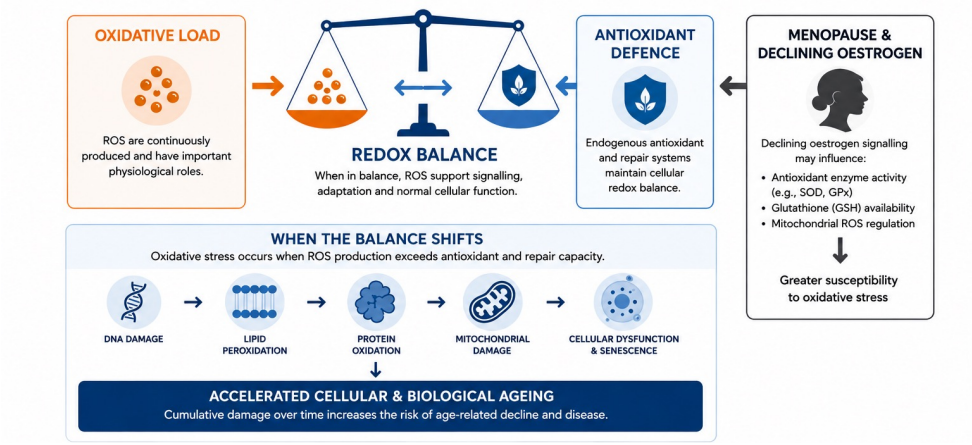
Mitochondria & oxidative stress



16

Redox balance: when load exceeds defence

The balance between ROS production and antioxidant defence influences cellular resilience and healthy ageing.



17

Earlier menopause & biological ageing

Three separate studies · different cohorts · different validated clocks · same direction of effect

1 · 4-COHORT POOLED	2 · NHANES	3 · UK BIOBANK
n ≈ 3,000 WHI, InCHIANTI, PEG, UK NSHD DNA methylation clock	n = 770 NHANES · postmenopausal, 50–85 y PhenoAge · GrimAge · DunedinPace	n = 117,763 UK Biobank · JAMA Netw Open, 2024 PhenoAge
Earlier menopause → accelerated epigenetic ageing	Premature menopause (~34 y) = highest-risk profile	Ever-use HT → younger biological age (≈ −0.17 y)
Surgical menopause → increased biological ageing	→ Faster pace of ageing (DunedinPace)	Strongest with later initiation (50–55 y), 4–8 y use
MHT → lower epigenetic age in some tissues	→ All-cause mortality HR ≈ 1.40	Effect greater with lower socioeconomic status
SNP rs11668344 linked to faster ageing	HRT → slower pace of ageing in some groups	Partially mediated mortality risk

Across ~121,000 women and multiple clocks: earlier menopause → faster biological ageing; HT → slower ageing.

18

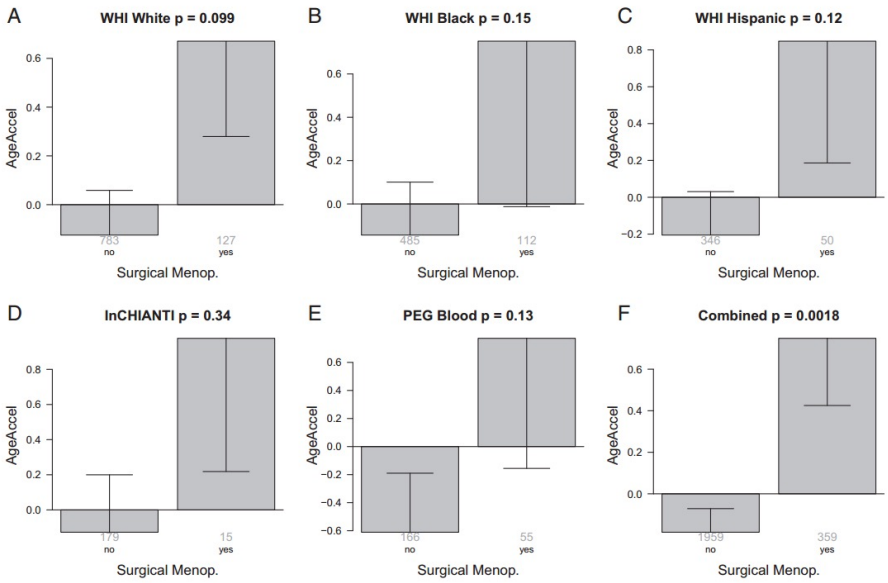
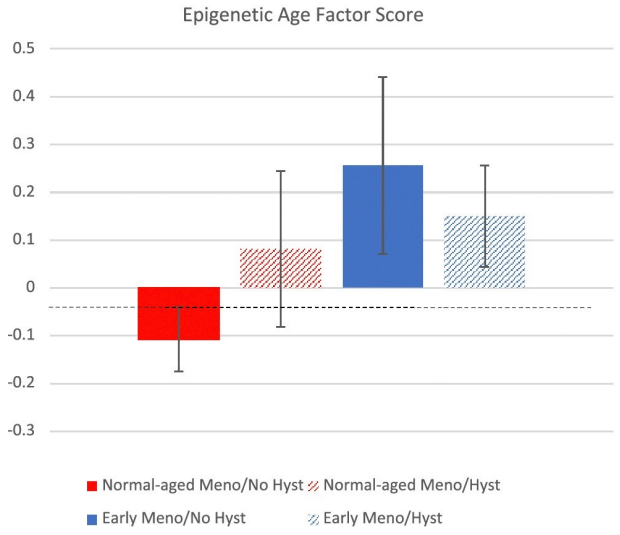


Fig. 1. Epigenetic AgeAccel versus surgical menopause status. The *x* axis of each plot reports surgical menopause status before age 50 y; i.e., "yes" denotes the group of women who experienced surgical menopause before age 50 y, and "no" corresponds to the group of women who did not undergo bilateral oophorectomy at any age before the blood draw. The bar plots report mean values of AgeAccel (± 1 SE) and the *P* value from a Student *t* test. The six panels show data from WHI (white) (*A*), WHI (black) (*B*), WHI (Hispanic) (*C*), InCHIANTI (*D*), and PEG (*E*) samples and all samples combined (*F*). A metaanalysis based on Stouffer's Z method indicates that AgeAccel is significantly positively associated with surgical menopause status (*P* = 0.0018).

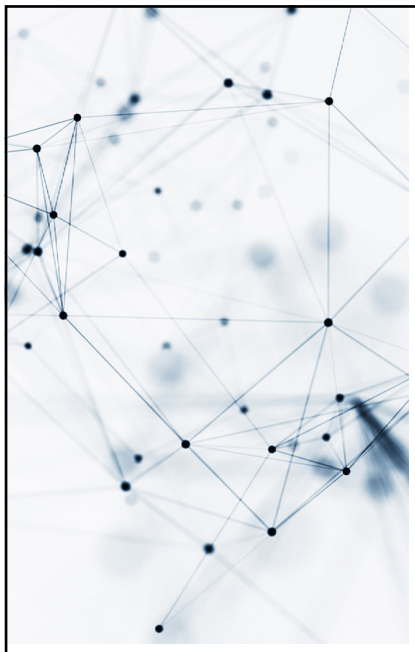
19

Biological age by timing of menopause & hysterectomy

- Women aged 56 and over in the Health & Retirement Study (HRS).
- 1,443 postmenopausal women
- Early menopause defined as menopause at 44 or younger.
- Epigenetic clocks
  - PhenoAge
  - GrimAge
  - DunedinPACE



20

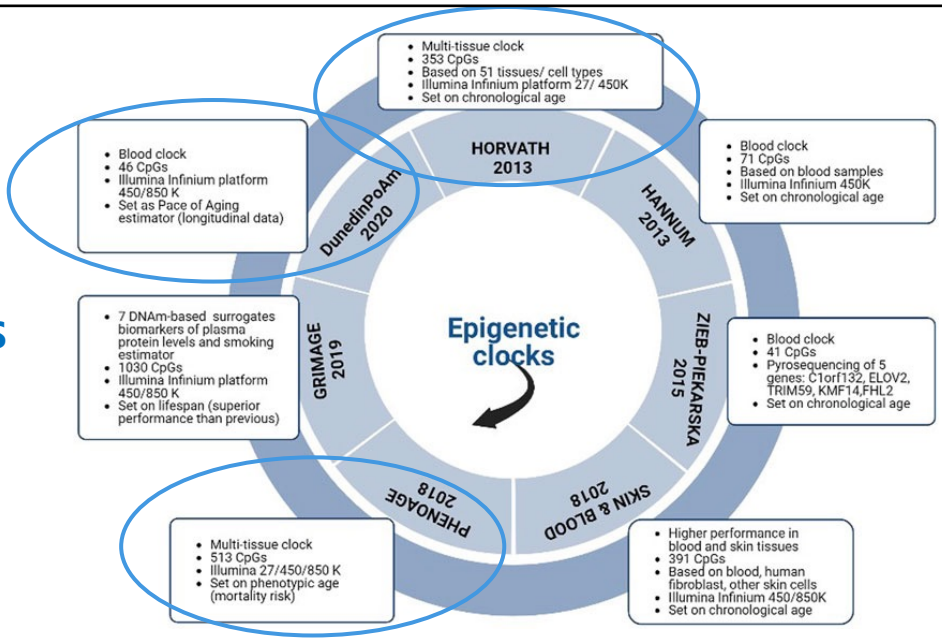


Biological Age Tests

21

22

EPIGENETIC AGE CLOCKS



Li Piani L, Vigano' P, Somigliana E. Epigenetic clocks and female fertility timeline: A new approach to an old issue? Front Cell Dev Biol. 2023

22

PhenoAge →

How old are you biologically?

DunedinPACE →

How fast are you ageing?

Covered in detail in my next talk: EPIGENETIC AGE: From Measurement to Intervention

23



Can MHT influence biological ageing?

24

What does the evidence suggest?

- Some studies associate MHT use with more favourable biological-age measures, but findings are mixed and vary by population, tissue and ageing measure.
- Levine, 2016: MHT was associated with younger epigenetic age in buccal cells, but not blood cells, a tissue-specific finding.
- UK Biobank, 2024: Historical HT use was associated with a modestly lower clinical phenotypic-age estimate; change over time was not measured.
- Ye, 2025: Findings varied by reproductive history and ageing measure, with mixed exploratory associations for hormone use.

25

Earlier menopause & biological ageing

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n ≈ 3,000 WHI, InCHIANTI, PEG, UK NSHD DNA methylation clock	n = 770 NHANES · postmenopausal, 50–85 y PhenoAge · GrimAge · DunedinPace	n = 117,763 UK Biobank · JAMA Netw Open, 2024 PhenoAge
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MHT → lower epigenetic age in some tissues	→ All-cause mortality HR ≈ 1.40	Effect greater with lower socioeconomic status
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26

Newer evidence, 2026

Study	Ageing measure	Main finding
Ma et al., 2026 · UK Biobank	KDM biological age: clinical biomarkers, blood pressure and lung function	Lower estradiol was associated with greater age acceleration; HRT users had more favourable biological-age estimates.
Wei et al., 2026 · Genetic analysis + NHANES	Epigenetic age acceleration: Horvath, Hannum, PhenoAge and GrimAge	Higher predicted ESR1 expression was associated with lower PhenoAge acceleration. HRT was associated with lower mortality, with the association modified by glucose status and epigenetic ageing.

27



Estrogen exposure & metabolism: individual differences matter

28

Hormone response reflects both exposure and how estrogen is metabolised

- **Exposure:** hormone production, MHT dose, formulation and route.
- **Metabolism:** Genetics, liver and gut function.
- **Elimination and recirculation:** conjugation, gut microbial activity and bowel function.

29

Estrogen metabolites have different biological effects

- **2-hydroxy:** generally weaker estrogenic activity; can undergo COMT-mediated methylation.
- **4-hydroxy:** can form reactive quinones capable of DNA damage; subsequent methylation and conjugation are important.
- **16α-hydroxyestrone:** has stronger estrogenic activity and can stimulate cell proliferation, its potential effects differ from the reactive 4-hydroxy pathway.
- Metabolism patterns have been associated with DNA damage, oxidative stress breast cancer risk.

30

What oestrogen metabolite testing shows

What dried urine testing measures

Parent hormones
Estrogens, progesterone and androgen metabolites

Phase I pathways
2-, 4- and 16-hydroxy oestrogens and their balance

Methylation
2-methoxy to 2-hydroxy ratio, a marker of COMT activity

Cortisol rhythm
Free cortisol across the day and total cortisol output

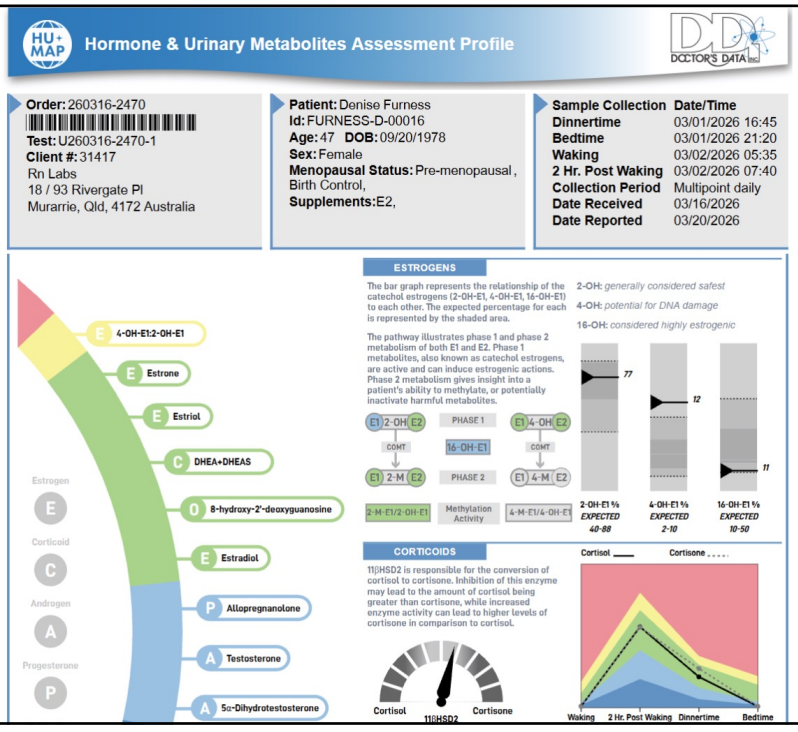
The method agrees with 24-hour urine
Four dried spot samples matched a full 24-hour collection for most hormone metabolites[1]

The 4-OH pathway links to DNA damage
Urinary estrogen–DNA adduct ratios were higher in high-risk women and women with breast cancer[2]

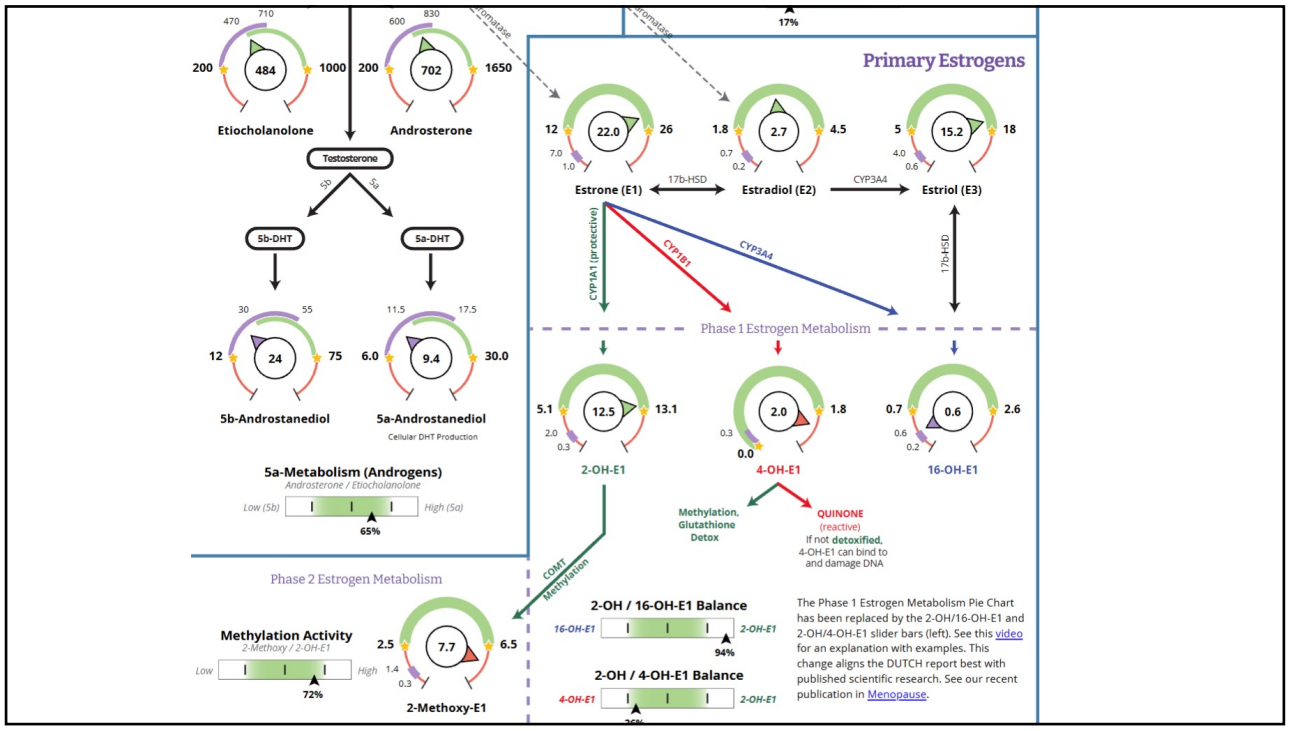
Nutrition can shift the pattern
Brassica vegetables and indole-3-carbinol raised the 2:16 ratio; results vary across trials[3]

Test, intervene, retest. Baseline in early menopause or before MHT, support, then retest. Not a diagnostic test for cancer.

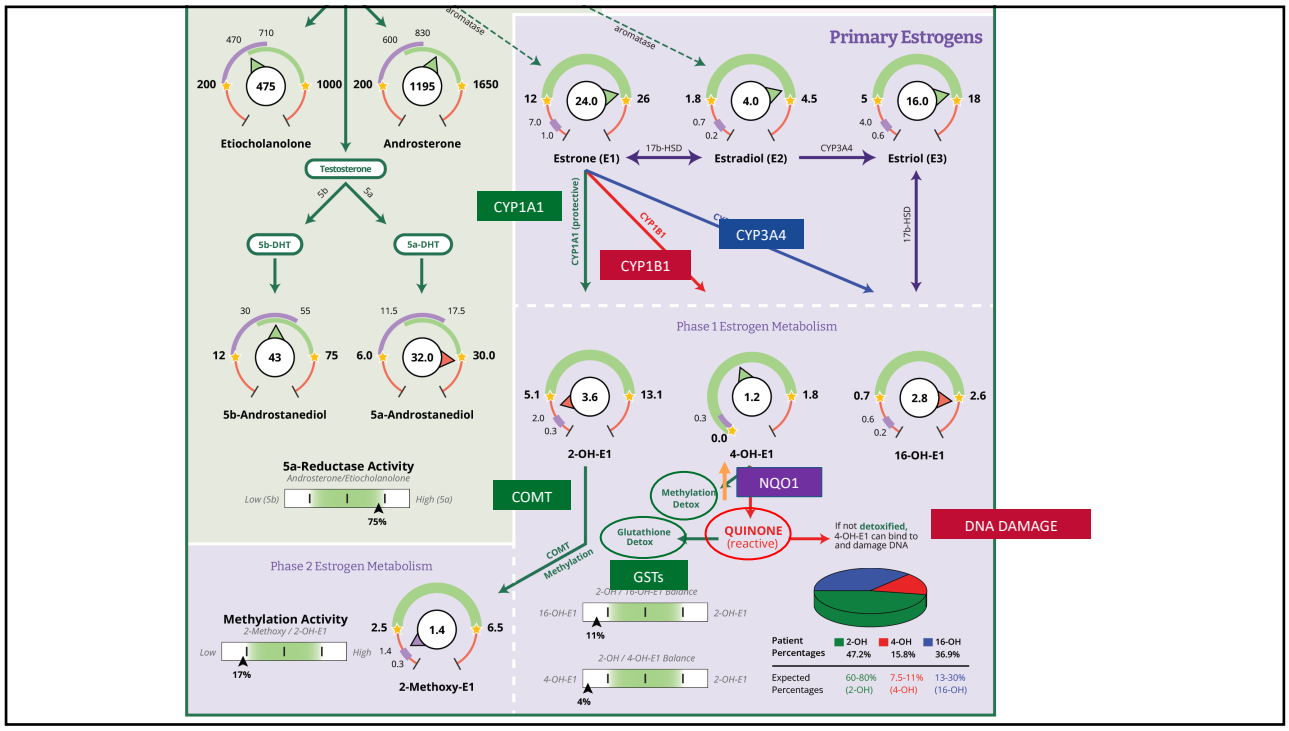
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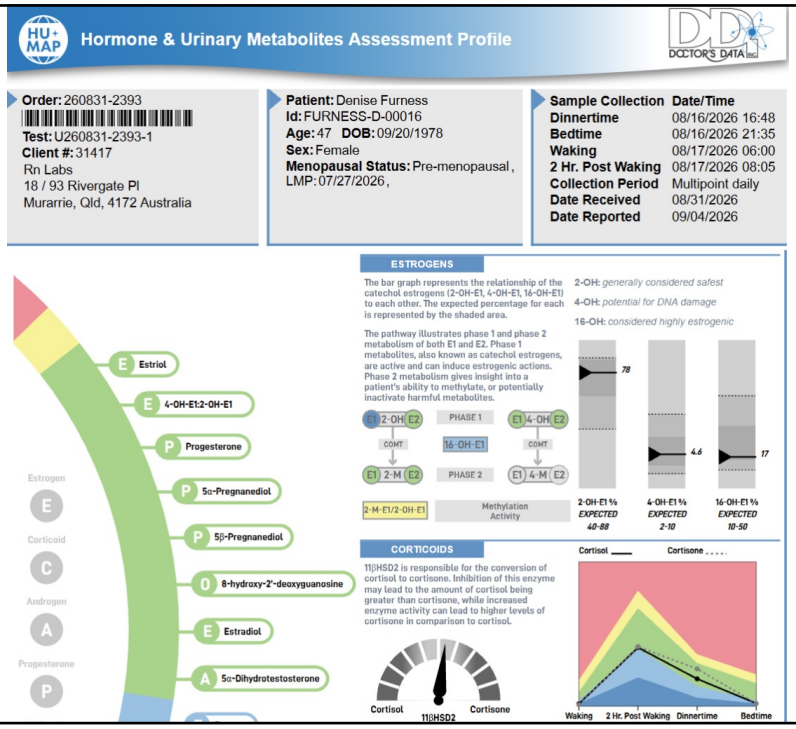
32


Primary Estrogens
Etiocholanolone
Androsterone
Testosterone
5b-DHT
5a-DHT
5b-Androstanediol
5a-Androstanediol
Cellular DHT Production
5a-Metabolism (Androgens)
Androsterone / Etiocholanolone
Low (5b)
High (5a)
65%
Estrone (E1)
Estradiol (E2)
Estriol (E3)
17b-HSD
CYP3A4
CYP1A1 (protective)
CYP1B1
Phase 1 Estrogen Metabolism
2-OH-E1
4-OH-E1
16-OH-E1
Methylation, Glutathione Detox
QUINONE (reactive)
If not detoxified, 4-OH-E1 can bind to and damage DNA
COMT Methylation
Phase 2 Estrogen Metabolism
Methylation Activity
2-Methoxy / 2-OH-E1
72%
2-Methoxy-E1
2-OH / 16-OH-E1 Balance
94%
2-OH / 4-OH-E1 Balance
The Phase 1 Estrogen Metabolism Pie Chart has been replaced by the 2-OH/16-OH-E1 and 2-OH/4-OH-E1 slider bars (left). See this video for an explanation with examples. This change aligns the DUTCH report best with published scientific research. See our recent publication in Menopause.

33


Primary Estrogens
Etiocholanolone
Androsterone
Testosterone
5b-DHT
5a-DHT
5b-Androstanediol
5a-Androstanediol
5a-Reductase Activity
Androsterone/Etiocholanolone
Low (5b)
High (5a)
75%
Estrone (E1)
Estradiol (E2)
Estriol (E3)
17b-HSD
CYP3A4
CYP1A1
CYP1A1 (protective)
CYP1B1
Phase 1 Estrogen Metabolism
2-OH-E1
4-OH-E1
16-OH-E1
COMT
Methylation Detox
NQO1
Glutathione Detox
QUINONE (reactive)
If not detoxified, 4-OH-E1 can bind to and damage DNA
DNA DAMAGE
GSTs
COMT Methylation
Phase 2 Estrogen Metabolism
Methylation Activity
2-Methoxy / 2-OH-E1
17%
2-Methoxy-E1
11%
4%
Patient Percentages
2-OH 47.2%
4-OH 15.8%
16-OH 36.9%
Expected Percentages
60-80% (2-OH)
7.5-11% (4-OH)
13-30% (16-OH)

34



35

HRT (MRT) and thrombophilia genes

Thrombophilia:

- A predisposition to developing venous blood clots due to genetic factors.
- Common genetic mutations include **Factor V Leiden (F5)** and **Prothrombin G20210A (F2)**.
- The MTHFR 677 TT genotype is associated with mild-moderate risk.

Oral Estrogen and Clotting:

- Undergoes first-pass metabolism in the liver, increasing the synthesis of clotting factors.
- Associated with a higher risk of venous thromboembolism (VTE), concern for those with inherited risk factors (F5, F2, MTHFR / high Hcy).

36

HRT Considerations with Inherited Thrombophilia

- Individuals with F5 or F2 mutations have an increased baseline risk of VTE, therefore any form of oestrogen therapy should be carefully considered.
- **Transdermal Oestrogen and Personalised Risk Assessment**:
  - Bypasses hepatic first-pass metabolism. Avoids the upregulation of hepatic clotting factors like fibrinogen and prothrombin, preferred for those at risk of clotting.
  - For individuals with **heterozygous** F5 or prothrombin mutations, transdermal HRT may be an option if no history of thrombosis exists.
  - For those with **homozygous mutations** or a personal/family history of thrombosis, HRT should be approached with greater caution, potentially with hematology consultation.

37

HRT Considerations with Inherited Thrombophilia

- **Progesterone Selection:**
  - Micronized progesterone (e.g., Prometrium) is generally considered safer than synthetic progestins like medroxyprogesterone acetate (MPA), which may have a pro-thrombotic effect.
- **Monitoring and Lifestyle Factors**:
  - Regular screening for additional risk factors (e.g., high homocysteine (Hcy) levels, inflammatory markers).
  - Ensuring optimal methylation support if required (inherited Hcy risk).
  - Maintaining a healthy lifestyle to reduce clotting risk (exercise, hydration, avoiding smoking, etc.).

38

Review > Post Reprod Health. 2023 Mar;29(1):33-41. doi: 10.1177/20533691221148036.
Epub 2022 Dec 27.

Hormone replacement therapy in women with history of thrombosis or a thrombophilia

Guy Morris [1], Vikram Talaulikar [2]

Affiliations + expand
PMID: 36573625 DOI: 10.1177/20533691221148036

Abstract

Findings from the Women's Health Initiative (WHI) randomised placebo-controlled trial (RCT) were published at the beginning of this century. They suggested that hormone replacement therapy (HRT) use increased the risk of cardiovascular disease and venous thromboembolism including pulmonary embolism and deep vein thrombosis The findings led to a decline in HRT prescriptions and negative publicity about the use of HRT for women with significant menopausal symptoms. Subsequent studies have shown that the risk of thrombosis with HRT relates to whether estrogen is combined with a progestogen and the route of administration of estrogen. In healthy women with no background medical problems, transdermal hormone replacement is not associated with an increased risk of thrombosis. However, much less is known about the safety of various HRT preparations in women with a high background risk of thrombosis. These cases can often be challenging for clinicians with uncertainties around testing for thrombophilia, use of anticoagulation and striking a balance between the risks and benefits of prescribing HRT. This article will review the mechanism of thrombosis with differing types of HRT and present the evidence from the relevant trials. The article will also present the evidence that specifically relates to women with a personal history of thrombosis or thrombophilia (heritable and acquired) to enable clinicians to better individualise the risk assessment for each woman requesting HRT and understand the role of thrombophilia screening or concomitant anticoagulation in such situations.

39

Review > Post Reprod Health. 2023 Mar;29(1):33-41. doi: 10.1177/20533691221148036.
Epub 2022 Dec 27.

Hormone repl… history of thr…

Guy Morris [1], Vikram Tala…

Affiliations + expand
PMID: 36573625 DOI: 10.

Abstract

Findings from the Women… published at the beginning… use increased the risk of c… embolism and deep vein t… publicity about the use of … have shown that the risk o… progestogen and the route… medical problems, transde… thrombosis. However, muc… with a high background ris… uncertainties around testi… the risks and benefits of p… differing types of HRT and… the evidence that specifica… (heritable and acquired) to… woman requesting HRT and understand the role of thrombophilia screening or concomitant anticoagulation in such situations.

- Limited data exist on HRT safety in women with hereditary or acquired thrombophilia or a personal history of VTE.
- Individualised risk assessment is crucial, and the balance between HRT benefits and potential risks.

Recommendations for Clinicians:

- Thorough evaluation of personal and family history of thrombosis before initiating HRT.
- Preference for transdermal oestrogen formulations, especially in women at increased thrombotic risk.
- Consideration of the type of progestogen used in combination therapy.
- Ongoing monitoring and reassessment of thrombotic risk during HRT.

40

Personalising MHT: what should we consider?

- **Clinical context:** symptoms, menop eatment goals.
- **Hormone exposure:** dose, formulat han transdermal oestrogen. Known thrombophilia or sessment.
- **Metabolic pathways:** genetic influe antioxidant defences.
- **Nutrition and gut function:** fibre int ination and recirculation.
- **Additional testing, where relevant:** stool β-gucuronidase can add context, interpreted alongside the clinical picture.

Consider the whole person including hormone exposure, metabolism and the foundations of healthy ageing.

41



Supporting Menopause Longevity with or without MHT

42

Four foundations for healthy ageing in menopause

Foundation	Main focus	Targeted support	Ageing outcomes
Nourish	Food quality, protein, fibre, plant diversity	Multinutrient where intake or testing shows a shortfall	Nutrient sufficiency, gut health, inflammation
Build	Muscle, bone, connective tissue, physical capacity	Creatine; collagen peptides, alongside resistance training	Sarcopenia, bone loss, insulin sensitivity
Restore	Sleep, stress load, recovery, symptom burden	Magnesium; botanical symptom support	Sleep quality, stress resilience, symptom relief
Protect	Cardiometabolic health, brain health, cellular defences	Omega-3, CoQ10/ubiquinol, B vitamins; broader risk management	Cardiovascular disease, dementia, oxidative damage

Supplements complement the foundations; selection depends on need, evidence, tolerability and medication use.

43

Nourish

- Prioritise whole foods and plant diversity (30 to 40 different plant-based foods each week).
- Include protein at each meal (individualised target: approximately 1.2–1.6 g/kg/day).
- Include fibre-rich foods (at least 25 g/day), increasing gradually, and 2 serves cruciferous vegetables.
- Ensure adequate energy, hydration and healthy fats.
- Identify nutrient deficiencies and supplement where needed.

44

Build: why muscle matters through menopause

- **Strength & function –** independence
- **Metabolic health -** glucose disposal
- **Mitochondrial capacity -** exercise-induced mitochondrial adaptation
- **Skin health -** skin elasticity, dermal structure & thickness
  - Nishikori S, et al. Resistance training rejuvenates aging skin by reducing circulating inflammatory factors and enhancing dermal extracellular matrices. Sci Rep. 2023



45

Build: how to train for muscle and bone

Lift heavy, progressively
2–3 sessions a week across major muscle groups; increase load as strength improves.

Add impact
Jumps and drop landings load the hip and spine; build up gradually.

Feed the adaptation
Protein at each meal; creatine ≥5 g/day with training adds to strength gains.

LIFTMOR TRIAL

+2.9%

lumbar spine BMD after 8 months, vs −1.2% in controls

101 postmenopausal women with low bone mass · 2 × 30-min supervised sessions a week · no vertebral fractures

Source: Watson SL, et al. LIFTMOR randomised controlled trial. J Bone Miner Res. 2018;33(2):211–220; vertebral fracture follow-up, J Bone Miner Res. 2019.

46

Creatine: What the evidence supports

Domain	What the evidence shows	Dose and conditions	Grade
Muscle and strength	Lean mass +0.37 kg; leg-press 1RM +7.5 kg in postmenopausal women	≥5 g/day combined with resistance training	Strongest
Cognition	Memory improved overall (SMD 0.29); larger effect in older adults (SMD 0.88). Frontal brain creatine rises with supplementation	2.2–20 g/day; dose did not predict effect size	Emerging
Bone	No change in BMD overall; 2 years of 3 g/day without training produced no bone or function benefit	Any benefit likely requires a loading stimulus	Limited
Safety	Adverse events mild and comparable with placebo; renal indices unchanged	Studied up to 20 g/day	Consistent

Naddafha S, Antonio J, Kreider RB, Stout JR. Creatine monohydrate for lean mass, strength, and bone density in postmenopausal women: a systematic review and meta-analysis. *J Int Soc Sports Nutr*. 2026;23(1):2668435. 7 RCTs (n = 608); Prokopidis K, et al. Effects of creatine supplementation on memory in adults: a systematic review and meta-analysis. *Nutrition Reviews*. 2023; Sales LP, Pinto AJ, Rodrigues SF, et al. Creatine supplementation (3 g/d) and bone health in older women: a 2-year, randomized, placebo-controlled trial. *Journal of Gerontology: Series A*. 2020;75(5):931–938; Korovljev D, et al. CONCRET-MENOPA: creatine hydrochloride and ethyl ester on cognition, clinical outcomes and brain creatine in peri- and menopausal women. *Journal of the American Nutrition Association*. 2026;45(3).

47

Collagen peptides: dose depends on target tissue

Target tissue	What is it / outcome studied	Studied dose	Evidence
MUSCLE & BODY COMPOSITION	Hydrolysed collagen peptides; muscle & body composition	15 g/day	RCTs with exercise: ↑ fat-free mass/body composition and improved strength
SKIN & DERMAL MATRIX	Specific bioactive collagen peptides formulation	2.5-5 g/day*	RCTs: ↓ eye wrinkles, ↑ skin elasticity; ↑ procollagen I & elastin
BONE HEALTH	Specific bioactive collagen peptides; bone	5 g/day	RCTs in postmenopausal women: ↑ BMD and favourable bone-marker changes
JOINT SUPPORT	Specific collagen peptides; joint/cartilage	5 g/day	RCTs: ↓ activity-related joint discomfort in physically active adults

**Skin trials used 2.5 g/day (eye wrinkles) or 2.5–5 g/day (elasticity).*

Muscle: Jendricke 2019, Nutrients 11(4):892 — 77 premenopausal women, 15 g/day + resistance training, 12 wks: ↑ fat-free mass, ↑ grip strength.
Skin: Proksch 2014, Skin Pharmacol Physiol 27(3):113–119 and 27(1):47–55 — ↓ eye wrinkles, ↑ elasticity, procollagen I +65%.
Bone: König 2018, Nutrients 10(1):97 — 131 postmenopausal women, 5 g/day for 12 months: ↑ BMD at spine and femoral neck.
Joint: Zdzieblik 2021, Nutrients 13(2):523 — 180 active adults, 5 g/day for 12 wks: ↓ exercise-induced knee pain vs placebo.

48

Restore: sleep and recovery in menopause

SLEEP

Regular sleep–wake times · dark, cool room

- Sleep disruption rises through the transition, driven by night sweats and early waking
- Short, broken sleep worsens insulin resistance, weight gain and cardiovascular risk
- Deep sleep supports memory and brain clearance; poor sleep is linked to faster biological ageing.

STRESS LOAD

Breathwork · time outdoors · social connection

- Falling estrogen changes the stress response as work and caring loads peak.
- Chronically raised cortisol drives abdominal fat, poor sleep, inflammation and bone loss
- Lowering stress load protects sleep, mood and metabolic health

SYMPTOM BURDEN

MHT where appropriate · magnesium · botanicals · CBT

- Hot flushes, mood change and brain fog erode sleep, work and quality of life
- Frequent, persistent hot flushes are linked to higher cardiovascular risk
- Treating symptoms restores sleep and recovery, the base for healthy ageing

Prioritise sleep and recovery: they shape symptoms now and ageing risk later.

49

Magnesium: supporting sleep and recovery

Why it matters

- Cofactor for GABA signalling and for COMT, which clears stress catecholamines.
- Women need **320 mg/day** (NHMRC); diets low in legumes, seeds, nuts and greens fall short.

Practical use

- **150 mg** daily as a baseline; **300 mg** for stress, muscle tension or poor sleep (elemental; upper limit 350 mg)
- **Glycinate:** first choice for sleep; gentle on the gut
- **Citrate:** well absorbed; relaxation and muscle recovery; looser stools at higher doses[4]
- **Oxide:** poorly absorbed; best used as a laxative
- Caution in renal impairment; space from bisphosphonates and levothyroxine

Sleep: small benefit, larger when intake is low
250 mg bisglycinate for 4 weeks cut insomnia scores more than placebo (−3.9 vs −2.3 ISI points)[1]

Older adults: faster sleep onset
Meta-analysis of RCTs: about 17 minutes shorter time to fall asleep; low-quality evidence[2]

Menopause symptoms
Review evidence suggests a role in preventing climacteric symptoms; controlled trials are limited[3]

1. Schuster J, et al. Nat Sci Sleep 2025;17:2027–40. 2. Mah J, Pitre T. BMC Complement Med Ther 2021;21:125. 3. Parazzini F, et al. Magnes Res 2017;30:1–7. 4. Walker AF, et al. Magnes Res 2003;16:183–91.

50

Protect: brain, heart and biological age

Brain and cardiovascular disease share the same underlying pathways; **oestrogen loss accelerates each one.**

Pathway	Why it matters after menopause	What protects
Inflammation and vascular health	Oestrogen loss raises LDL cholesterol, blood pressure and vascular inflammation	Omega-3 (EPA/DHA) · daily movement · polyphenol-rich plants
Methylation and homocysteine	High homocysteine is linked to dementia and heart disease; B vitamins slowed brain atrophy[1]	Folate, B12, B2 and B6 · test homocysteine
Mitochondria and oxidative stress	Lower oestrogen reduces mitochondrial efficiency and raises oxidative load, speeding cellular ageing	Ubiquinol · B vitamins · magnesium · selenium and zinc · exercise
Toxins and DNA damage	Cumulative exposures damage DNA and accelerate epigenetic ageing	No smoking · limit alcohol · fewer plastics · UV care · cruciferous vegetables
Social and cognitive connection	Social isolation is one of 14 modifiable dementia risks that together explain about 45% of cases[2]	Regular social contact · purpose · new learning · treat hearing loss

1. Smith AD, et al. PLoS One 2010;5:e12244 (VITACOG). 2. Livingston G, et al. Lancet 2024;404:572–628 (Lancet Commission on dementia).

51

What to do, and who for

NOURISH

Whole foods, plant diversity and adequate protein. Multinutrient where intake or testing shows a shortfall.

Consider for: low or restricted intake, poor appetite, absorption issues.

BUILD

Resistance training 2–3×/week plus impact. Protein at each meal. Creatine 3–5 g/day; collagen peptides 2.5–15 g/day by tissue.

Consider for: muscle and bone loss, low strength, cognitive concerns, joints, skin.

RESTORE

Sleep regularity, stress load and active recovery. Magnesium 150–300 mg/day; botanical symptom support.

Consider for: poor sleep, high stress, night sweats, low dietary magnesium.

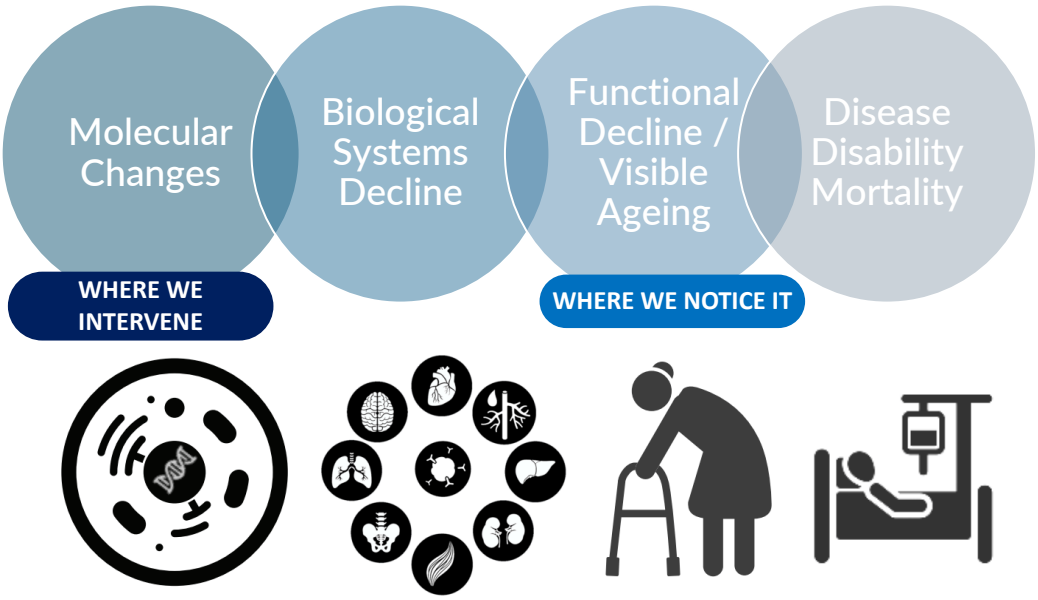
PROTECT

Omega-3, active B vitamins, ubiquinol 100–150 mg/day. Social connection. Reduce / avoid smoking, alcohol and toxin exposure.

Consider for: everyone; test homocysteine; ubiquinol with statins.

Foundations first. Food, movement, sleep and connection act at the molecular level, before decline shows. Test, intervene, retest: targeted supplements build on the foundations, not replace them.

52



53

Summary

1. **Menopause timing shapes biological ageing.**
   Earlier and surgical menopause are linked with faster epigenetic ageing.
2. **Estrogen loss affects many systems at once.**
   Mitochondria, inflammation, metabolism, vascular and brain health shift together.
3. **Response to MHT is individual.**
   Dose, route, estrogen metabolism and clotting risk guide personalised prescribing.
4. **Testing makes ageing measurable.**
   Biological age clocks and hormone metabolite testing personalise and track the plan.
5. **Nourish, build, restore, protect.**
   With or without MHT, the foundations act early, at the molecular level.

54

Thank you!

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55

Genes to consider for hormone metabolism

- CYP17A1 rs743572
  - GG (CC) increased enzyme activity genotype exhibited higher irritability and anxiety scores. Symptoms measured using Menopause Rating Scale (MRS) and Hospital Anxiety and Depression Scale (HADS). PMID: 27117436.
- CYP1B1 rs1056836
  - G allele associated with increased enzyme activity may increase risk for hot flashes and night sweats (not conclusive). PMID: 32797194
- COMT rs4680 (Val158Met)
  - AA (Met) slow enzyme activity, linked with increased sensitivity to pain and emotional instability (mood disturbances) which may impact perimenopause symptoms.
  - Oestrogen down-regulates COMT.

56

APOE 4 allele and estrogen replacement

- Emerging evidence suggests women with the e4 allele may benefit from oestrogen in **early menopause.** PMID: 36624497, PMID: 10822435, PMID: 37846476
- Women's Health Initiative Memory Study (WHIMS) and HRT Timing: showed that conjugated equine estrogens plus medroxyprogesterone acetate increase dementia risk in women **aged 65 years and above.** PMID: 22612612
- Studies in perimenopause are currently limited. Initiating oestrogen therapy in perimenopause and early transition phase before menopause may offer cognitive benefit, but existing studies have investigated HRT in postmenopause.

57