Dr AnnaBurrows

medical specialist in gynaecology

HRT update 2025

MENOPAUSAL HORMONE THERAPY - 2025

This presentation is for a general informative read and should **never** be a substitute for a consultation with your general practitioner or Dr Burrows.

Much of the information on this document is based upon the best world knowledge, past literature and the latest research from around the globe. I attended the Intenational Menopause Society 19th World Congress – nearly 3000 gynaecologists, endocrinologists, primary health care doctors, scientists and allied health professsionals presented or attended.

THE MENOPAUSE TRANSITION

- Vasomotor
- Irregular Bleeding
- Urinary Incontinence
- Sleep disturbance
- Dyspareunia
- Depression
- Anxiety
- Labile Mood
- Fatigue
- Headache
- Myalgias
- Arthralgias
- Weight gain
- Poor memory
- Dry Skin
- Dry eyes
- Vaginal Dryness
- Thin scalp hair
- Hirsutism

Understanding the Perimenopause Journey

The menopause transition (MT)is a major milestone for women, and adaptive process to lowering hormone levels. Women need time to accommodate lowering of oestrogen levels. Abrupt changes in levels can be problematic, depending on individual adaptability, genetic, environmental and psychological factors.

Early perimenopause

- Commences with clinically silent reduced ovarian reserve with less AMH and inhibin A
- Less restraint on FSH (follicle stimulating hormone)
- Leading to 'rapid' cycles, short follicular phases, follicle maturation beginning before the next menses
- More frequent menses
- Longer luteal phases
- Wider hormone fluctuations

Late MT

- periods can be 60 to 364 days apart
- prolonged stretches of low estradiol, failure to produce progesterone
- accelerated 'typical' symptoms (hot flushing, vaginal dryness, mood changes, sleep changes)

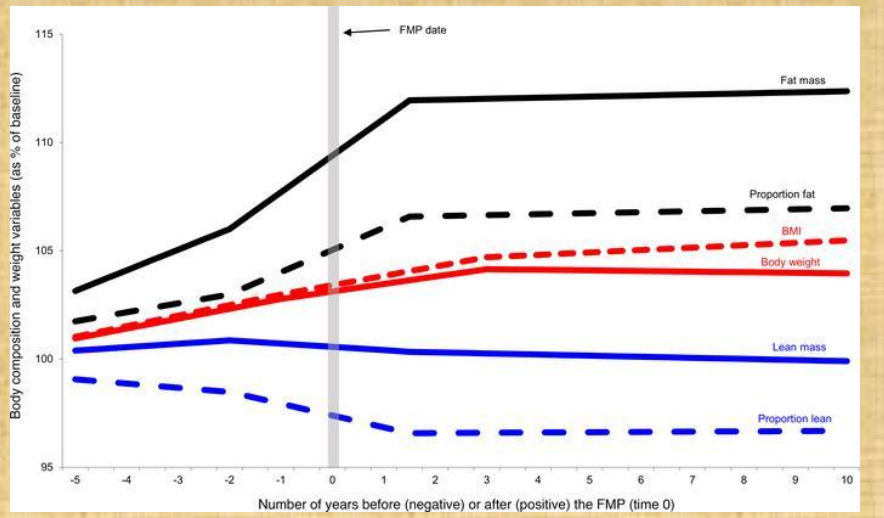
Understanding the Perimenopause Journey

Mood :The good news is that menopause transition and menopausal status is not a significant predictor of first episode of major depression.
Depressive symptoms (not major depression) is associated with stressful life events and other personal factors (general health, education, past history of depression).

Weight : This can be a struggle. *Jansen et al Arch Intern Med 2008* follow up 949 women over 9 years. The **metabolic** syndrome increases dramatically over the menopause transition. It is a constellation of related factors eg insulin resistance, abdominal obesity, lipid issues and hypertension. The loss of the protective role of oestrogens changes body fat distribution and leads to abdominal obesity.

Changes in body composition and weight during the menopause transition

The good news is that many of these processes have a short curve of worsening and then restabilize.



MHT/HRT BENEFITS

MHT/HRT is usually helpful if you experience problems with hot flushes and night sweats. Mood, sleep and sex drives may also improve. Oestrogen with natural progesterone early after the menopause will be protective for cardiac disease. Women can find improvements in joint and muscle aches, vaginal dryness and urine incontinence. There is long term protection of the heart, bones and vaginal mucosa.

MHT/HRT RISKS

Oestrogen

Oral (not transdermal) could increase thrombosis (blood clots in the legs or lungs).

Progestogen

Androgenic progesterone (used rarely in 2025) may lead to a slightly increased risk of developing breast cancer and cardiac disease.

Prometrium (body identical) or micronized progesterone is preferred

The Mirena intrauterine device is neutral with respect to systemic progesterone effects.

Overall, menopausal hormone treatment has the benefits of However, it can prevention of other conditions such as osteoporosis, heart disease, fractures, diabetes and some types of cancers.

Current international recommendations:

The benefits outweigh the risks in women who are having significant symptoms from menopause, and that MHT is effective and safe for most healthy women.
Some side effects include fluid retention, bloating, breast tenderness and swelling, and irregular bleeding. These often go away with time.

Precautions include:

breast, endometrial cancer, hormone dependent cancer
•undiagnosed vaginal bleeding
•untreated uterine lining thickening
•raised risk of thrombosis
•coronary heart disease, stroke or dementia
•blood clots in the legs or lungs
•untreated hypertension (if you have high blood pressure that is treated, talk to your doctor about MHT)
Other risk factors: Talk to your own doctor about your medical history.

BALANCING THE BENEFITS AND AND POSSIBLE RISK TO YOU IS PART OF SHARED DECISION MAKING WITH YOUR DOCTOR.

MENOPAUSAL HORMONE THERAPY

- MHT is the most effective treatment for moderate to severe menopausal symptoms and is most beneficial before the age of 60 years or within 10 years after menopause.
- ***The dose and duration of MHT should be consistent with treatment goals***.
- Oestrogen only is appropriate therapy for women after a hysterectomy.
- Oestrogen plus a progestogen should be used when the uterus is present.
- Topical low dose oestrogen is preferred for those women whose symptoms are limited to vaginal dryness and dyspareunia.

IMS Recommendations. Baber et al Climacteric ;19: 109-150
Global Consensus Statement. De Villiers et al Climacteric 19:313-315)

•OESTROGEN

•Oral tablet -oestrogen -for symptoms
•Gels or patches (oestrogen absorbed through the skin)
•creams and tablets (oestrogen) placed in the vagina (60-80% improvement)
•Selective Oestrogen Receptor Modulators SERM

•PROGESTERONE

•a hormonal intrauterine device (IUD)(Mirena). Minimal systemic progesterone effects, a contraceptive for the perimenopause as well as a treatment for bleeding.
•Micronised progesterone (Prometrium) natural- body identical,preferred over androgenic progesterone agents. Better risk profile for coronary disease, venous clotting and breast cancer risk.
•Synthetic androgenic progestogens.

•TESTOSTERONE

•Androfeme has approval in Australia for hypoactive sexual desire disorder.

•The 19th Annual International Menopause Society IMS World Congress was held in Melbourne, Oct 2024.
•The presentations confirmed unequivocal evidence that Androfeme improves female sexual function. Hormone levels confirm accurate safe dosing, and avoids dose related androgenic (male type) side effects.
• Anecdotally, there are other benefits, but this requires caution - the literature does not support testosterone for other indications. Large randomized controlled trials found no changes for mood disorders, wellbeing, cognitive (‘brain fog’ – *Climacteric 2023 vol 26),* dementia, muscle mass and bone density over placebo.

INTRAROSA – new to Australia 2024

A steroid (DHEAS or prasterone) daily insertion, 6.5 mg pessary blister pack was approved by the TGA in 2023. It provides a 40-80% improvement in symptom severity.
DHEAS is produced in the adrenal glands, gonads and brain and is converted intracellularly into active metabolites of estrogens and androgens (male type hormones).

The 19th Annual International Menopause Society World Congress had demonstrated the Canadian extensive experience with Intrarosa. The studies showed a 36% improvement in elastin density (improved elasticity for sexual comfort), 152% increase in nerve ending density to the vaginal mucosa(increased sensation and communication to the brain), improved nitrous oxide mediated cGMP responsible for relaxation of smooth muscle vessels – to improve lubrication).
The literature also cofirms improved bladder symptoms- it decreased frequency of bladder uti symptoms, and overactive bladder symptoms.

Daily vaginal administration
This is to treat the genitourinary syndrome of menopause. It is an alternative to vaginal oestrogen.

REF- ***Med Lett Drugs Ther. 2017 (1529. 149-150); Maseroli, El et al Sex Med Rev 2020, 8:379; Mattarazo, 2021 (European J Obs Gynae and reproductive Biology).***

ISSUES TO ADDRESS

1. What is the effect of HRT on hot flushes, the genitourinary syndrome of menopause (also formerly known as vaginal atrophy) and other menopause symptoms?

2. What are the risks or risk reduction for osteoporosis, cardiovascular disease, breast, endometrial and colon cancer?

3. Does HRT slow the decline in cognitive function and prevent Alzheimer's disease? What can be done about brain fog – or cognitive issues.

4. What about weight gain ?

5. How is sleep impacted by the perimenopause/menopause?

6. How can I address mood disorders and depressive or anxiety symptoms?

7. What is a safe recommendation for me – what to take and for how long?

SLEEP DISTURBANCES

POOR SLEEP

- **45% Perimenopausal Women**
- **Increased awakening, poor quality sleep, waking up alert**
- **Insufficent sleep, difficulty falling asleep, waking up early.**
- **Common – In 2024, the National Health and Wellness Survey of 27,621 women across the globe found up to 56% of post-menopausal and up to 60.1% of perimenopausal women reported sleep issues.**

CAUSES

- **Hot Flushes night sweats from menopausal oestrogen loss** (in 2024, Dr Makim, a neuroscientist from Chicago USA showed 78% of women will wake with a night flush, even if not subjectively aware of the flush -
- **Nocturia (waking to pass urine)**
- **Anxiety/Depresson/Mood**
- **Life stressors**
- **Primary Sleep Disorders/ restless leg syndrome/obstructive sleep apnoea/partner disturbance**

SLEEP DISTURBANCES

POOR SLEEP – CONSEQUENCES

Sleep Disturbances, Hot Flusing and Moods are interrelated.

-Depressed Mood is a risk for sleep disturbance & vice versa

-Sleep disturbance is suggested to be a potential mediator of the relationship between hot flusing and mood

-Mood can impact women's experience of menopause – those with depressive symptoms are more likely to report flushing, and negative mood can lead to more severe symptom severity**.**

Poor sleep impacts many aspects of health as well as overall quality of life.

(1)Cognitive, (2) Bone Health (3) immune function (4) metabolic health (5) mental health (6) cardiovascular health (7) dementia risk

Menopause Brain Fog and Sleep

'Constellation of cognitive symptoms experienced by women around the menopause which most frequently manifest in memory and attention difficulties'. (Maki et al, Menopause 2024; 31 – 724-33).

SLEEP DISTURBANCES - Management Strategies

Menopausal Hormone Treament (Oestrogen) has a favourable effects on the Circadian Rhythm **(Citron et al, Endocrine 2017, reprinted IMS 2024)**

- Improved sleep quality
- Improved length of REM sleep
- Improved latency (time from awake to sleep – the lightest of the non –REM sleep)
- Improved sleep quality

Other – Cognitive Behavioural Therapy has been helpful in randomized controlled trials.

Your family doctor or specialist will exclude other conditions- eg thyroid, autoimmune conditions, iron deficiency, stress, sleep apnoea, restless legs, anxiety and depression, reflux, alcohol, caffeine, chronic pain etc.

DEPRESSION

- Harvard Study of Moods – depression during the menopausal transition- women entering the perimenopause had a 2 fold increased risk for the first onset of depression or depressive symtoms

  Premenopausal 5.1%, perimenopausal 9.1%, postmenopausal 9.8%

- SWAN (Study of Women's Health Across the Nation) – increased psychologic distress

- Depression more likely:

1. Latter phases of perimenopause
2. History of postnatal depression and PMDD
3. Sleep disorders and hot flushes
4. Chronic health conditions
5. Life stressors

DEPRESSION

- Treatment with transdermal oestradiol success -KEEPS (Krono Early Prevention Study) :
- HRT can improve
  1. Depression
  2. Anxiety
  3. Sexual function
- Your gp/ psychiatrist might also consider
- Consider Cognitive behavioural therapies
- SSRI's (fluoxetine, sertraline, escitalopram, citalopram, vortioxetine)
- SNRI's (venlafaxine, desvenlafaxine, duloxetine)
- Others –mirtazapine, quetiapine

NEUROLOGICAL FUNCTION (dementia), ALZEHIMER'S DISEASE

Vascular dementia
Endostage repetitive minor or major vascular incidents in diseased vessels – leading to repetitive minor or major thrombosis or haemorrhage in brain vessels – leading to loss of neurons and ultimately dementia
Alzheimers' disease
Loss of neurons due to toxicity of amyloid and Ptau accumulation – leads to repetitive damage of susceptibe brain neurons-leading to dementia

The effects of hormones on cognitive function varies enormously between trials with inconsistent outcomes. It is agreed that early treatment with menopausal hormones is protective due to the vasodilatory effect of oestrogen.

Nerattini (*Frontiers in neuroscience 2023)* reviewed hormones on 21 065 treated and 20 997 placebo patients).
Oestrogen use in midlife is associated with a 32% reduced risk of Alzheimers and oestrogen use in late life has a smaller reduced risk.
Combined oestrogen progesterone use in midlife leads to a non-statistically significant risk reduction .
Commencing combined MHT in late life leads to a non-statistically significant risk increase.

NEUROLOGICAL FUNCTION (dementia), ALZEHIMER'S DISEASE

How oestogen works on the brain

(1) Synaptic plasticity –Oestrogen stimulates an increase of dendritic synapses in hippocampus
(2) Free radicals - Oestrogen provides neuroprotection against oxidative stress by antioxidant effect
(3) Cholinergic Neurotranmitter system –Oestrogen stimulate the enzyme that produces acetylcholine (a neurotransmitter important for memory functions and whose levels are reduced in Alzheimers)
(4) Cellular maintenance and survival-Oestrogen enhances the survival of neurons via modulation of neurotrophins (growth factors responsible for survival and maintenance of neurons
(5) Amyloid beta protein – is decreased by oestrogen to protect against amyoid mediate cell death
(6) Tau protein – estrogen prevents hyperphosphorylation of this protein which would have caused decreased neurofibrillary tangles.

(*Depypere H et al, Maturitas 2016 – BELGIUM)*

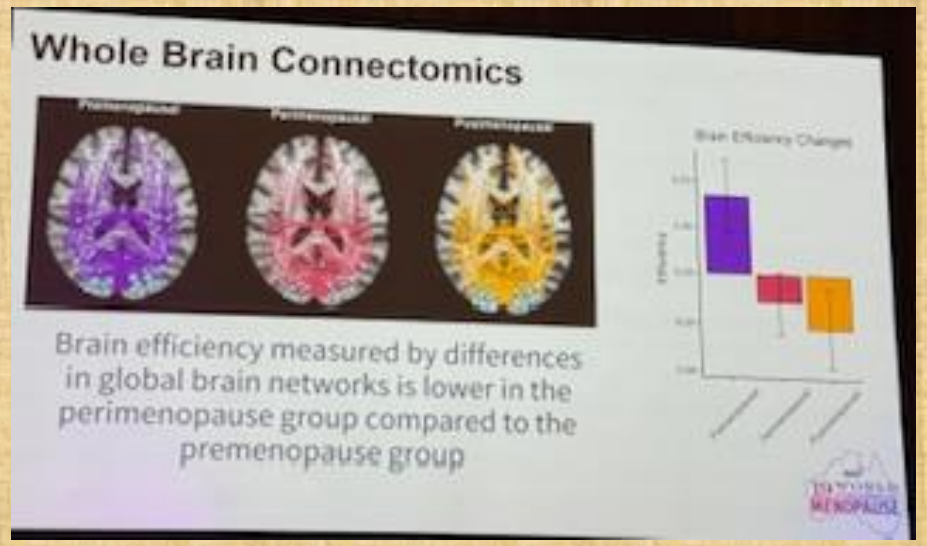
COGNITIVE ISSUES ‘BRAIN FOG’ AT THE PERIMENOPAUSE (1)

Characterized by irregular menstrual cycles (oligo or anovulation - not ovulating frequently)
Irregular cycles
Increased psychosocial symptoms – eg mood swings , anxiety, memory changes, sleep disturbances, ‘brain fog’
Often referred to as ‘brain fog’ , symptoms include memory loss, clouding of thinking processes, word finding difficulties and losing ones’ train of thought.
Variable vasomotor symtoms – eg hot flusing and night sweats
Typically oestrogen levels **FLUCTUATE,** sometimes the levels are unopposed and extremely high and sometimes the levels are absent or very low.

COGNITIVE ISSUES 'BRAIN FOG' AT THE PERIMENOPAUSE (2)

Cognitive performance is maintained in the normal range for most women. About 10% will have a clinically significant change that can persist into the post-menopause *(Maki et al, Menopause 2021, April)*
To maintain memory function, the perimenopausal brain may compensate for low oestradiol levels by increasing hippocampus connectivity across the hemispheres.

Altered congition and brain fog is also very closely linked to
1) Mood changes
2) Sleep issues – it is not surprising that clinical trials show declines in verbal learing and memory with poor sleep
3) Vasomotor flushing – hot flushes are associated with memory
Decline- correction of this symptom has been proven to improve memory



OESTROGEN/COGNITION AND PERIMENOPAUSE

The greater changes and fluctuations in oestrogen levels increase risk of depression. Oestrogen treatment will lessen this effect and improve brain function.

COGNITIVE ISSUES 'BRAIN FOG' AT THE PERIMENOPAUSE (3)

Cognitive performance - Strategies for Brain Health *Maki et al, 'Brain Fog in Menopause: a healthcare practitioners' guide for decision making and counselling for cognition.'*

1) Heart health is brain health – aim to normalise blood pressure, lipids, blood sugars
2) Train the body to boost the brain – an exercise regime of at least 150 minutes of moderate intensity aerobic exercise weekly
3) Slow mid life weight gain – follow a balanced mediterranean type diet -
4) 2) and 3) combined – weight management and physical exercise will lower your dementia risk
5) Don't smoke
6) Stay connected – maintain your social connections
7) Exercise your brain – eg reading, learn a new language, volunteer, learn a new skill

https://www.imsociety.org/wp-content/uploads/2022/09/ENGLISH-WMD-Leaflet.pdf

This link to this leaflet published for the world menopause day is very useful.

GENITOURINARY SYNDROME OF MENOPAUSE

Consensus of 2 medical societies ISSWSH (Int society for the Study of Women's Sexual Health) and NAMS(North American Menopause Society).

Effect of sex steroids on the female genitourinary tract, including the vaginal, labia, urethra and bladder.
The term includes vulvovaginal atrophy (VVA), lower urinary tract symptoms and sexual symptoms.
At least 50% of women have symptoms, starting at the perimenopause and progressing after menstural cessation.

Vaginal Oestrogen Creams –work to thicken the urogenital mucosa, increase vaginal secretion, lower vaginal pH and protect from pathogens.
Intrarosa (DEHA) vaginal pessary
Androfeme cream- Female Hypoactive Desire Disorder (libido)
Strata MGT – silicone gel, awaiting availability in Australia
Vagina laser as third line treatment

OSTEOPOROSIS

- Oestrogen deficit results in increased osteoclast activity and bone resorptio
- Bone mass peaks third decade of life
- Accelerated loss starts 2 years before menopause and can continue for 2-4 years
- Oestrogen will reduce fractures by 65%:
    - HRT vs placebo
    - RR 0.66 hip fracture
    - RR 0.66 vertebral fracture
    - RR 0.77 fragility fractures any site
- Consider alternatives to HRT if no other indication than primary prevention of osteoporosis

-Calcium and Vit D;weight bearing and resistance exercises; work on balance and flexibility to avoid falls;moderate alcohol intake and cease smoking.

OSTEOPOROSIS

- Management
- (1) Antiresorptive

  oestrogens and SERMS

  bisphosphonates-* the only treatment that keeps working after cessation

  RANKL targeted therapy
- (2) Anabolic

  Parathyroid peptides

  PTH – Teriparatide (PTH 1-34(

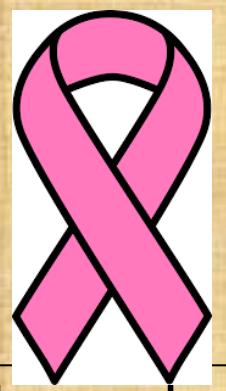
  PTHrP – Abaloparatide

  Anti- sclerostin - Romosozumab

CARDIOVASCULAR DISEASE

- Accounts for 30.7% of female deaths
- The lifetime risk of dying from ischaemic heart disease is 10 times that of risk of dying from:
  - Breast cancer
  - Reproductive cancer
  - Osteoporotic fracture
- American Heart Association does not recommend HRT to be used for primary prevention of heart disease- but with early menopause –menopausal hormone treatment can protect from cardiovascular disease.
- Observational and randomized studies suggest younger women starting HRT at menopause are **not** at increased risk. T
- Cardiovascular benefits of oestrogen is a vasodilator (to protect from heart disease), increases HDL cholesterol, improves insulin resistance, reduces atheroma formation
- KEEPS Study 2012;DOPS Study 2012 (BMJ);Elite Study 2014 (younger women attenuation carotid intima-media thickness)

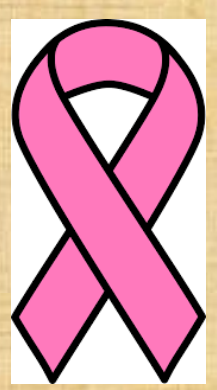
BREAST CANCER



- Oestrogen may promote pre-existing breast cancer
- Unknown if it will induce the growth of new cancers.
- Nurses' Health Study – slight increased risk
- WHI (CCE /MPA) combined HRT
  - Excess 8 cases /10 000 users per year
  - WHI (CCE alone) no increased risk

- Epidemiologic meta analysis of 21 Studies – increased risk over time
- Iowa Women's Health Study and other – no increased risk
- Million Women Study (observational) - increased risk

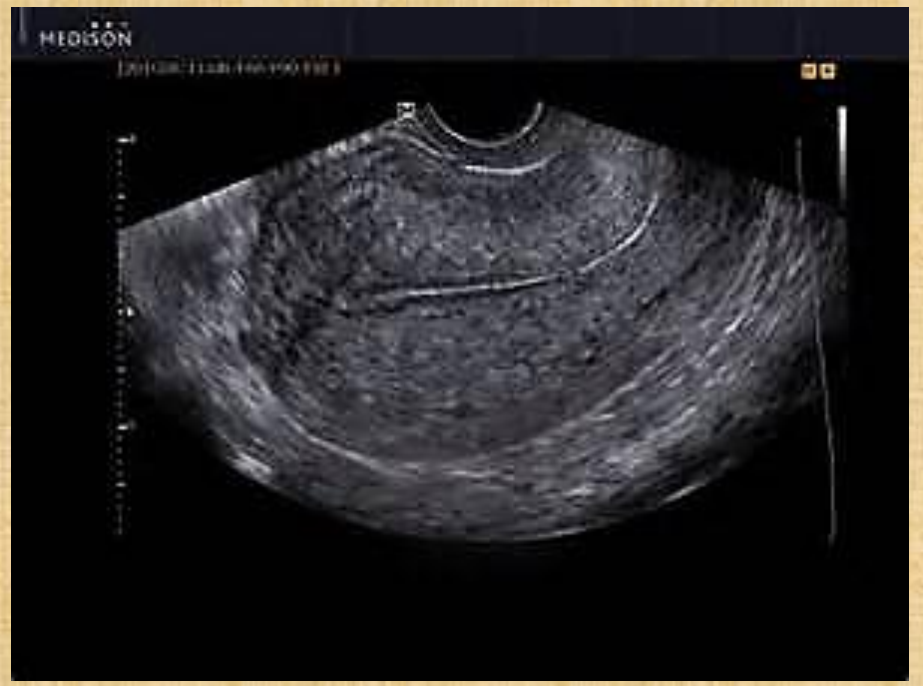
BREAST CANCER



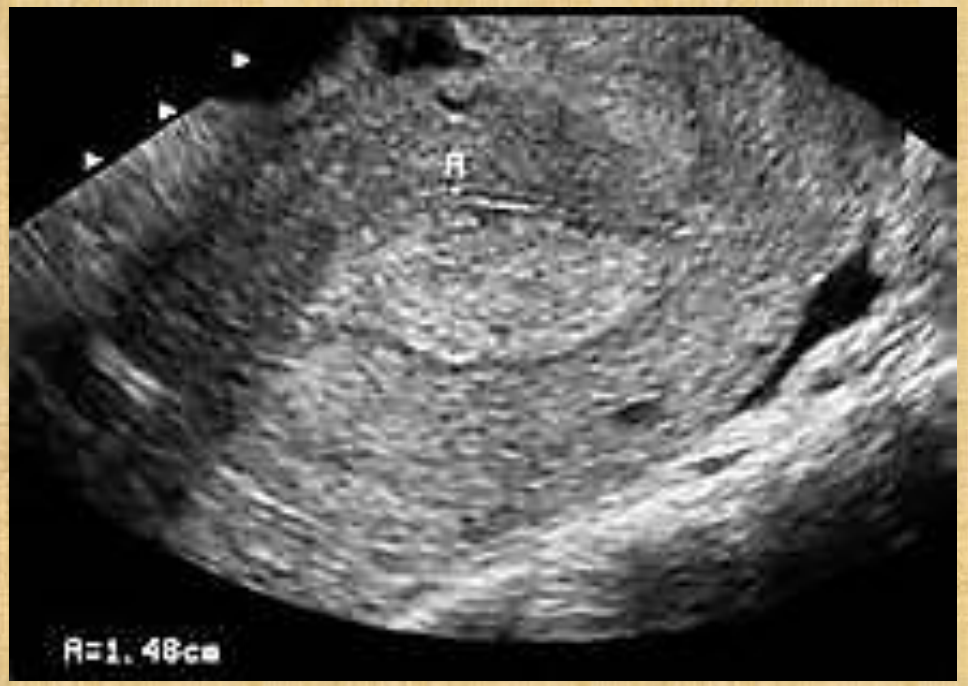
- No randomized studies to evaluate different progestogens
- BRAC 1 and 2
  - Prophylactic oophorectomy
  - HRT improves quality of life
  - HRT does not increase risk of genetically determined breast cancer
- History of breast cancer avoid HRT
- Family history (first degree relative with pre-menopausal breast cancer)
  - HRT will not increase the risk

ENDOMETRIAL CANCER

The lining should be suppressed (thin). Any thickening of the lining or bleeding must be investigated. Dr Burrows will discuss your circumstances and ways to take hormones in a safe manner.



THIN ENDOMETRIUM



ABNORMAL ENDOMETRIUM

VENOUS THROMBOEMBOLISM

- National Collaborating Centre for Women's and Children's Health concluded
  - Important Guidelines

1. Oral HRT increases VTE risk and can occur immediately (with or without progesterone)
2. Transdermal HRT does not significantly increase this risk
3. Risk increases substantially with age
4. Risk discontinues when HRT stopped

Global Consensus Statement

- RCT and observational data provide strong evidence that oestrogen only MHT may decrease coronary disease and all-cause mortality in women younger than 60 years of age and within 10 years of menopause*Data on oestrogen – progestogen therapy in this population show a similar trend but with less precision*
- The risk of breast cancer in women over 50 years associated with MHT is a complex issue but *is primarily associated with the addition of a progestogen to estrogen therapy and to the duration of use*

(Global Consensus Statement. De Villiers et al Climacteric 2016;19:313-315)

BESINS HEALTHCARE
Innovating for Wellbeing

UPDATE ON THE USE OF

Micronised Progesterone:

Hormone Replacement

Prometrium®
micronised progesterone

Achieving Endometrial Atrophy with Micronised Progesterone in Oestrogen Replacement Therapy

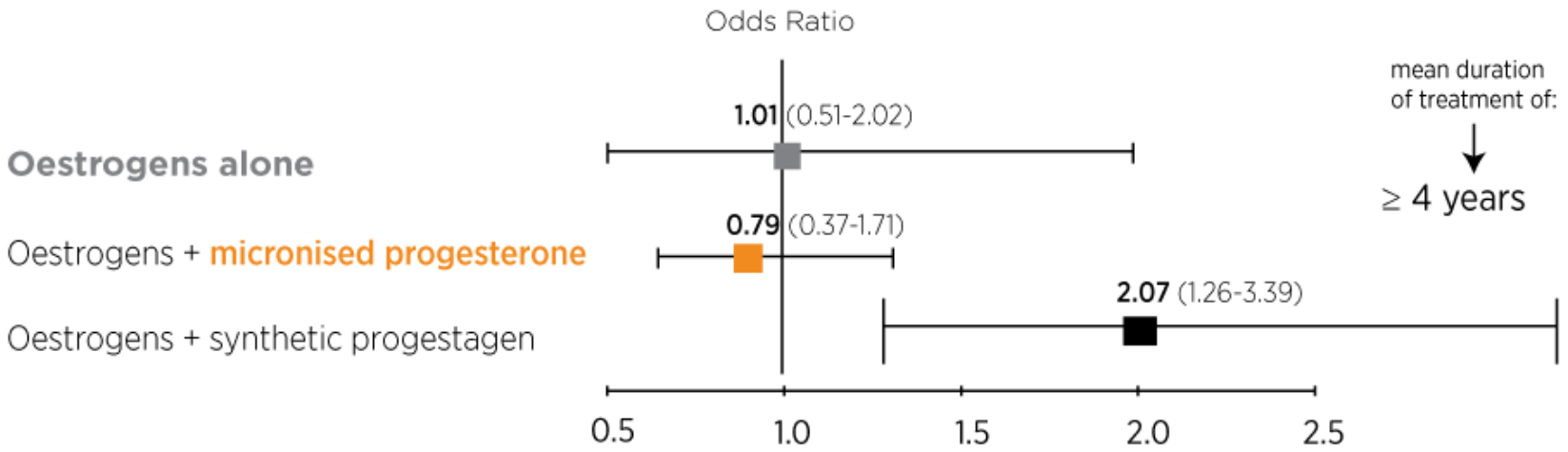
200 mg/day for 1st 12 days (PEPI 1996)
or
100 mg/day for days 1-25 (Darj et al 1991)

Endometrial atrophy (or quiescent)

Study Group for the PEPI Trial. JAMA 1996;275(5):370-375
Darj et al. Maturitas 1991;13:109-115

Breast Cancer Risk and HRT – CECILE Study

Odds ratios for breast cancer among current users of menopausal hormone therapy with treatment duration ≥4 years

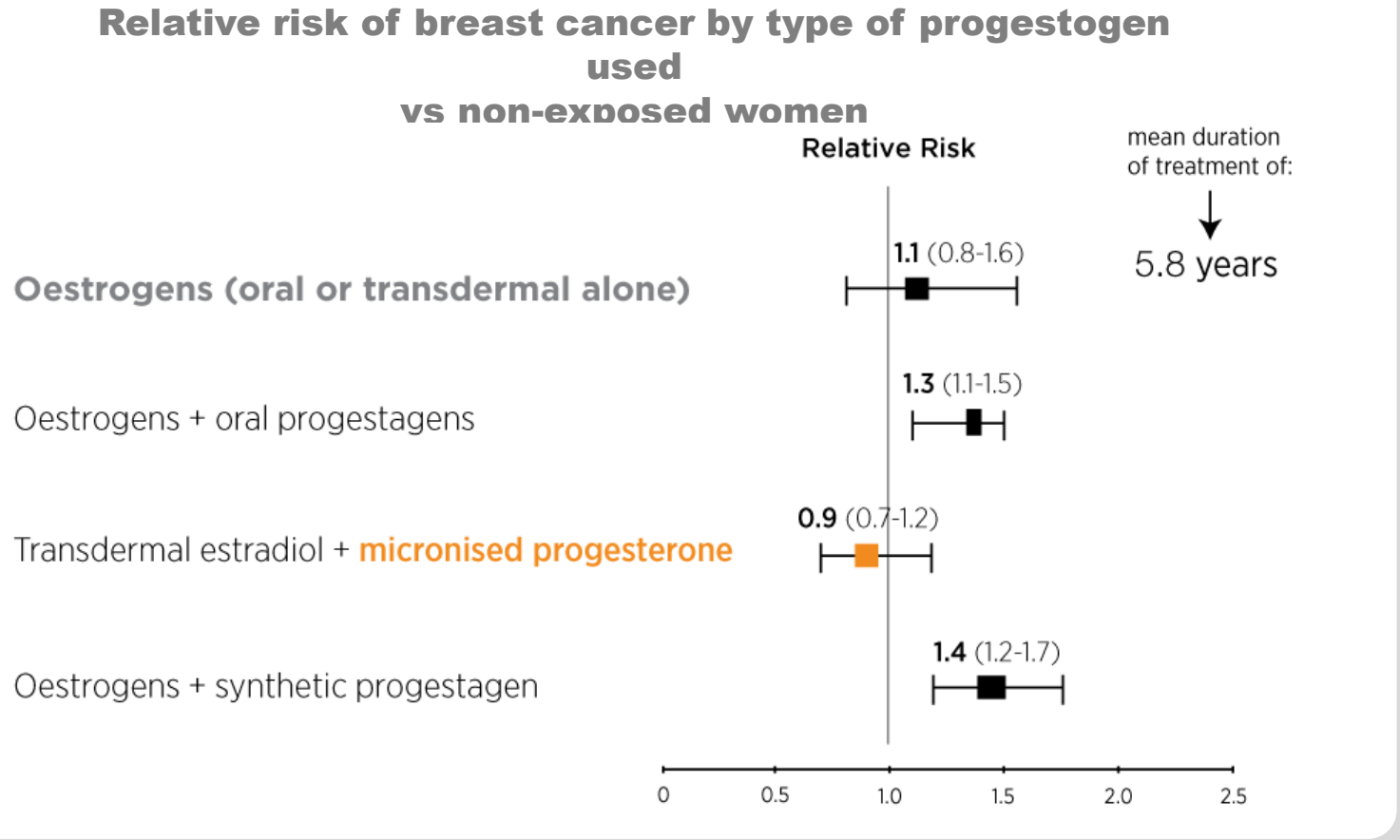


Adapted from Cordina-Duverger E, PLoS One 2013

Odds ratios adjusted for study area/ age at reference date / age at menarche / parity / age at first full-term pregnancy / breast feeding /history of benign breast disease / family history of breast cancer in first-degree relatives / BMI / oral contraceptive use

Cordina-Duverger E et al. PLoS One 2013;8(11) e78016

Breast Cancer Risk and HRT – E3N Study

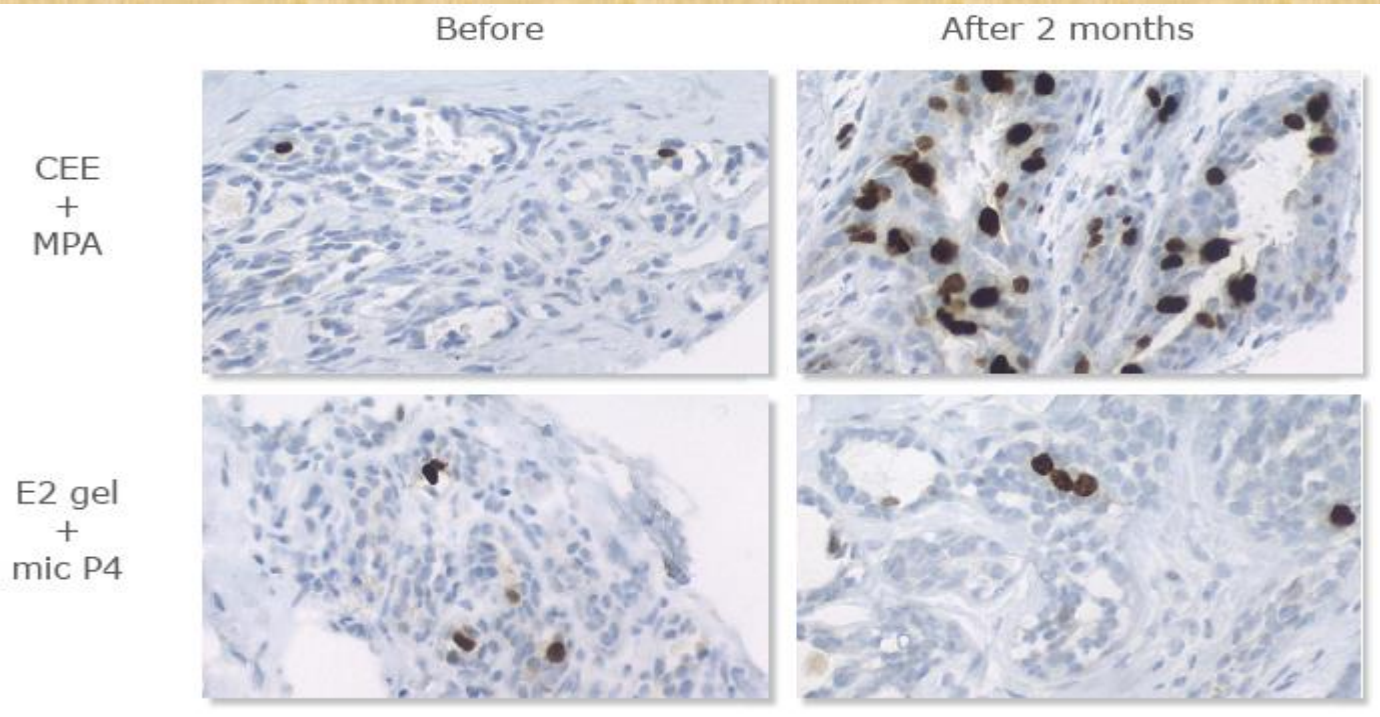


The test for heterogeneity between micronised progesterone and synthetic progestins was significant (p <0.001).

Adapted from Fournier A et al. 2005

Fournier A et al. Int. J. Cancer: 2005;114:448–454

Effects of percutaneous E2 - oral mic.P4 versus oral CEE + MPA on breast cell proliferation and bcl-2 protein in healthy women



Breast histologic findings from two individual women before (left) and after (right) 2 months of sequential treatment with either oral conjugated equine oestrogens–MPA (top) or percutaneous E2–oral micronised P (bottom). Nuclei of proliferating cells staining brown by Ki-67 MIB-1 antibody. (Original magnification X200)

Murkes D et al. **Gynaecol Endocrinol** 2012;28(S2):12-15

Breast cancer and progestogen: Guidelines

- "…It is not clear whether there is a class effect from the progestogen or whether the specific agent used influences breast cancer risk. Data from a large observational study suggest that **EPT with micronised progesterone carries a low risk of breast cancer with short-term use** *(meaning up to 5 years)* but carries an increased risk of breast cancer with all EPT formulations with long-term use."[1]

- "Emerging data …..report that **progesterone** (and perhaps **dydrogesterone**) in combination with oestrogen does **not increase breast cancer risk** if given for 5 years or less." (Level of Evidence C)[2]

- **A large European observational study** suggested that **micronised progesterone** or dydrogesterone used in association with oral or percutaneous estradiol may be associated with **a better risk profile** for breast cancer than synthetic progestogens**.**[3]

- The risk may be lower with micronised progesterone or dydrogesterone than with a synthetic progestogen.

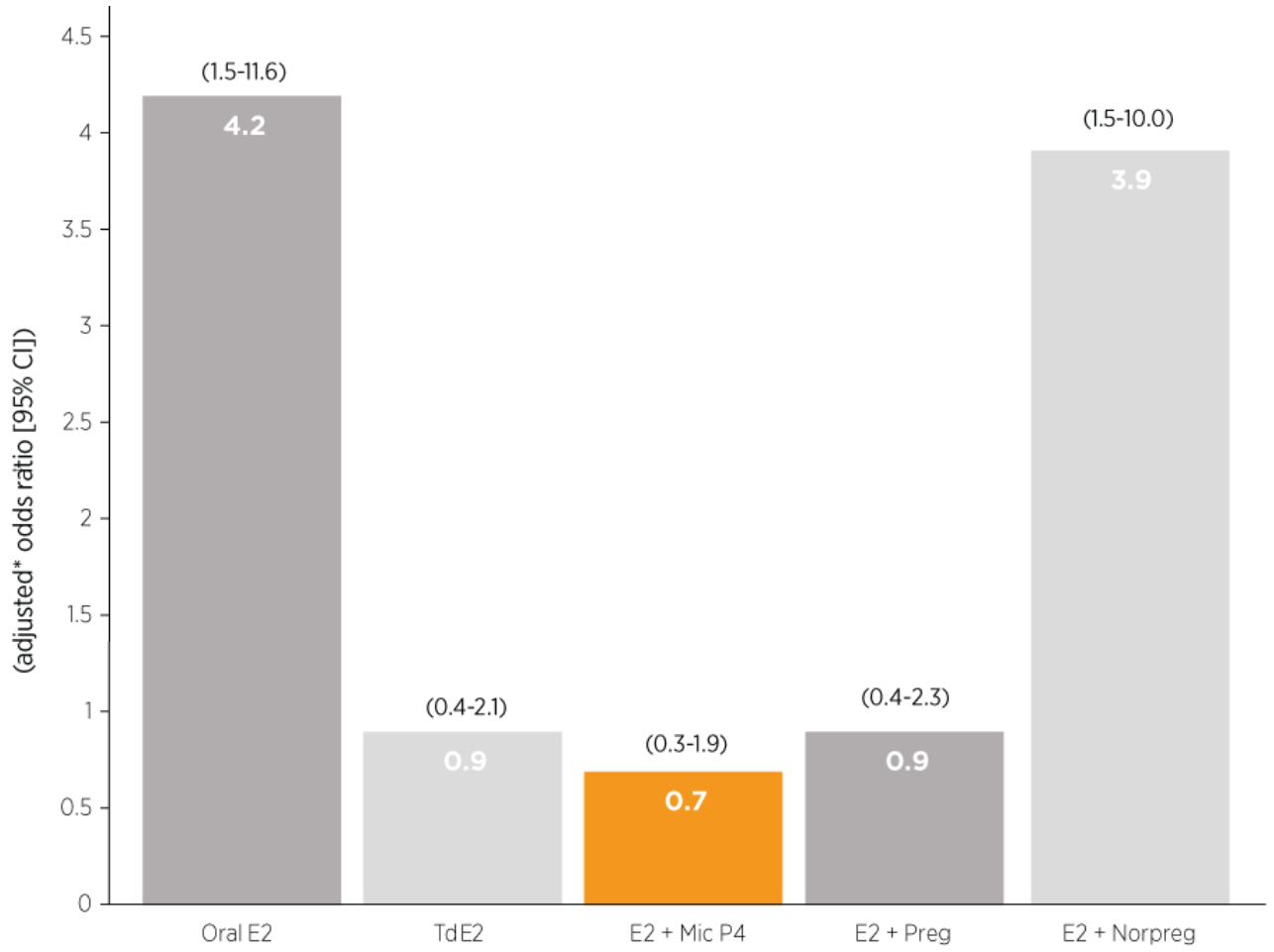
1. Schmidt P. Menopause. 2012; 19(3): 257-271
2. Santen RJ. JCEM.2010:95,(1):S1-S66
3. De Villiers TJ et al. Climacteric 2013;16:316–337

BESINS HEALTHCARE
Innovating for Wellbeing

Micronised Progesterone on VTE risk

Prometrium®
micronised progesterone

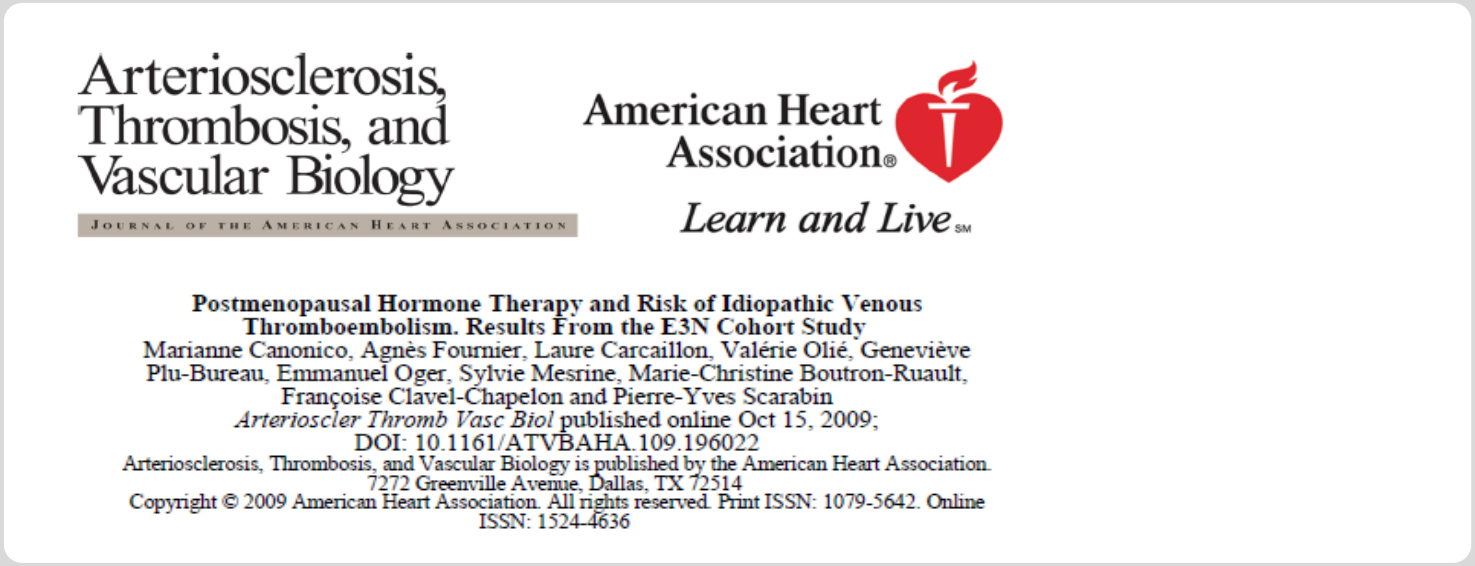
Impact of Hormone Therapy on VTE Risk by Route of Oestrogen Administration and Type of Progestogens **(ESTHER study)**



*Adjusted for obesity status, familial history of VTE, history of varicose veins, education, age at menopause, hysterectomy and cigarette smoking. Td E2 (Transdermal estradiol), Mic P4 (micronised progesterone), Preg (Pregnane derivatives), Norpreg (Norpregnanes derivatives)

Adapted from **Canonico M, et al.** *Circulation 2007*

Canonico M, et al. *Circulation 2007;**115**:840-845*



Arteriosclerosis, Thrombosis, and Vascular Biology
Journal of the American Heart Association
American Heart Association®
Learn and Live℠

Postmenopausal Hormone Therapy and Risk of Idiopathic Venous Thromboembolism. Results From the E3N Cohort Study

Marianne Canonico, Agnès Fournier, Laure Carcaillon, Valérie Olié, Geneviève Plu-Bureau, Emmanuel Oger, Sylvie Mesrine, Marie-Christine Boutron-Ruault, Françoise Clavel-Chapelon and Pierre-Yves Scarabin

Arterioscler Thromb Vasc Biol published online Oct 15, 2009;
DOI: 10.1161/ATVBAHA.109.196022
Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 1079-5642. Online ISSN: 1524-4636

Conclusions

"In this large study (from **E3N cohort study**), we found that route of oestrogen administration and concomitant progestogens type are two important determinants of thrombotic risk among postmenopausal women using hormone therapy.

Transdermal oestrogens alone or combined with progesterone might be safe with respect to thrombotic risk."

Canonico et al. *Arterioscler Thromb Vasc Biol. 2010;30:340–345*

BIJUVA 1/100 – oral estradiol and progesterone

The first and only fixed dose ccMHT treatment with micronised progesterone, like other combinations are helpful for many menopausal symptoms. As a combined continuous bleed free regime, it is usually commenced one year after the last period.

BENEFITS – Symptom Relief
Hot flushes, night sweats, vaginal dryness, sleep/mood disturbances, muscle aches , vaginal and bladder problems

BENEFITS – Bone Health
MHT helps maintain bone density and reduces the risk of osteoporosis and fractures

BENEFITS – Quality of Life
MHT can improve menopause specific quality of life in women experiencing menopausal symptoms

BIJUVA 1/100 – oral estradiol and progesterone

The first and only fixed dose ccMHT treatment with micronised progesterone

BENEFITS

BREAST CANCER RISK

Risk of breast cancer is slightly increased (figures Iprevent July 2023, Theramex data)

-Lifetime risk of breast cancer is 86 in 1000 (55 year old never used MHT)

-Risk after using ccMHT for 5years – lifetime risk of breast cancer is 91 in 1000 (5 extra cases per 1000 women)

-This data can be compared to other risk factors which include but are not limited to

a) Drinking 3 x alcohol units daily (7 extra cases per 1000)

b) Body Mass Index over 30 (12 extra cases per 1000)

c) Family history

-The use of body identical estradiol and micronised progesterone will reduce these numbers (*Baber et al Climacteric 2016 19(2) pp109; Fournier et al Breast Ca Res Treat 2008*)

BIJUVA 1/100 – oral estradiol and progesterone

VENOUS THROMBOEMBOLISM RISK (VTE)

Both oral oestrogen-only and combined oestrogen-progestogen therapy can slightly increase the risk of VTE. The risk is highest in the first year of use.
(figures Iprevent July 2023, Theramex data)

-Risk of VTE in a 55 year old woman who has never used MHT is 1 in 1000
-Risk after using oral MHT is 2 in 1000 (1 extra cases per 1000 women)
(Baber et al 2016 International Menopause Society Recommendations, Climacteric 2016; Vinogradova British Medical Journal, 2019; Thermex data)

-The above level of VTE risk is defined as rare, and can be reduced by the use of body identical estradiol and micronised progesterone, or vaginal and transdermal MHT *(2022 Position Statement North American Menopause Society Advisory Panel; Vinogradova BMJ 2019; Canonico et al Thromb Vas Biol 2010).*

NON HORMONAL OPTIONS

Hot Flushing and Vasomotor Symptoms

Lifestyle - weight loss, (cooling techiques, exercise, yoga, diet – less proven but helps)
Mind Body Techniques-Cognitive Behavioural Therapy, Clinical Hypnosis
Prescription therapies – Fezolinetant (Veoza),
SSRIs/SNRIs, gabapentin, oxybutynin (moderate effect and limited by side effects)
Other – herbal, soy and over the counter supplements are of limited benefit in trials. Purity and safety can be an issue due to lack of regulation.

Herbal

Promensil PERI For perimenopause - plant based *Rheum rhaponticum* (Siberian Rhubarb)- once daily tablet
Promensil 0 Standardised herbal extract for of red clover for menopause (*Trifolium pratense*)
Olive and Bee
100% natural intimate cream(*Olea Europa and Cera Alba* – olive oil and pure Australian beeswax) suitable to use internally and externally. Pharmacy or online.

VEOZA (FEZOLINETANT 45 mg) NON HORMONAL TREATMENT

Veoza is not a hormone. It works at the body's natural temperature control centre to control hot flushing. During menopause/perimenopause, declining oestrogen effects the thermostat. Veoza rebalances the thermostat. It is a daily tablet taken with or without food.

In clinical trials Veoza resulted in a 60% reduction in the number of vasomotor symptoms (hot flushing, night sweats, better sleep) but also the episodes were of less intensity resulting in better comfort.

As it is not typical menopausal hormone treatment, there are very few patients not suited to commence this treatment (CYP1A2 inhibitors, liver disease, renal impairment). There is a body of safety evidence. A blood test to check at 3 months is needed. No other special management is required. Less than 5% discontinue the treatment and there were no serious adverse effects related to the treatment in trials.

The benefits perisist long term if the treatment continues. A negative is that Veoza has does not treat vaginal symptoms, nor improve bone health. This would be factored into a shared decision making process with you and Dr Burrows exploring all options available.

New to Australia in 2025

NON HORMONAL TREATMENT

StrataMGT (Stratpharma, Switzerland).

A new silicone based lubricant (non hormonal) for the treatment of menopausal vaginal dryness and lichen sclerosus. – Therapeutic Goods Australia approval is pending.

Unlike traditional hormones, Strata MGT does not absorb and has no systemic hormonal risks. It is inert, has no measurable pH, contains no steroids, hormones, alcohol, parabens or fragrance, for long term use.

Mucosal healing –apply direct to dry, wet, cracked and sensitive mucosal tissue.
Faster healing – provides a moist healing environment – for re-epithelialization, reduction in acute inflammation with a barrier restoration
Early studies showed Strata MGT relieves itch, tenderness, dryness, buring, dyspareunia, dysuria.

WEIGHT MANAGEMENT

Physiological responses oppose weight loss

Appetite hormones, CNS activation of mesolimbic reward pathways, energy expenditure

Medications are indicated

In conjunction with lifestyle interventions – eating changes, physical activity, sleep and stress management

BMI over 30 kg/m2 or over 27 kg/m2 with weight related complication

Semaglutide and Tirzepatide has the ability to achieve the goal – 10% weight loss at 1 year (New England J Medicine)

Glp1 Agonists also have secondary health benefits

improved blood pressure

improved triglycerides and LDL-cholesterol

improved physical function score

improved HbA1C

improved fasting glucose

Semaglutide reduces cardiovascular events in non-diabetics with obesity, and has FDA approval for this

LITERATURE

- WHI (Women's Health Initiative) RCT 1993-2002
- PEPI (Post menopausal Estrogen/Progestin Interventions) 1989-94
- HERS (Heart and Estrogen Replacement) 1993-98
- NHS (Nurses Health Study)
- SWAN (Study of Women's Health Across the Nation) 1996-current
- MWS (Million Women Study) 1996- current
- WISDOM (Womens International Study of long Duration Estrogen after Menopause 1992-2002
- ELITE (Early Vs Late Intervention trial Estradiol) 2004-2013
- KEEPS (Kronos Early Estrogen Prevention Trial) 2005-2012
- Harvard mood study 1995-2006
- DOPS Danish Oestoporosis prevention Study 1990-2008
- Revised Global consensus statement on menopausal hormone treatment. Marutirus 2022
- EMAS (European)Consensus Statement
- NAMS (North American Consensus Statement) 2022
- The 2023 Practitioners Toolkit for Managing Menopause.

Dr AnnaBurrows

medical specialist in gynaecology

This presentation is for a general informative read and should **never** be a substitute for a consultation with your general practitioner other health care specialists, or Dr Burrows