

CLINICAL WEBINAR

Navigating Modern Menopause Therapy (MHT) and Integrative Co-Prescribing



Presented by:
Tracee Blythe, Naturopath

Presenter | Tracee Blythe



Tracee Blythe is a dedicated practitioner and educator specialising in the evolution of Menopause hormone therapy (MHT) and integrative co-prescribing. With an extensive background in naturopathic interventions, Tracee empowers practitioners with rigorous, science-backed clinical frameworks.

Tracee teaches professionals how to confidently integrate evidence-based nutrition and herbal medicine alongside MHT to safely manage risks, reduce side effects, and optimise therapeutic outcomes for menopausal women.

Host | Linda Dal Molin



Linda Dal Molin is the Director of Sales and Education for Designs for Health Australia.

Linda has a Masters in Human Nutrition, Bachelor of Health Science (Complementary Medicine), Advanced Diploma Naturopathy. She has been a practitioner for over 26 years and worked in the natural health space for 30 years having owned and managed health food stores and a large multi-modality allied health clinic. Linda practices on Saturday mornings in a busy clinic in Sydney's inner city with a focus on women's and gut health.

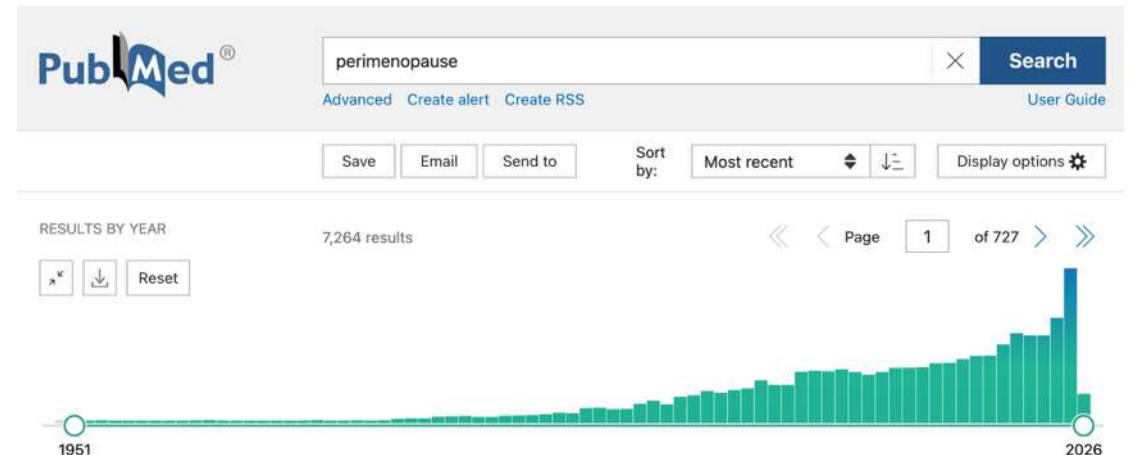
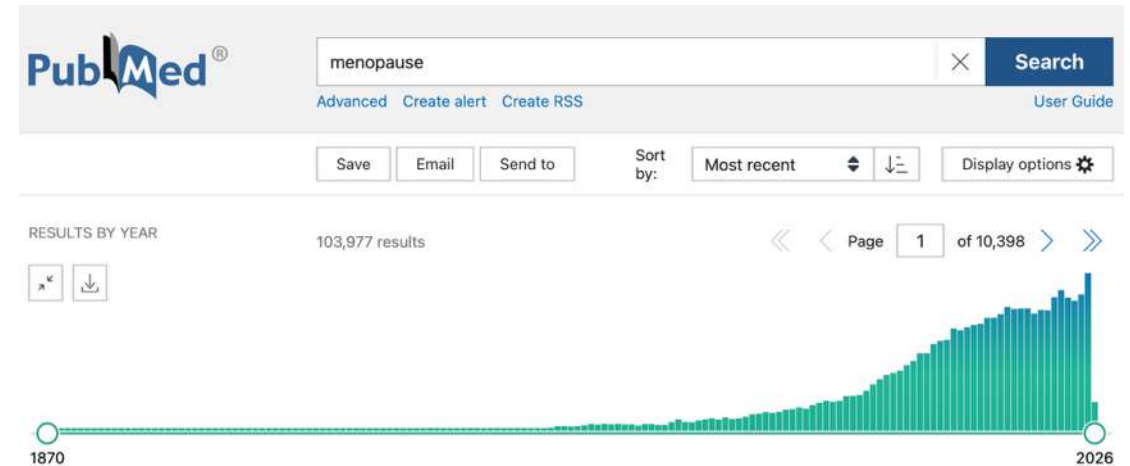
Linda has developed a strong relationship with the Designs for Health practitioner community. She will moderate the Q&A discussion with Tracee in this webinar and engage our live Designs for Health practitioner community to bring insight and practical clinical pearls for all.

Learning Objectives

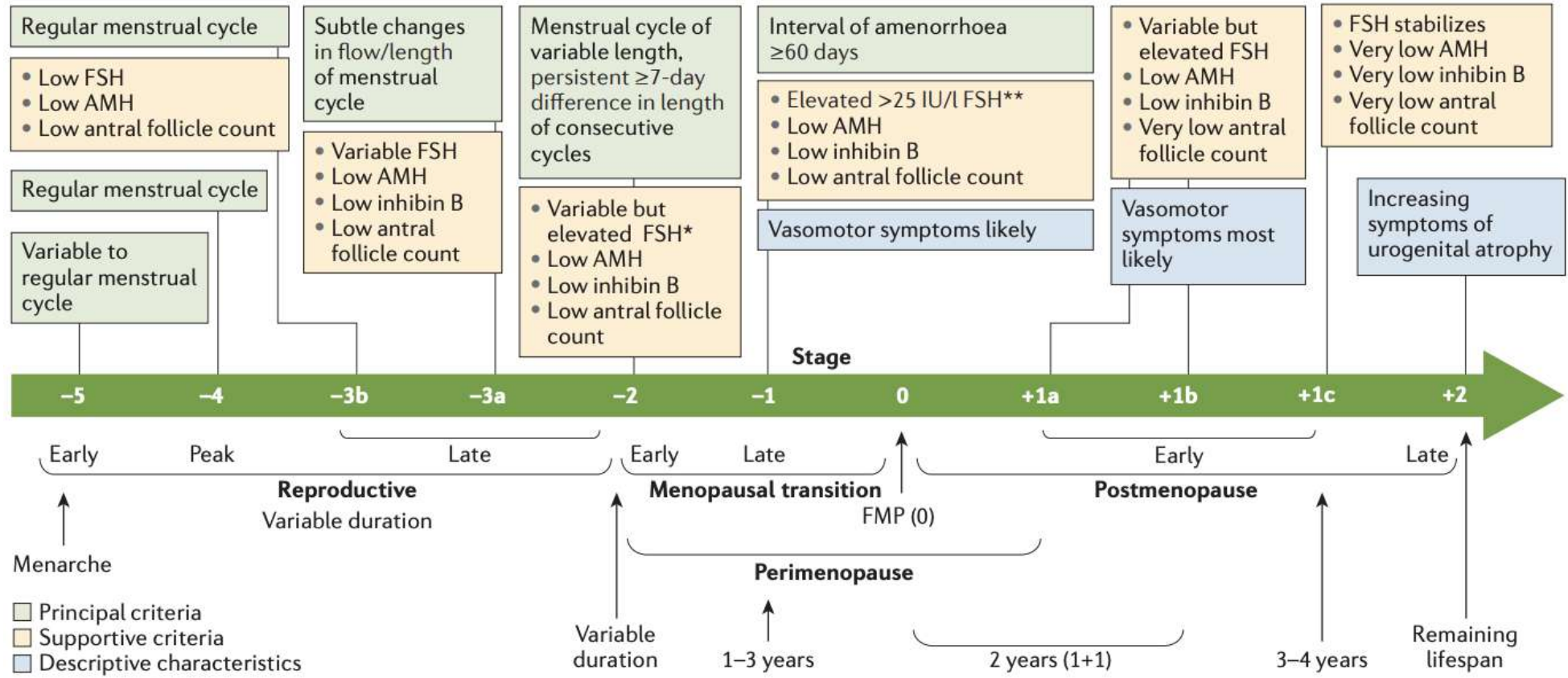
- 1 Analyse menopausal hormone therapy (MHT);** the pharmacokinetic and pharmacodynamic differences between oral, transdermal, and vaginal preparations.
- 2 Evaluate the safety profiles** of MHT according to route of administration and patient comorbidities.
- 3 Apply strategies to prevent or manage common adverse effects** associated with MHT using integrative co-prescribing approaches.
- 4 Develop integrative management plans** that incorporate evidence-based nutritional, herbal, and lifestyle interventions alongside MHT.
- 5 Identify clinically significant herb–nutrient–drug interactions, contraindications,** and considerations when co-prescribing complementary medicines with MHT.

| Understanding peri/menopause

- Limited research last century.
- Significant increase in the last 20 years – more than 60%.
- Surge in patient awareness, social media.
- Changes to medicine, guidelines, recommendations.



Peri/menopause – Defined



Davis, S. R., Lambrinoudaki, I., Lumsden, M., Mishra, G. D., Pal, L., Rees, M., Santoro, N., & Simoncini, T. (2015). Menopause. *Nature reviews. Disease primers*, 1, 15004

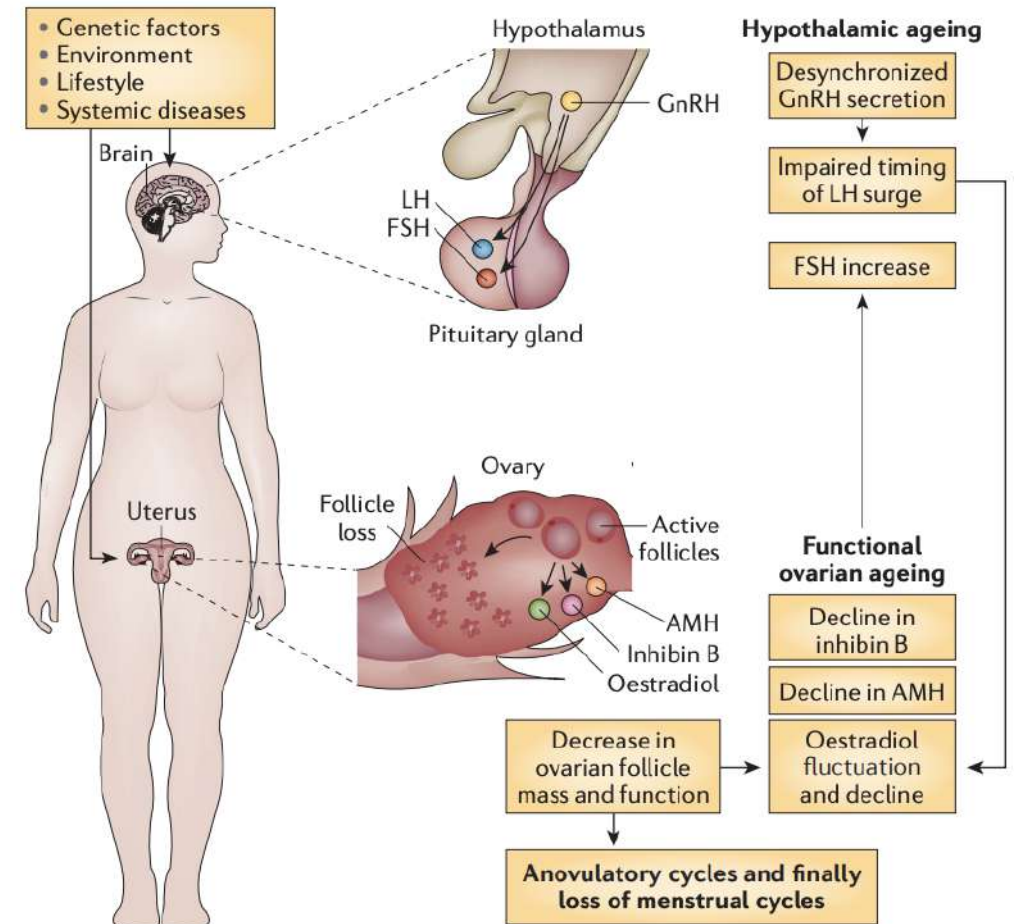
Perimenopause is defined more by hormonal shifts than calendar age.

'Menopause' once amenorrhoea is 12 months +.

Variable duration 2-10 years, onset also variable age 35-50.

Signs and Symptoms

- **Vasomotor (VMS):** hot flushes, night sweats.
- **Cardio-metabolic changes:** increased central adiposity, lipid changes, altered glucose and insulin sensitivity.
- **Mood changes:** anxiety, irritability, mood swings, sleep issues, memory lapses, poor concentration, low energy and fatigue, higher emotional reactivity.
- **Estrogen excess;** heavy bleeding, sore breasts, headaches and bloating.
- **Genitourinary syndrome of menopause (GSM)** Changes to libido, vaginal dryness/atropy.
- Muscle/joint pain, loss of bone density, skin changes.



Davis, S. R., Lambrinoudaki, I., Lumsden, M., Mishra, G. D., Pal, L., Rees, M., Santoro, N., & Simoncini, T. (2015). Menopause. *Nature reviews. Disease primers*, 1, 15004

| Drug Treatment Options

Hormonal

- **Combined MHT** – estradiol with progestogen or progesterone – cyclical progestogen/progesterone if less than 12m amenorrhoea
- **Estrogen only** – post hysterectomy or presence of mirena
- **Progesterone only** – if oestrogen unsuitable
- **Tibolone** – synthetic steroid
- **DHEA**
- **Testosterone**

Delivery methods vary – Estrogen via tablet, transdermal patch, gel, pessary, vaginal cream. Progestogen/progesterone available in capsule/tablet, DHEA as a pessary and testosterone as a cream.

Non Hormonal

- SSRIs and SNRIs
- Clonidine
- Oxybutynin
- Gabapentin
- Fezolinetant

AMS guide to MHT/HRT doses

CYCLIC MENOPAUSAL HORMONE THERAPY (MHT)

Use continuous oestrogen and cyclic progestogen combinations at peri-menopause or if less than 12 months amenorrhoea

Low Dose		
PRODUCT	PRESENTATION	COMPOSITION
Femoston	Tablet	1mg oestradiol/10mg dydrogesterone
Estrogel Pro	Combination pack of oestradiol transdermal gel, with micronised progesterone capsules.	1 pump (0.75mg oestradiol) daily, and 2 capsules (200mg) micronised progesterone orally for 12 days out of a 28-day cycle
Medium dose		
Trisequens*	Tablet	1 and 2mg oestradiol hemihydrate/1mg norethisterone acetate
Femoston	Tablet	2mg oestradiol/10mg dydrogesterone
Estalis sequi 50/140)	Transdermal patch	50mcg 17β oestradiol/140mcg norethisterone acetate (twice weekly application)
Estalis sequi 50/250 (same oestrogen, more progestogen than Estalis sequi 50/140)	Transdermal patch	50mcg 17β oestradiol/250mcg norethisterone acetate (twice weekly application)
Estrogel Pro	Combination pack of oestradiol transdermal gel, with micronised progesterone capsules	2 pumps (1.5mg oestradiol) daily, and 2 capsules (200mg) micronised progesterone orally for 12 days out of a 28-day cycle

CONTINUOUS COMBINED MENOPAUSAL HORMONE THERAPY (MHT)

Should be used if 12 months since LMP or after 12 months cyclical MHT

LOW DOSE		
PRODUCT	PRESENTATION	COMPOSITION
Angeliq 1/2*	Tablet	1mg oestradiol hemihydrate/2mg drospirenone
Femoston-conti*	Tablet	1mg oestradiol/5mg dydrogesterone
Kliovance*	Tablet	1mg oestradiol hemihydrate/0.5mg norethisterone
Bijuva*	Capsule	1mg oestradiol/100mg micronised progesterone
Estrogel Pro	Combination pack of oestradiol transdermal gel, with micronised progesterone capsules.	1 pump (0.75mg oestradiol hemihydrate) daily, and 1 capsule (100mg) micronised progesterone orally for 25 days out of a 28-day cycle ¹
OTHER LOW DOSE HORMONAL OPTIONS		
Livial*, Xyvion*	Tablet	2.5mg tibolone
Duavive* (oestrogen/ SERM combination)	Tablet	0.45mg conjugated equine oestrogens / 20mg bazedoxifene acetate
MEDIUM DOSE		
Kliogest*	Tablet	2mg oestradiol hemihydrate/1mg norethisterone
Estalis continuous 50/140	Transdermal patch	50mcg 17β oestradiol/140mcg norethisterone acetate (twice weekly application)
Estalis continuous 50/250 (same oestrogen, more progestogen than Estalis continuous 50/140)	Transdermal patch	50mcg 17β oestradiol/250mcg norethisterone acetate (twice weekly application)
Estrogel Pro	Combination pack of oestradiol transdermal gel, with micronised progesterone capsules.	2 pumps (1.5mg oestradiol hemihydrate) daily, and 1 capsule (100mg) micronised progesterone orally for 25 days out of a 28-day cycle ¹

¹Can be given daily if adherence is an issue

<https://hub.menopause.org.au/Play?pid=6eceed60-db26-4dfc-a662-794d7b39ef59>

AMS guide to MHT/HRT doses

OESTROGEN ONLY THERAPY:

Only use these if patient has had a hysterectomy or in combination with a progestogen or Mirena if intact uterus

LOW DOSE		
PRODUCT	PRESENTATION	COMPOSITION
Estrofem*	Tablet	1mg oestradiol hemihydrate
Progynova	Tablet	1mg oestradiol valerate
Premarin*	Tablet	0.3mg conjugated equine oestrogens
Estradot 25, 37.5	Transdermal patch	25mcg or 37.5mcg oestradiol (twice weekly application)
Estraderm 25 MX	Transdermal patch	25mcg oestradiol hemihydrate (twice weekly application)
Estrogel	Gel	0.75mg oestradiol hemihydrate = 1 pump daily
Sandrena	Gel	0.5mg oestradiol daily
MEDIUM DOSE		
Estrofem*, Zumenon	Tablet	2mg oestradiol hemihydrate
Progynova	Tablet	2mg oestradiol
Premarin*	Tablet	0.625mg conjugated equine oestrogens
Estradot 50	Transdermal patch	50mcg oestradiol (twice weekly application)
Estraderm 50 MX	Transdermal patch	50mcg oestradiol hemihydrate (twice weekly application)
Sandrena	Gel	1mg oestradiol daily
Estrogel	Gel	1.5mg oestradiol hemihydrate = 2 pumps daily
HIGH DOSE		
Estradot 75, 100	Transdermal patch	75 or 100mcg oestradiol (twice weekly application)
Estraderm 75, 100 MX	Transdermal patch	75 or 100mcg oestradiol hemihydrate (twice weekly application)
Sandrena	Gel	1.5mg oestradiol = 1mg + 0.5mg sachets daily
Estrogel	Gel	2.25mg oestradiol hemihydrate = 3 pumps daily or 3.0mg oestradiol = 4 pumps daily

VAGINAL THERAPY

If prescribing vaginal oestrogen rather than systemic hormone therapy, a progestogen is not required.

PRODUCT	PRESENTATION	COMPOSITION
Ovestin	Cream	0.5mg oestrinol = 1 application; daily for first 14 days, then twice weekly ongoing
Ovestin	Pessary	0.5mg oestrinol; daily for first 14 days, then twice weekly ongoing
Vagifem Low	Pessary	10mcg oestradiol hemihydrate; daily for first 14 days, then twice weekly ongoing
Intrarosa*	Pessary	6.5mg dehydroepiandrosterone (DHEA) daily (prasterone)

PROGESTOGEN THERAPY

Suggested alternative doses for use with the oestrogen preparations above where fixed dose therapy is not suitable

LOW DOSE for use with low dose oestrogen		
PRODUCT	PRESENTATION	COMPOSITION
Provera (1/2 of 5mg tablet)	Tablet	2.5mg medroxyprogesterone acetate
Provera 2.5mg tablet*	Tablet	2.5mg medroxyprogesterone acetate
Primolut N (1/4 of 5mg tablet)	Tablet	1.25 mg norethisterone
Prometrium	Capsule	100mg micronised progesterone orally for 25 days out of a 28-day cycle ¹ or 200mg orally daily for 12 days out of a 28-day cycle
Mirena* (PBS indication for contraception/ menorrhagia)	Intrauterine system	Levonorgestrel 52mg (approx. 20mcg daily over 5 years)
MEDIUM DOSE for use with medium dose oestrogen ²		
PRODUCT	PRESENTATION	COMPOSITION
Primolut N (1/4 of 5mg tablet)	Tablet	2.5mg norethisterone
Provera, Ralovera	Tablet	5mg medroxyprogesterone acetate
Prometrium	Capsule	100mg micronised progesterone orally for 25 days out of a 28-day cycle ¹ or 200mg orally for 12 days out of a 28-day cycle
Mirena* (PBS indication for contraception/ menorrhagia)	Intrauterine system	Levonorgestrel 52mg (approx. 20mcg daily over 5 years)
HIGHER DOSE (for use in cyclic therapy or continuous therapy with high dose oestrogen) ²		
PRODUCT	PRESENTATION	COMPOSITION
Primolut N (1/2 5mg tablet)	Tablet	2.5mg norethisterone
Prometrium	Capsule	100mg micronised progesterone orally for 25 days out of a 28-day cycle ¹ or 200mg orally for 12 days out of a 28-day cycle
Provera, Ralovera	Tablet	10mg medroxyprogesterone acetate
Mirena* (PBS indication for contraception/ menorrhagia)	Intrauterine system	Levonorgestrel 52mg (approx. 20mcg daily over 5 years)

<https://hub.menopause.org.au/Play?pid=6eceed60-db26-4dfc-a662-794d7b39ef59>

Oral Estradiol (valerate and hemihydrate)

Pharmacokinetics

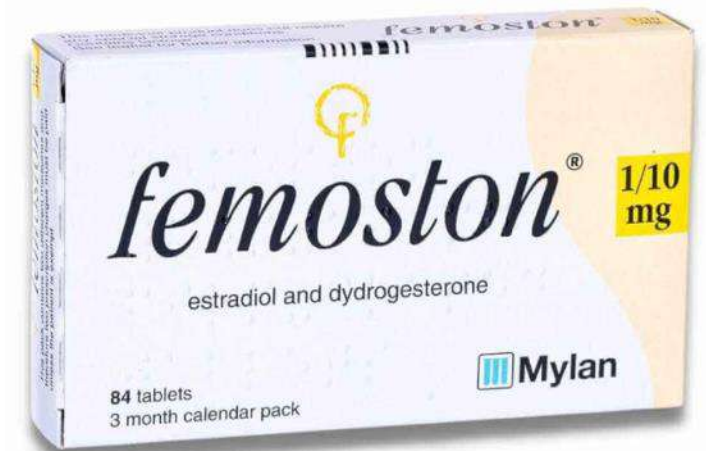
- Absorbed via gut to portal circulation with extensive first-pass hepatic metabolism.
- T_{max} 6–8 h, Bioavailability ~2–10%, Half-life ~14–17 h.
- Converted partly to estrone and conjugates.
- Metabolised via CYP1A1 and CYP3A4.

Impact

- Agonist at ER α and ER β receptors, impact on thermoregulation, neurovascular signalling, vaginal epithelium, bone turnover.
- Hepatic exposure increases SHBG, clotting factors, CRP, TBG, CBG.
- Fluctuating serum levels.
- Nausea, breast tenderness, headaches, gallbladder disease

Consider

- Higher hepatic effect – increased VTE risk, triglycerides and gallbladder disease risk.
- Caution for smokers, migraine history.



| Hepatic Effects of Oral Estradiol

LIPID METABOLISM

- ↓ LDL-C (↑ hepatic LDL receptors)
- ↑ HDL-C (↑ ApoA-I, ↓ hepatic lipase)
 - ↓ Lipoprotein(a)
- ↑ Triglycerides (↑ VLDL production)

BINDING PROTEINS

- ↑ SHBG → ↓ free testosterone
- ↑ TBG → ↑ total thyroid hormones
- ↑ CBG → ↑ total cortisol

COAGULATION

- ↑ Fibrinogen
- ↑ Factors VII, VIII, X
- ↓ Protein S
- Prothrombotic shift
- ↑ VTE risk

INFLAMMATION

- ↑ C-reactive protein (CRP)
- Hepatic synthesis increase

SYSTEMIC CONSEQUENCES

- Improved LDL/HDL profile but ↑ triglycerides
- Reduced free testosterone (via SHBG increase)
 - Increased thromboembolic risk
 - Elevated CRP (hepatic marker)

| Transdermal Estradiol (gel/patch/spray)

Pharmacokinetics

- Enters systemic circulation via skin
- largely avoids first pass liver metabolism
- produces steady state estradiol

Impact

- Similar ER antagonism but minimal hepatic stimulation
- reduced VTE risk, minimal coagulation, lipid, CRP and SHBG neutral

Consider

- Preferred in women with VTE risk, obesity, migraine, or metabolic syndrome.
- Lower thrombotic and hepatic risk profile than oral estrogen
- Adherence issues
- Local skin irritation (much higher for patch)
- Additional progesterone may be needed



| Vaginal Estradiol (pessary, tablet, cream)

Pharmacokinetics

- Local vaginal absorption.
- Minimal systemic estradiol levels, especially when placed in lower third of vagina.
- Serum levels usually remain in postmenopausal range.



Impact

- Local estrogen receptor activation in vaginal epithelium, urethra and bladder, improved lubrication, epithelial thickness, pH and microbiome.

Consider

- First-line therapy for genitourinary syndrome of menopause (GSM).
- Does not require progestogen for endometrial protection at low doses. Minimal systemic risks.

MHT Route Comparison Summary

	Oral Estradiol	Transdermal Estradiol	Vaginal Estradiol
Absorption	Gut to liver circulation	Skin to systemic circulation	Local vaginal tissue
First-pass liver metabolism	Yes	Minimal	Minimal
Estrone : estradiol ratio	5:1 – 7:1 higher	2:1 lower	Minimal systemic
SHBG, clotting factors, CRP	Increased	Minimal change	None
VTE risk	Higher	Neutral	None
Lipid effects	Higher HDL & TG, lower LDL	Neutral	None
Clinical use	Systemic symptom control	Systemic symptom control	GSM only

| Naming the Progestogens

Progestogen – the umbrella term for all.

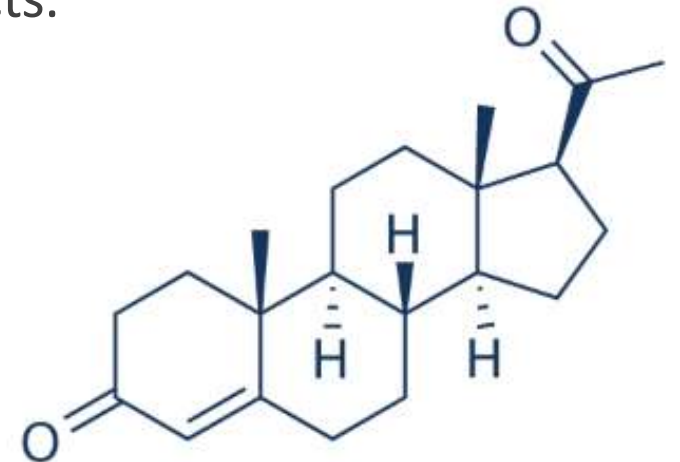
Progesterone – naturally occurring hormone In MHT micronized progesterone.

Progestins – synthetic compounds that mimic progesterone.

They have different metabolic effects, often with more side effects.

Available in Australia currently;

- Medroxyprogesterone.
- Drospirenone.
- Levonorgestrel (as IUD).
- Norethisterone.



| Micronised Progesterone (Prometrium)

Pharmacokinetics

- Rapid GI and hepatic metabolism.
- Up to 30 metabolites.
- T_{max} 4h.
- Food can double absorption.
- Shorter half-life.

Pharmacodynamics

- Metabolised to pregnanolones, positive modulation of GABA_A receptors, sedative/anxiolytic effects.
- Selective progesterone receptor activity.

Additional notes

- “Body-identical”.
- Night dosing preferred due to sedation.
- Effective endometrial protection.



| Medroxyprogesterone Acetate

Pharmacokinetics

- Higher progestogenic potency and bioavailability than progesterone.
- T_{max} 1–4h.
- Long half-life 40–60h.

Pharmacodynamics

- High progesterone receptor affinity.
- Also binds androgen and glucocorticoid receptors.

Additional notes

- Strong endometrial protection.
- Longer duration of action.
- Greater metabolic and receptor cross-activity.



| Drospirenone

Pharmacokinetics

- Rapid absorption.
- T_{max} 1–2h.
- 76% bioavailability.
- Half-life 25–33h.

Pharmacodynamics

- Strong antimineralocorticoid activity.
- Increased sodium excretion.
- Increased potassium retention.
- Anti-androgenic effects.

Additional notes

- May reduce fluid retention/BP.
- Monitor potassium in high-risk patients.



| Levonorgestrel (LNG-IUS)

Pharmacokinetics

- IUD delivery.
- Serum peak 180 pg/mL within 2 weeks, declining over 5 years.
- Systemic half-life 14–20h.

Pharmacodynamics

- Predominantly local endometrial effect.
- minimal systemic exposure compared with oral agents.

Additional notes

- Highly effective endometrial protection.
- Contraceptive.
- Reduced systemic side effects.



| Norethisterone

Pharmacokinetics

- Oral bioavailability 40–80% (higher when fasted).
- T_{max} 1h.
- Half-life 9.5h.

Pharmacodynamics

- High androgen receptor affinity.
- Weak androgenic effects.

Additional notes

- May cause acne, oily skin, hirsutism in susceptible individuals.
- Effective endometrial protection.



| Androgens – Testosterone (Androfeme 1% Cream)

Pharmacokinetics

- Serum rise of testosterone takes around 6-12 weeks.
- Metabolised mainly in liver to inactive metabolites and estradiol via aromatase.
- 5mg dose restored total and free testosterone toward premenopausal ranges – aim to keep to female physiologic range.

Impact

- Action primarily via androgen receptors in CNS, muscle and Genital tissue.
- Enhances sexual desire, arousal and central reward pathways.



Consider

- Acne/oily skin, hirsutism, lipid changes dose related.
- Lacking long term safety data for cardiometabolic and breast tissue safety.

| Androgens – DHEA (6.5mg Vaginal Intrarosa)

Pharmacokinetics

- Local conversion from DHEA to androgens/estrogens, systemic levels of DHEA and metabolites remain within typical postmenopausal ranges.

Impact

- Local intracrine conversion, improving vaginal epithelium, pH and dyspareunia and other impacts of GSM.
- Nil systemic impact.

Consider

- Local vaginal discharge/irritation can occur, as can unexpected bleeding (rare).



| Benefits (and Risks) of MHT

- **VMS** – 70-90% reduction in frequency & severity.
- **GSM** – restore vaginal epithelium, increased lubrication and improved pH balance, significant improvements in dyspareunia and urinary symptoms (vaginal application).
- **Cardiovascular benefit depend on route, dose, duration and timing** – MHT within 10 years of menopause or before age 60 (maintaining epithelial integrity).
- **Cancer risks** – combined MHT increases breast cancer risk, estrogen alone may reduce (bioidentical may reduce risk) reduced colorectal cancer risk.
- **Bone protection** – reduction in fracture risk by 20-40% (ER-mediated inhibition of osteoclastogenesis).
- **Non-alcoholic fatty liver** – prevalence increased in oral administration and decreased in transdermal.
- **Sleep quality, mood regulation, sexual function, QoL** – modest benefits.
- **Mortality** – no change.

| Common Side Effects

Most adverse effects of MHT are dose-related and route-dependent.

Side effects are common in the first 3–6 months and can resolve with dose or formulation adjustment.

Serious risks are uncommon in healthy women under 60 when therapy is appropriately prescribed.

Most common early complaints are:

- Breast tenderness/mastalgia
- Bloating / fluid retention
- Breakthrough bleeding
- Nausea
- Headache



| Less Common Adverse Effects

Serious adverse events are uncommon in appropriately selected women under 60.

Venous Thromboembolism (VTE)

- Risk with oral estradiol, obesity, smoking, thrombophilia.
- Transdermal estradiol has minimal VTE risk in observational data.

Stroke

- Small increased risk with oral estradiol in women >60 or >10 years post menopause.
- Risk is low in healthy women <60 within 10 years of menopause.

Breast Cancer Risk

- Combined estradiol and progestogen shows a small increased risk.
- Estradiol only either minimal or possibly reduced risk in some data.
- Risk increases with duration >5 years (particularly combined therapy) and micronised progesterone may have a more favourable profile than MPA).

Gallbladder Disease

- More common with oral estrogen, lower risk with transdermal.
- Through altered bile composition and hepatic first-pass effect.

| Side Effect Support – Mastalgia

Up to 25% of MHT users, particularly with estrogen initiation or dose increase. Driven by increased or fluctuating estrogen (and progesterone) leading to ductal proliferation.

Consider

Flax (seeds/oil) – ALA, lignans, mucilage gum. anti-inflammatory, antioxidant. 30g ground seed daily.

Vitamin E & evening primrose oil (EPO) – benefit in cyclic mastalgia, reduction in severity through antioxidant/anti-inflammatory and prostaglandin modulation effect. Vit E 200–400 IU/day and EPO 1000mg BD.

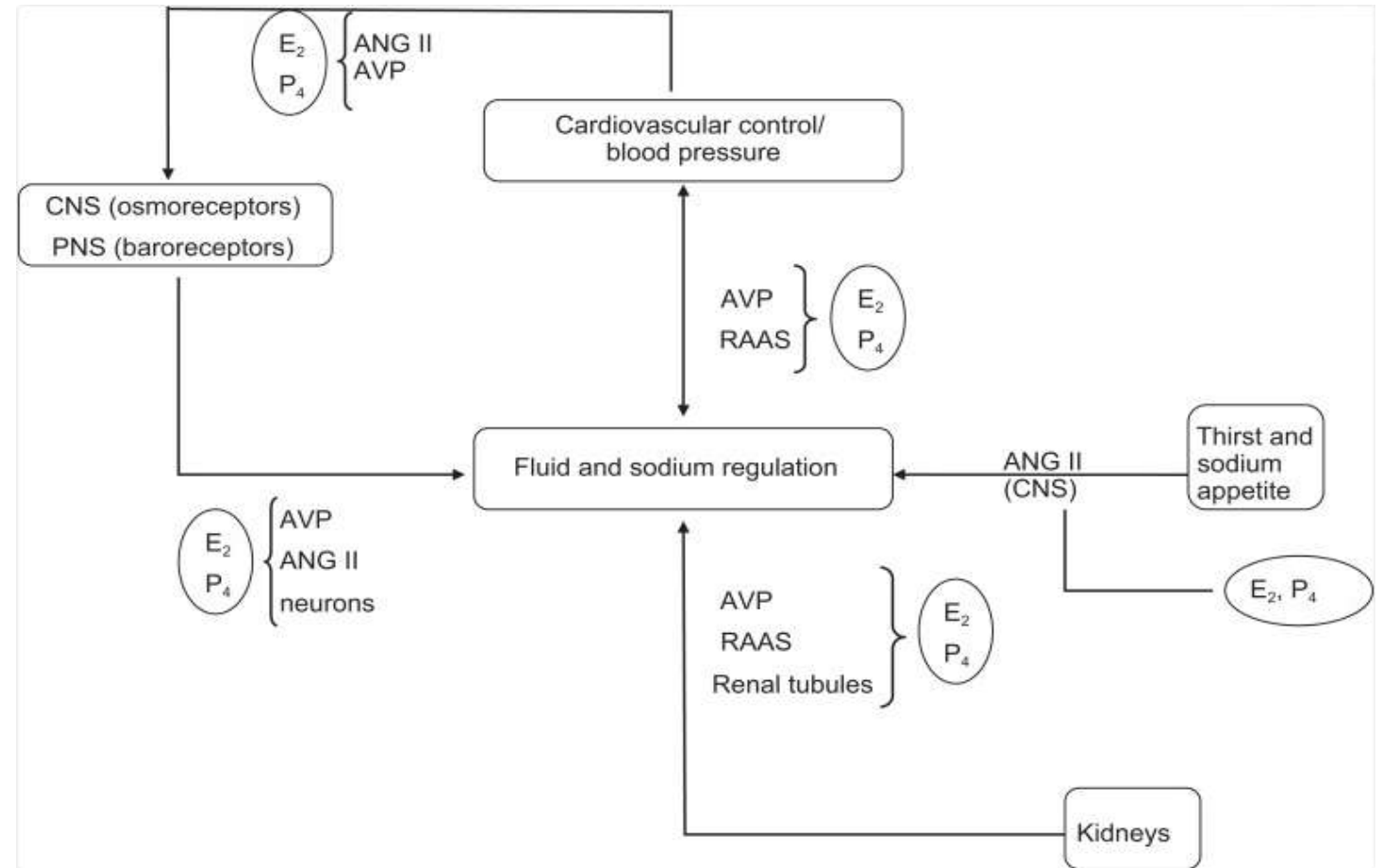
Vitex agnus castus – pain relieving, prolactin inhibiting, ER blocking. Dose 2ml fluid extract or 1800mg dry herb daily. (on rising).

Dietary interventions – reduce caffeine, and saturated fat, increasing unsaturated fats and fibre.



Side Effect Support – Fluid Retention

- Impacting up to 20% of users.
- More common with oral estrogen, progestins (esp. androgenic ones) and in the early treatment phase.
- Shift in the regulatory set-point for aldosterone/RAAS system mean kidneys hold onto more sodium.



Stachenfeld NS. Hormonal changes during menopause and the impact on fluid regulation. *Reprod Sci.* 2014 May;21(5):555-61. doi: 10.1177/1933719113518992. Epub 2014 Feb 3. PMID: 24492487; PMCID: PMC3984489.

| Side Effect Support – Fluid Retention

Consider

- **Magnesium**
 - modulates aldosterone sensitivity.
 - improves vascular tone.
 - Reduces hormonally mediated fluid retention.
 - 200-250mg/day dosing.
- **Vitamin B6**
 - also modulates aldosterone
 - 40-100mg/day dosing - short term use (neuropathy risk at 100mg/day longer term).
- **Sodium** – moderate sodium intake.
- **Daily movement** – support lymphatics.
- **If drospirenone, lower dosage consideration** (due to antimineralocorticoid activity).



| Side Effect Support – Headache & Migraines

Caused by rapid changes to estrogen levels, similar to menstrual migraine mechanisms.

Oral MHT and inclusion of progestogens had greater impact due to higher peak and more fluctuations.

Consider

- **First consider dose and form** – switching to transdermal and/or lower dose.
- **Magnesium** – NMDA modulation and stabilizes vascular tone, substance P inhibitor, 400-600mg/day.
- **Riboflavin (B2)** – improves mitochondrial energy metabolism, 200-400mg/day.
- **CoQ10** – reduces neuroinflammation and mitochondrial support, 300mg/day.
- **Other interventions to consider** – consistent sleep, hydration, blood glucose level stability, regular aerobic activity and stress regulation.

| Side Effect Support – Nausea

Estrogen influences the chemoreceptor trigger zone (CTZ), vomiting centre and serotonergic signalling. Rapid rise in estrogen increases sensitivity similar to early pregnancy.

Consider

- **First consider dose and form** – switching to transdermal and/or lower dose, always take with food
- **Ginger** – modulates the serotonergic signalling and is prokinetic
- **Vitamin B6** – neurotransmitter modulation, reduces sensitivity. Research indicates that ‘active’ form P5P is required. 25-50mg TDS, short term use only
- **Peppermint oil** – antispasmodic and smooth muscle relaxer, taken as an inhalation twice daily



| Improving Outcomes for Women

Goal is for an integrative management plan. Nutrition, herbal medicines and lifestyle advice can serve either alongside or as an alternative to MHT.

Focus

- **Optimise MHT** – dose, route, timing, progestogen choice, adherence capability.
- Apply **symptom-targeted, evidence-based interventions** to improve quality of life.
- Use integrative care **to enhance symptom control and improve tolerability/adherence.**
- **Reduce long term comorbidity** – particularly cardiometabolic and musculoskeletal.



| Improving Outcomes for Women

Core principles

- **Enhance symptom control – improve medicine tolerability/adherence**
 - Vasomotor symptoms
 - Mood/anxiety/stress/sleep
 - Sexual function & GSM
- **Address/consider comorbidities of peri/menopause**
 - Cardiovascular and metabolic disease
 - Musculoskeletal conditions (osteoporosis/fragility, sarcopenia, arthralgia/myalgia)
 - Skin and hair changes
- **Whole person support**
 - Gut health
 - Cognitive health

| Integrative Management Framework

Integrative management framework for menopause.

(Stepwise approach to optimise outcomes and support MHT).



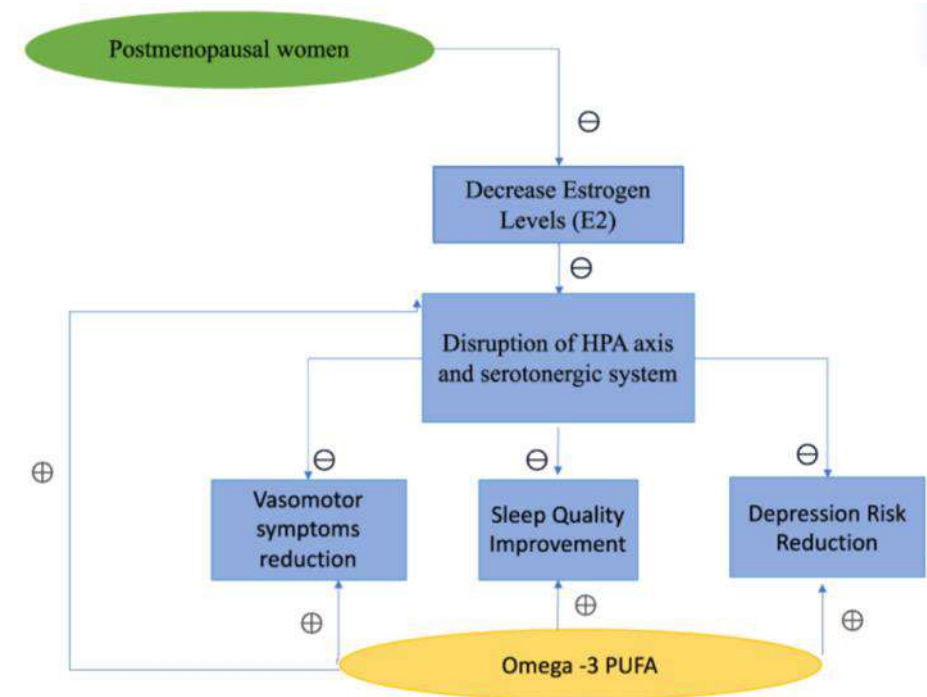
| Omega 3 Essential Fatty Acids

Mechanisms

- Anti-inflammatory and triglyceride-lowering effects.
- May influence serotonergic and dopaminergic pathways relevant to mood.

Evidence

- A 2023 review (Iqbal, et al) found benefit in VMS, **sleep and depression**.
- Masoumi et al (2016) reported increased benefit when omega 3 was combined with citalopram for postmenopausal women.
- Another 2023 review (Wang, et al) found significant **reductions in TG** for menopausal women.
- Minihane et al (2025) found an ‘increase in EPA and DHA intake and status is associated with **improved brain function**’.



Iqbal AZ, Wu SK, Zailani H, Chiu WC, Liu WC, Su KP, Lee SD. Effects of Omega-3 Polyunsaturated Fatty Acids Intake on Vasomotor Symptoms, Sleep Quality and Depression in Postmenopausal Women: A Systematic Review. *Nutrients*. 2023 Sep 30;15(19):4231. doi: 10.3390/nu15194231. PMID: 37836515; PMCID: PMC10574492.

| Omega 3 Essential Fatty Acids

Symptoms supported

- Cardiometabolic risk.
- Hypertriglyceridaemia
- Mood support/brain function.
- Possibly night sweats in some women.

Role with MHT

- Consider for long-term cardiometabolic intervention alongside MHT.
- Benefit for brain function/mood support requires EPA over 1000mg/daily.

Safety / cautions

- Generally safe with MHT.
- Use caution with anticoagulants / antiplatelet therapy at higher doses.



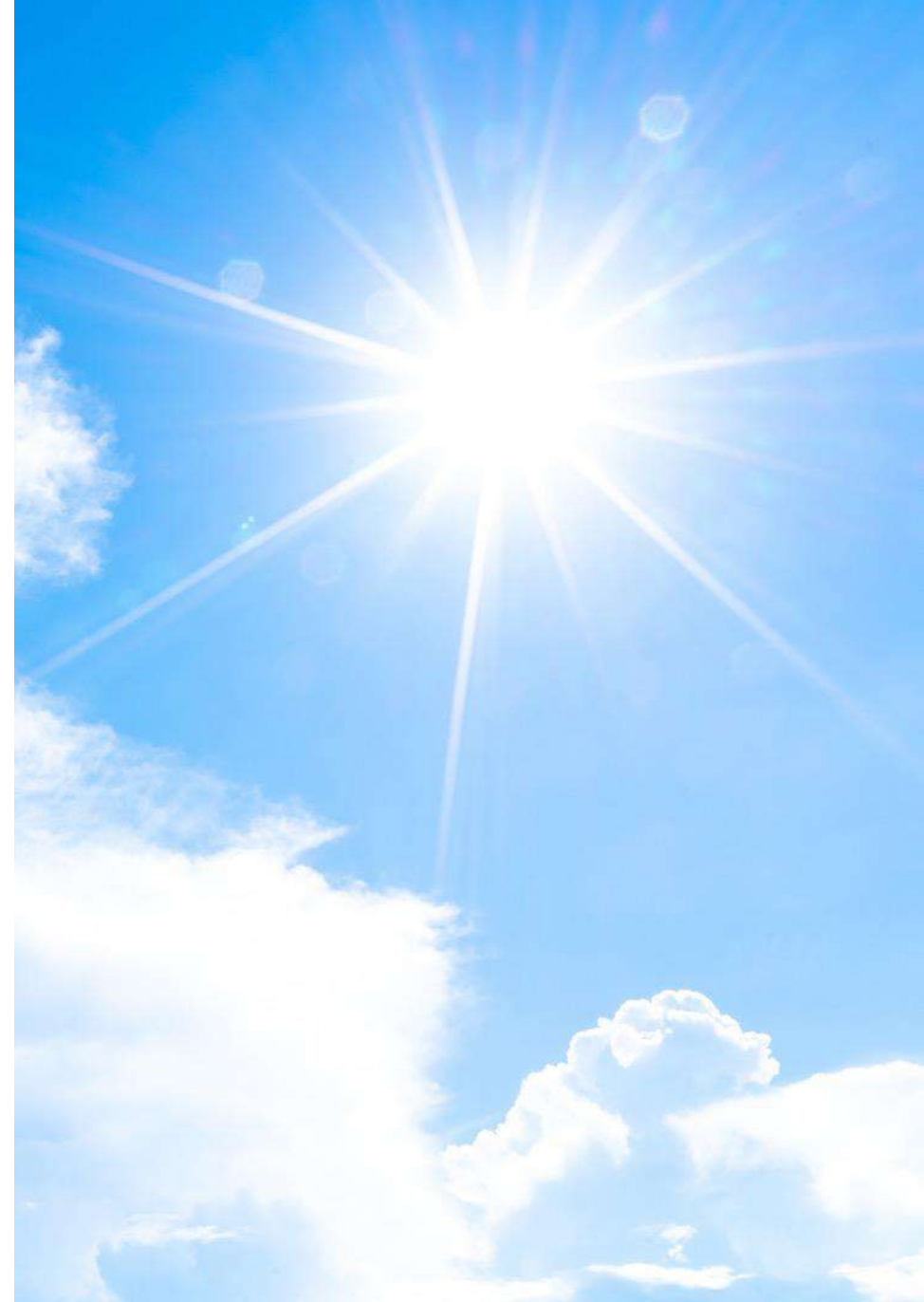
| Vitamin D

Mechanisms

- Central to calcium homeostasis and bone metabolism.
- Deficiency is common and may contribute to poor musculoskeletal health.
- Growing evidence for role in immune regulation and as an anti-oxidant.

Evidence

- Reviews of menopausal health consistently support identifying and **correcting vitamin D deficiency** in postmenopausal women.
- Multiple studies have found **benefit on GSM**, particularly in post menopausal women with deficiency – improved muscle strength and vulvovaginal atrophy symptoms.



| Vitamin D

Symptoms supported

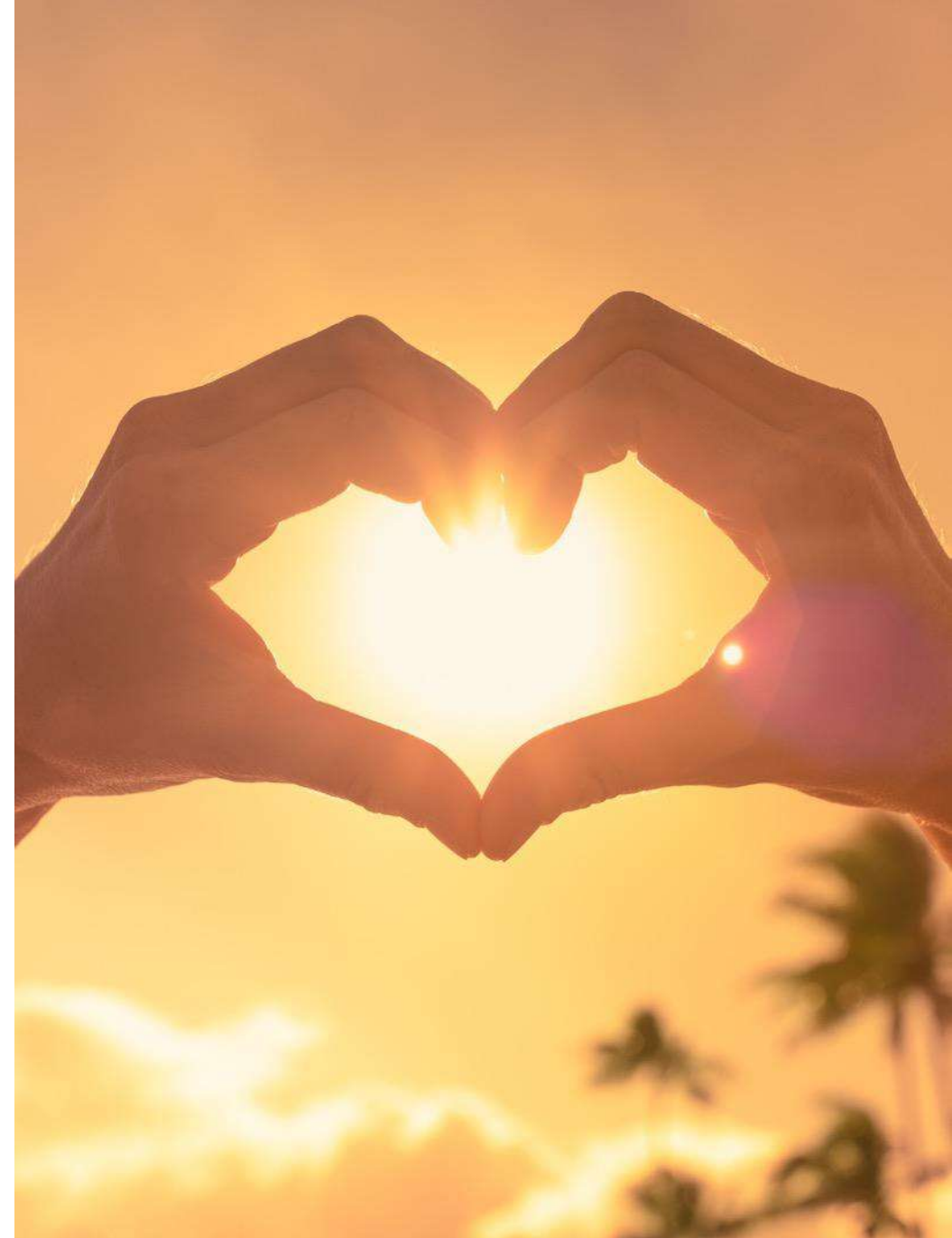
- Bone health / fracture risk reduction strategies.
- Deficiency-related muscle symptoms.
- GSM symptoms.

Role with MHT

- Consider with MHT when bone health is a priority or deficiency is present.
- Additional therapy to support GSM.

Safety / cautions

- Safe with MHT.
- Avoid chronic excessive dosing without testing.



| Magnesium

Mechanisms

- Involved in neuromuscular relaxation, GABA-related signalling, sleep regulation, cortisol reduction through HPA regulation and energy metabolism.
- Declining estrogen reduces magnesium retention capacity, leading to depletion.

Evidence

- A 2024 review (Rawji et al) concluded magnesium is likely useful for **mild anxiety and insomnia**, especially in people with low magnesium status.
- In a placebo-controlled trial, Abbasi et al. (2012) found magnesium improved subjective insomnia measures in older adults.
- Depletion of magnesium has been found to be more prevalent in those with **recurrent migraine**.



| Magnesium

Symptoms supported

- Sleep disturbance
- Anxiety and stress
- Headaches, migraine
- Muscle tension/pain
- Metabolic support

Role with MHT

- Addition when sleep, tension, constipation, or headache remain problematic.

Safety / cautions

- Diarrhoea is the most common adverse effect.
- Use caution in significant renal impairment.



| Creatine

Mechanisms

- Supports phosphocreatine energy buffering in both muscle and brain.
- Most useful when paired with resistance training.

Evidence

- A 2021 meta-analysis by Dos Santos et al, found older females supplementing with creatine had **significant gains in muscle strength**, over 24 weeks.
- In a 2015 RCT, Chilibeck et al. found creatine plus resistance training preserved femoral neck BMD and improved bone geometry.
- Reviews suggest the strongest evidence is for muscle, with bone and **cognition more mixed/emerging**.



| Creatine

Symptoms supported

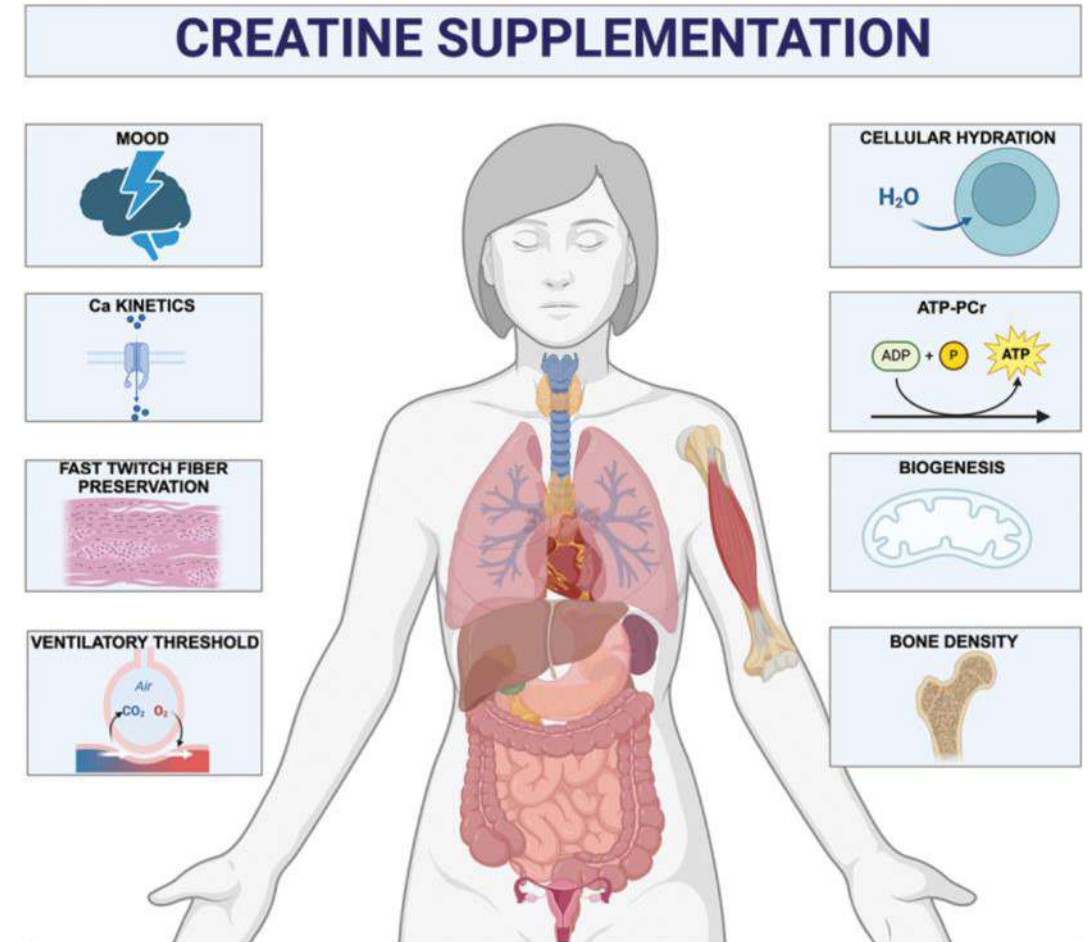
- Sarcopenia risk.
- Strength and function.
- Possibly bone strength.
- Emerging cognitive support.

Role with MHT

- MHT for musculoskeletal health, particularly with resistance training.

Safety / cautions

- Generally safe in healthy adults.
- Monitor in significant renal disease, particularly at high doses and ensure adequate hydration.



Smith-Ryan AE, DeBiondo GM, Brown AF, Kleiner SM, Tran NT, Ellery SJ. Creatine in women's health: bridging the gap from menstruation through pregnancy to menopause. *J Int Soc Sports Nutr.* 2025 Dec;22(1):2502094. doi: 10.1080/15502783.2025.2502094. Epub 2025 May 15. PMID: 40371844; PMCID: PMC12086928.

| Soy (isoflavones)

Mechanisms

- Modulate key signaling pathways, reducing release of inflammatory mediators.
- Antioxidant properties allow scavenging of ROS (slow aging).
- Act as phytoestrogens, binding mostly to Erb – agonist/antagonist effects.

Evidence

- A 2012 meta-analysis by Taku et al. found extracted or synthesised soy isoflavones **reduced hot-flash frequency and severity**.
- On safety, a 2025 meta-analysis found soy isoflavones had **no significant effects on endometrial thickness**, vaginal maturation index, FSH, or estradiol, and long-term trials reported minimal overall risk in healthy postmenopausal women.



| Soy (isoflavones)

Symptoms supported

- Modest VMS reduction.
- Headache.
- Depression/low mood.
- Bone and cardiometabolic support(including palpitations).

Role with MHT

- Adjunct or alternative, 50-100mg isoflavones daily.

Safety / caution

- Food soy is generally well tolerated unless allergy is present.
- Evidence to date does not suggest clinically meaningful estrogenicity on endometrium at studied doses in postmenopausal women.
- Caution to remain for those with estrogen related disease.



| Soy (isoflavones)

Dietary Sources

Soy Food	Typical Serving	Total Isoflavones (mg)	Approx mg / 100 g	Notes
Whole soybeans (boiled)	½ cup (85 g)	~47 mg	~55 mg	Among the richest dietary sources
Edamame (green soybeans)	½ cup	~18–25 mg	~18 mg	Immature soybeans
Tempeh (fermented)	85 g (3 oz)	~10–38 mg	~60 mg	Fermentation alters aglycone content
Tofu (firm)	85 g (3 oz)	~17–33 mg	~22 mg	Depends on coagulant and firmness
Soy milk	1 cup (240–275 ml)	~24–30 mg	~10–12 mg	Highly variable depending on dilution
Miso paste	½ cup	~59 mg	~40 mg	Fermented soybean paste
Roasted soy nuts	28 g (1 oz)	~38 mg	~135 mg	Concentrated due to dehydration
Soy flour	¼ cup	~33 mg	~120 mg	Used in baking
Textured vegetable protein (TVP)	¼ cup	~27 mg	~90 mg	Processing reduces content slightly
Soy protein isolate	100 g	~91 mg	~91 mg	Processing can remove up to ~90% of original isoflavones
Soy yoghurt	½ cup	~21 mg	~16 mg	Depends on formulation

| Vitex agnus castus

Mechanisms

- Dopaminergic effects with prolactin modulation best evidence is in cyclical mastalgia and PMS-type symptoms.
- modulate key neuroendocrine pathways involved in menopause through dopaminergic, phytoestrogenic, opioidergic, and indirect serotonergic mechanisms.

Evidence

- A placebo-controlled RCT by Halaska et al. (1999) showed **benefit for cyclical mastalgia**.
- A 2020 review (Ooi, et al) concluded Vitex was effective in **relieving breast pain intensity** and reducing cyclical mastalgia symptoms.



| Vitex agnus castus

Symptoms supported

- Cyclical mastalgia / breast tenderness.
- PMS-like irritability or cyclical symptom clustering.
- More useful in perimenopause rather than postmenopause.

Role with MHT

- Most relevant for women with cyclic/progestogen-phase symptoms or breast tenderness on sequential regimens.

Safety / cautions

- Use caution with dopamine agonists/antagonists because of theoretical pharmacologic overlap.



| Shatavari (asparagus racemosus)



Mechanisms

- Traditional Ayurvedic herbal medicine, data remains limited, but emerging.
- Contains steroidal saponins, phytoestrogens and antioxidants.

Evidence

- In a 2024 randomized, double-blind, placebo-controlled trial, Gudise et al. found **significant improvements in hot flashes, night sweats, insomnia, anxiety, vaginal dryness, loss of libido, and Utian QoL versus placebo.**
- In a 2025 RCT, Mahajan et al. also found shatavari root extract **improved perimenopausal symptom scores and was safe.**
- O’leary et al (2021) found no benefit for bone turnover in post menopausal women but **improvement in muscle function** and contractility.

| Shatavari (asparagus racemosus)

Symptoms supported

- Vasomotor symptoms.
- Sleep, anxiety.
- GSM.
- Muscle function.
- Quality of life.

Role with MHT

- Adjunct or alternative.

Safety / cautions

- Trials reported good tolerability and no major safety issue.



| Holy Basil (*ocimum tenuiflorum*)

Mechanisms

- Demonstrated to have anti-stress, adaptogenic, anti-oxidant, analgesic and anti-inflammatory properties, through constituents including eugenol.

Evidence

- In a 2022 double-blind, placebo-controlled RCT, **Lopresti et al.** found holy basil reduced objective and subjective stress markers and improved subjective sleep quality in stressed adults.
- Jamshidi et al (2017) completed a systematic review and among 24 human studies, found **significant cardiometabolic benefits, including normalising blood pressure, lipid markers and blood glucose, in addition to stress support.**



| Holy Basil (*ocimum tenuiflorum*)

Symptoms supported

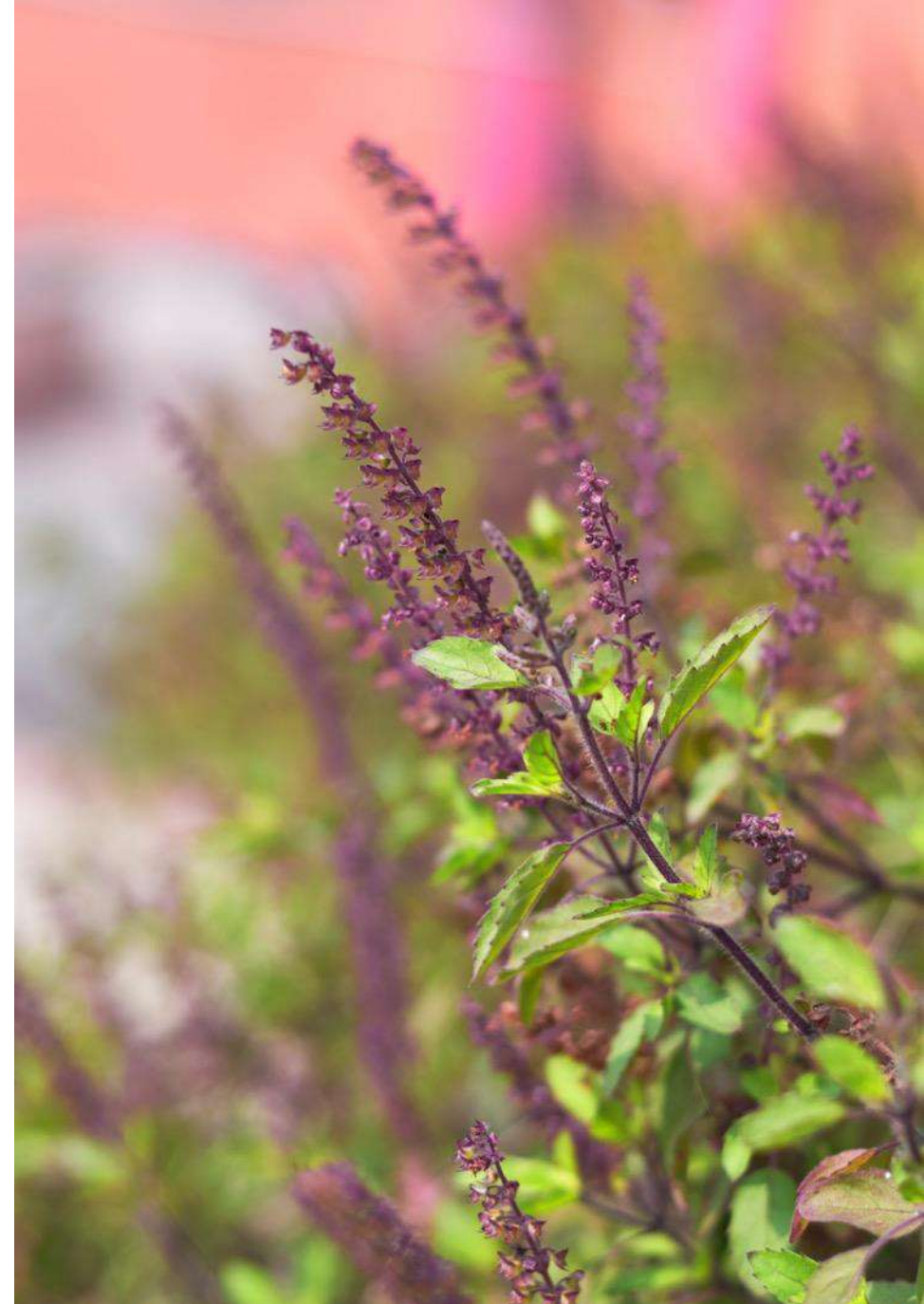
- Stress
- Sleep disturbance
- Anxiety “wired and tired” presentations
- Consider where stress amplifies VMS
- Cardiometabolic health

Role with MHT

- Supportive adjunct for stress/sleep

Safety / cautions

- Generally well tolerated in the human trials reviewed.



| Soluble Fibre

Mechanisms

- Improves LDL reduction through bile acid binding, and supports bowel regularity.

Evidence

- Ganji et al. (2008) both reported favourable lipid responses in postmenopausal women in 6 weeks with 5g TDS in cookie form. (recipe to the right).
- Jakeman et al (2017) found significant increases in bone calcium retention with 20g/daily of soluble corn fibre.

Fibre Cookies

Ingredients:

- 250 g psyllium fibre
- 250 g plain flour
- 300 g sugar
- 300 g brown sugar
- 480 g shortening
- 200 g eggs
- 1 tsp baking soda

Method

Combine all ingredients.

Divide into 50 cookies.

Cook at 170C for 11-14 minutes.

Each cookie contains 5 g fibre.

| Soluble Fibre

Symptoms supported

- Constipation.
- LDL reduction.
- Cardiometabolic risk.
- Gut-health support.

Role with MHT

- Useful alongside MHT where oral estrogen is being used and broader cardiometabolic risk reduction is desired.

Safety / cautions

- Start low and increase gradually.
- Separate from medications if absorption is a concern.



| Mediterranean Diet

Mechanisms

- Anti-inflammatory diet rich in fibre, polyphenols, unsaturated fats, legumes, nuts, fish, and olive oil.
- Supports insulin sensitivity, lipid profile, vascular health, mood and cognition.



Evidence

- The 2020 EMAS position statement concluded that **the Mediterranean diet may improve vasomotor symptoms, mood, cardiovascular risk factors, and long-term outcomes including bone and cognitive health.**
- Australian observational work published in 2024 (Byrne-Kirk et al) found that higher Mediterranean-style diet adherence was not associated with lower menopause symptom severity in one cohort.
- Another (Herber-Gast, 2013) found a lower symptoms with mediterranean diet in a 6000 women.

| Mediterranean Diet

Symptoms / domains supported

- Cardiovascular and metabolic risk.
- Cognitive health.
- Bone health.
- Possibly mood and vasomotor symptom burden.

Role with MHT

- Strong role alongside MHT for long-term risk reduction.
- Comorbidity-modifying intervention.



| MediDiet / MEDAS tool

Score 1 for adherence and
0 for non adherence

10 or more = high adherence

5 or less = low adherence

1	Uses olive oil as the main cooking fat	<input type="checkbox"/>
2	≥2 serves vegetables daily	<input type="checkbox"/>
3	≥3 serves fruit daily	<input type="checkbox"/>
4	≥3 serves legumes per week	<input type="checkbox"/>
5	≥3 serves fish/seafood per week	<input type="checkbox"/>
6	≥3 serves nuts per week	<input type="checkbox"/>
7	Whole grains most days	<input type="checkbox"/>
8	Red meat <1 serve/day	<input type="checkbox"/>
9	Processed meats rarely (<1/week)	<input type="checkbox"/>
10	Butter/cream <1 serve/day	<input type="checkbox"/>
11	Sugary drinks rarely (<1/day)	<input type="checkbox"/>
12	Commercial sweets/pastries ≤2/week	<input type="checkbox"/>

García-Conesa MT, Philippou E, Pafilas C, Massaro M, Quarta S, Andrade V, Jorge R, Chervenkov M, Ivanova T, Dimitrova D, Maksimova V, Smilkov K, Ackova DG, Miloseva L, Ruskovska T, Deligiannidou GE, Kontogiorgis CA, Pinto P. Exploring the Validity of the 14-Item Mediterranean Diet Adherence Screener (MEDAS): A Cross-National Study in Seven European Countries around the Mediterranean Region. *Nutrients*. 2020 Sep 27;12(10):2960. doi: 10.3390/nu12102960. PMID: 32992649; PMCID: PMC7601687.

| Exercise

Mechanisms

- Anti-inflammatory, enhances metabolic health.
- Thermoregulation, maintaining bone and muscle density through mechanical loading, improving vascular function through increased nitric oxide bioavailability.

Evidence

- in a 2019 RCT, Berin et al. found that 15 weeks of resistance training **reduced the frequency of moderate–severe hot flushes** in postmenopausal women.
- A 2023 systematic review (Capel-Alcaraz, et al) of strength exercise in menopausal women found **benefits for strength, bone density, metabolic and hormonal measures**.
- Another 2023 systematic review (Sanchez-Delgado) found benefits with **lowered blood pressure** when combined with oral HRT.



| Exercise

Symptoms supported

- Cardiometabolic risk.
- Bone health / sarcopenia.
- Mood and sleep.
- Possibly vasomotor symptoms in some women.

Role with MHT

- Foundational therapy alongside MHT, especially for long-term cardiometabolic and musculoskeletal risk reduction.

Safety / cautions

- Generally safe when tailored to baseline fitness, joint health, and fracture risk.
- In symptomatic women, hot flashes may transiently worsen during some exercise sessions.



| Cognitive Behaviour Therapy

Mechanisms

- Targets maladaptive sleep behaviours, hyperarousal, conditioned wakefulness, and dysfunctional beliefs about sleep.
- Can also reduce the interference caused by vasomotor symptoms.

Evidence

- The 2023 NAMS nonhormone statement recommends CBT for '**reducing the bother and interference associated with VMS**'.
- A 2024 scoping review (Niktaudi et al) found that CBT-I consistently **improved sleep quality** and insomnia severity in menopausal women.
- In RCTs by McCurry et al. (2016) and Drake et al. (2019), CBT-I **improved insomnia** more than sleep hygiene education alone.



| Cognitive Behaviour Therapy

Symptoms supported

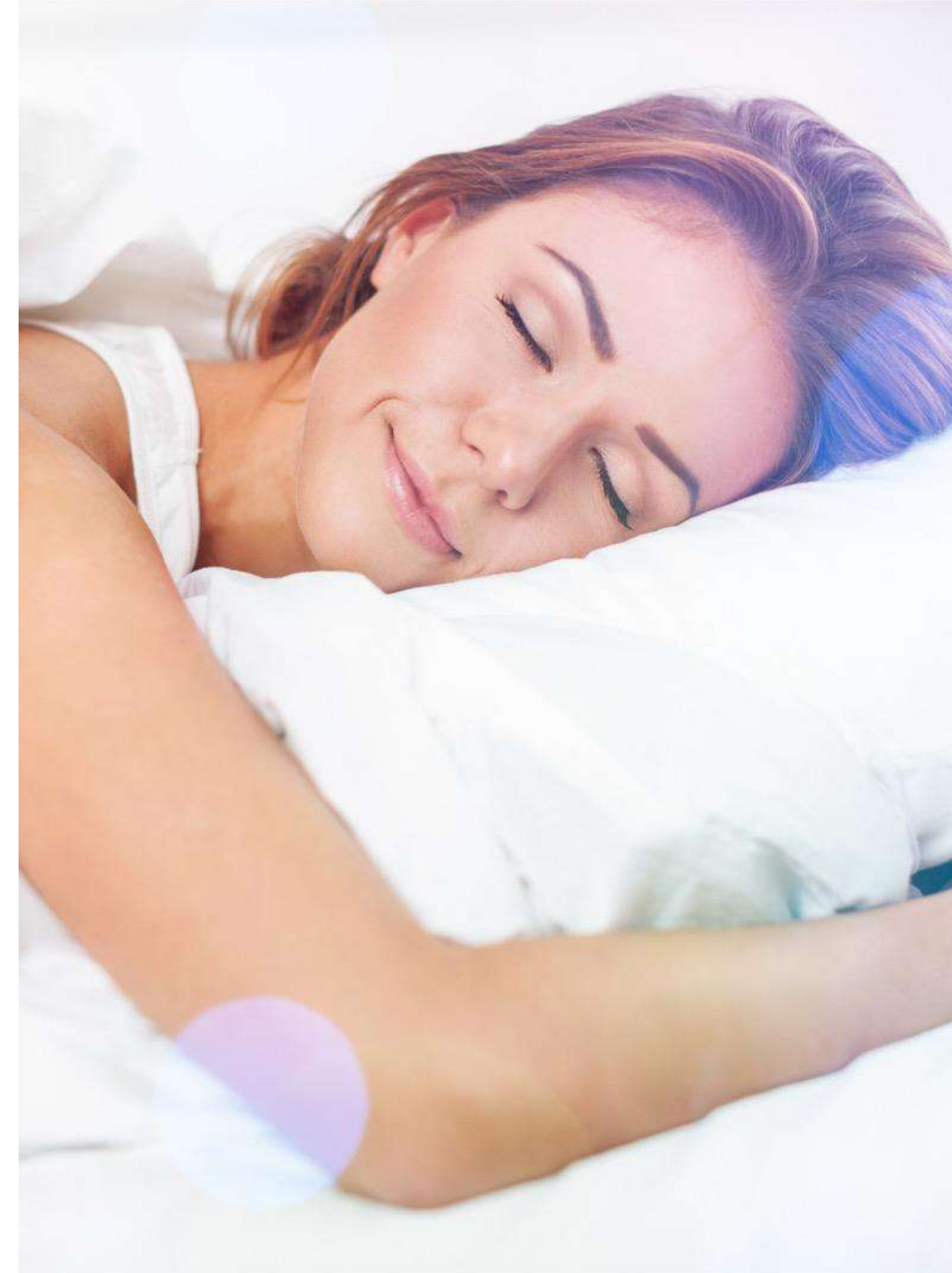
- Insomnia
- Sleep fragmentation
- Distress related to hot flushes / night sweats
- Mood and daytime functioning

Role with MHT

- Excellent adjunct to MHT, particularly when sleep remains poor despite improved VMS.
- Especially useful in women who cannot or do not want to escalate hormonal therapy.

Safety / cautions

- Safe with MHT.
- Access and adherence can be barriers.



| Herb/Drug/Nutrient Interactions

Most complementary therapies can be used safely alongside MHT when evidence-based products are selected and key interaction categories are considered.

- CYP modulation (inhibit/induce)
- Bleeding risk, sedation
- Hormone sensitivity

Summary interaction

	Issue	Clinical relevance
St John's wort	CYP3A4 induction	May reduce oral estrogen levels
Grapefruit	CYP3A4 inhibition	May increase oral estradiol levels
Black cohosh	Rare hepatotoxicity	Avoid in liver disease
Skullcap + progesterone	Additive sedation	Falls risk in susceptible patients
High dose vitamin E / omega-3	Bleeding tendency	Monitor if anticoagulated

| Herb / Drug / Nutrient Interactions – Estradiol (oral)

Complementary medicine / food	Caution or contraindication	Why	Clinical notes	Key reference(s)
St John's wort	Caution / usually avoid	CYP3A4 and P-gp induction may reduce oral estrogen exposure and symptom control	Most clinically important herb interaction for oral HT; watch for return of VMS or bleeding change	Berri-Bibee et al, 2024
Grapefruit / grapefruit juice	Caution	Can increase oral estradiol bioavailability by inhibiting presystemic CYP3A4 metabolism	May raise estrogen exposure and side effects;	Schubert et al. 1994
Red clover / high-dose soy isoflavones / other phytoestrogens	Caution in hormone-sensitive settings	Potential additive hormone-active effects are theoretical; not proven harmful with routine MHT	Main concern is women with current/past estrogen-sensitive cancer or those on tamoxifen/AIs, rather than routine co-use with MHT	AMS review
Black cohosh	Caution	Liver injury concern complicates use because active liver disease is a contraindication to systemic HT	Not a direct PK interaction; avoid if abnormal LFTs/active liver disease	LiverTox

Herb / Drug / Nutrient Interactions – Estradiol (oral)

Complementary medicine / food	Caution or contraindication	Why	Clinical notes	Key reference(s)
Vitamin E (high dose)	Caution	May increase bleeding tendency, especially if also anticoagulated	Relevant if patient also uses anticoagulants, antiplatelets or has heavy bleeding	2013, Pastori et al.
Omega-3 (high dose)	Caution	Slight additive bleeding concern at high doses, especially with anticoagulants	Standard doses are usually compatible; focus caution on anticoagulated patients	Javaid et al. 2024
Fibre supplements	Caution (timing)	May delay/reduce absorption of co-administered oral medicines	Separate by a few hours from oral HT and other medicines if possible	General medication absorption guidance;
Calcium-D-glucarate	Caution	Theoretical reduction in enterohepatic estrogen recycling; no meaningful menopause/MHT outcomes data	Avoid presenting as evidence-based co-therapy with oral HT	Mechanistic literature only

Herb/Drug/Nutrient Interactions – Estradiol (transdermal)

Complementary medicine / food	Caution or contraindication	Why	Clinical notes	Key reference(s)
St John's wort	Caution	Enzyme induction is less likely to matter than with oral HT because transdermal bypasses first-pass gut/liver metabolism	Risk lower than with oral estrogen, but direct menopause interaction studies are lacking	See Oral Estradiol
Grapefruit / grapefruit juice	Generally not relevant	Grapefruit interaction is mainly with orally absorbed CYP3A4 substrates	Usually no clinically relevant concern for patches/gels/sprays	See oral estradiol
Black cohosh	Caution	Liver concern relevant as systemic HT is contraindicated/ cautioned in liver disease	Not a direct route-specific interaction	LiverTox
Red clover / soy isoflavones / phytoestrogens	Caution in hormone-sensitive settings	Same principle as oral estrogen: concern is mainly oncology context, not routine MHT co-use	Not an established contraindication with transdermal estrogen in otherwise appropriate women	AMS review

| Herb/Drug/Nutrient Interactions – Estradiol (transdermal)

Complementary medicine / food	Caution or contraindication	Why	Clinical notes	Key reference(s)
Vitamin E / high-dose omega-3	Caution if anti-coagulated / heavy bleeding	Additive bleeding concerns are patient-factor issues, not route-specific estrogen interactions	More relevant with anticoagulants, procedures, or heavy bleeding	Pastori; Javaid;
Psyllium / fibre	No meaningful interaction	Transdermal route bypasses GI absorption	Timing separation not needed for estrogen patch/gel itself	Route pharmacology

Herb/Drug/Nutrient Interactions – Estradiol (vaginal)

Complementary medicine / food	Caution or contraindication	Why	Clinical notes	Key reference(s)
Phytoestrogens (soy, red clover, shatavari)	Caution in hormone-sensitive settings	Concern is theoretical/additive hormone-active context in sensitive patients	Not generally a reason to avoid in routine practice unless oncology/history dictates caution	AMS review
Black cohosh / hepatotoxic herbs	Usually not route-specific issue	Vaginal estrogen is local, but liver disease may still change broader treatment decisions	More relevant if other systemic hormones are also being used	livertox
Bleeding-risk supplements (vitamin E, high-dose omega-3)	Caution if unexplained bleeding or anticoagulated	Not because of vaginal estrogen interaction, but because abnormal bleeding requires assessment	Don't attribute bleeding automatically to supplements or local estrogen; investigate	As for oral estradiol

Herb/Drug/Nutrient Interactions – Micronised Progesterone

Complementary medicine / food	Caution or contraindication	Why	Clinical notes	Key reference(s)
Grapefruit / grapefruit juice	Caution	May increase bioavailability of orally administered progesterone	Could increase sedation or dizziness in sensitive patients	Fingerová et al. 2003
Skullcap / Valerian / kava / alcohol	Caution / sometimes avoid	Additive sedation/CNS depression	Particularly relevant when oral micronised progesterone is used at bedtime	Progesterone sedation literature
St John's wort	Caution / usually avoid	Enzyme induction could theoretically reduce oral progesterone exposure	Strongest concern with oral rather than vaginal/transdermal routes	Berri-Bibee et al, 2024
Psyllium / high-fibre supplements	Caution (timing)	May reduce absorption of co-administered oral medicines	Separate dosing where practical	General absorption principles

Herb/Drug/Nutrient Interactions – Progestins

Complementary medicine / food	Caution or contraindication	Why	Clinical notes	Key reference(s)
St John's wort	Caution / usually avoid for oral progestins	Enzyme induction may reduce exposure to oral progestins	Best established from contraceptive literature; most relevant to oral regimens	Berri-Bibee et al, 2024
Grapefruit	Caution for oral progestins	May increase oral progesterone/progestogen exposure variably	More relevant to oral forms than LNG-IUS	Fingerová et al.
Phytoestrogens	Caution in hormone-sensitive settings	Not because of direct progestin interaction, but because whole hormonal context is more complex	Not usually a routine contraindication	Menopause guidance
Psyllium / high-fibre supplements	Caution (timing)	May reduce absorption of co-administered oral medicines	Separate dosing where practical	General absorption principles

| Herb/Drug/Nutrient Interactions – Testosterone

Complementary medicine / food	Caution or contraindication	Why	Clinical notes	Key reference(s)
Saw palmetto / spearmint / licorice	Caution	Potential antiandrogenic effects may counter desired clinical response	Not a proven contraindication, but may efficacy	Smith et al 2021
Phytoestrogens (soy, red clover)	Usually compatible	No established direct interaction with transdermal testosterone in women	Main issue is keeping testosterone in female physiologic range, not herb-food interaction	AMS review
Biotin	Caution (labs)	Not a testosterone interaction, but high-dose biotin can interfere with immunoassays	Relevant when monitoring hormones with blood tests	Lab interference principle

Herb/Drug/Nutrient Interactions – Vaginal DHEA

Complementary medicine / food	Caution or contraindication	Why	Clinical notes	Key reference(s)
St John's wort	No established interaction	Product information suggests interactions are not expected at clinically relevant concentrations	Data limited, but concern is much lower than with oral HT	TGA PI
Black cohosh	No established direct interaction	If systemic symptoms or LFT issues arise, reassess all products	More general safety monitoring than known interaction	EMA/TGA PI

Key Takeaways

1

Route of hormone therapy matters

2

Adverse effects are often improved by adjusting dose, route, or progestogen choice. Integrative co-prescribing can improve outcomes.

3

Lifestyle, nutrition and targeted complementary therapies may

- enhance symptom control
- improve tolerability and adherence to MHT
- support cardiometabolic and musculoskeletal health

4

Implement a structured approach

- optimise MHT (dose, route, formulation)
- build lifestyle foundations (diet, movement, sleep, stress)
- add targeted nutrients or herbal interventions
- monitor response, safety and interactions

Integrative menopause care should be personalised, evidence-informed and regularly reviewed to optimise symptom control and long-term health.

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CBTI

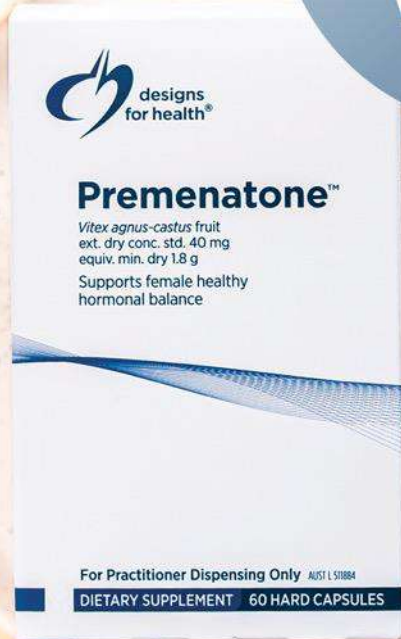
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