"Essential Info on HRT and Menopause; Your Questions Answered"

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Menopause Society
OF IRELAND

Declarations

I am a regular speaker for:

Besins, Bayer, Consilient Health & other Pharma sponsored meetings.

I have attended numerous meetings in Ireland and abroad thanks to educational grants from Consilient Health, Astellas, Bayer, Besins & many other pharmaceutical companies.

The information in these slides comes from peer reviewed sources and not the pharmaceutical industry.

What is happening at Menopause/ Perimenopause ?

- The word ‘menopause’ means end of menstruation- it usually occurs by 51 yoa and marks the end of reproductive ability BUT.....
- Ovarian function becomes less predictable as we pass 35yoa &
- **Levels of AMH & Inhibin B start to decline which will impair follicle maturation & ovulation as a result**
- The Hypothalamic-Pituitary-Ovarian hormone cascade may be disrupted at times (but at other times it may be functioning typically) and symptoms may start to arise well before the final menstrual bleed - this is **Perimenopause**

WHY IS MENOPAUSE IMPORTANT FOR YOU?

- Menopause is not considered a ‘disease’ unless occurring at a very early age
- It is a natural transition from reproductive capability to post reproductive life - but for many it can be a struggle
- All body systems can be impacted so it is best managed by well trained GP and prescription medication(s) are a common component of management
- So if you are a pharmacist and females are among the patient population, you need to know about menopause and perimenopause as more than half the population will experience it If they are lucky enough to live into their mid life

Perimenopause

MIDDLE-AGED BARBIE

- Symptoms often precede the Final Menstrual Bleed by Years but typically, start in our 40's- anything younger is POI and <u>needs</u> urgent management
- Average duration of symptoms is 7-10 years, but 30% patients have longer episodes of significant symptoms - some are symptomatic into their late 60's. *(Avis 2015)*
- HCPs can't out rule menopause just because patient still has periods = therefore, there are <u>NO RELIABLE BLOOD TESTS TO DIAGNOSE MENOPAUSE TRANSITION (perimenopause)</u>
- Patient often juggling Contraception needs and Menopause symptoms
- Use of HRT is almost <u>NEVER contraindicated</u> and should be offered if only to confirm diagnosis; you put a patient in far more 'danger' with the COCP than you could ever do with HRT (esp if she is still menstruating)

Diagnosis is Clinical- rarely need blood tests

- NIGHT SWEATS &
- HOT FLUSHES
- MENSTRUAL CHANGES:
- MENORRHAGIA, IRREGULARITY
- DECREASE IN METABOLISM
- LOSS OF VAGINAL ELASTICITY & LUBRICATION "GUSM"
- INCREASE INCIDENCE OF METABOLIC SYNDROME
- HAIR & SKIN CHANGES
- JOINT ACHES & PAINS
- BLADDER COMPLAINTS
- DEPRESSION,
- MOOD SWINGS
- IRRITABILITY, RAGE
- ANXIETY
- CHRONIC FATIGUE
- MEMORY LOSS, CONCENTRATION ISSUES &
- BRAIN FOG
- LOSS OF LIBIDO
- PMS-TYPE SYMPTOMS

Management of Menopause/ Perimenopause

Hormone replacement Therapy (HRT) is the most effective intervention for control of (peri) menopausal symptoms

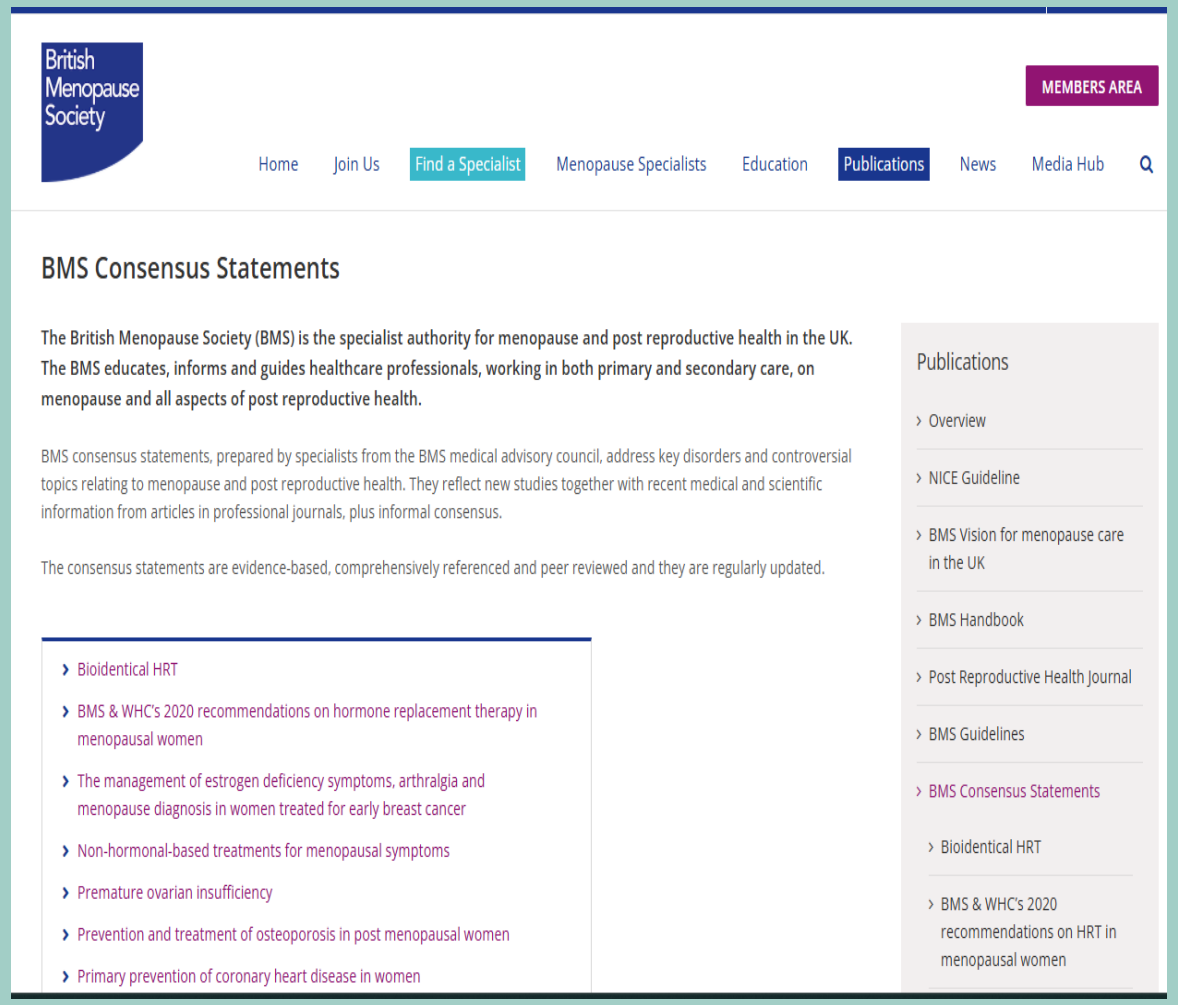
All patients should be able to access advice on how they can optimise their menopause transition and the years beyond

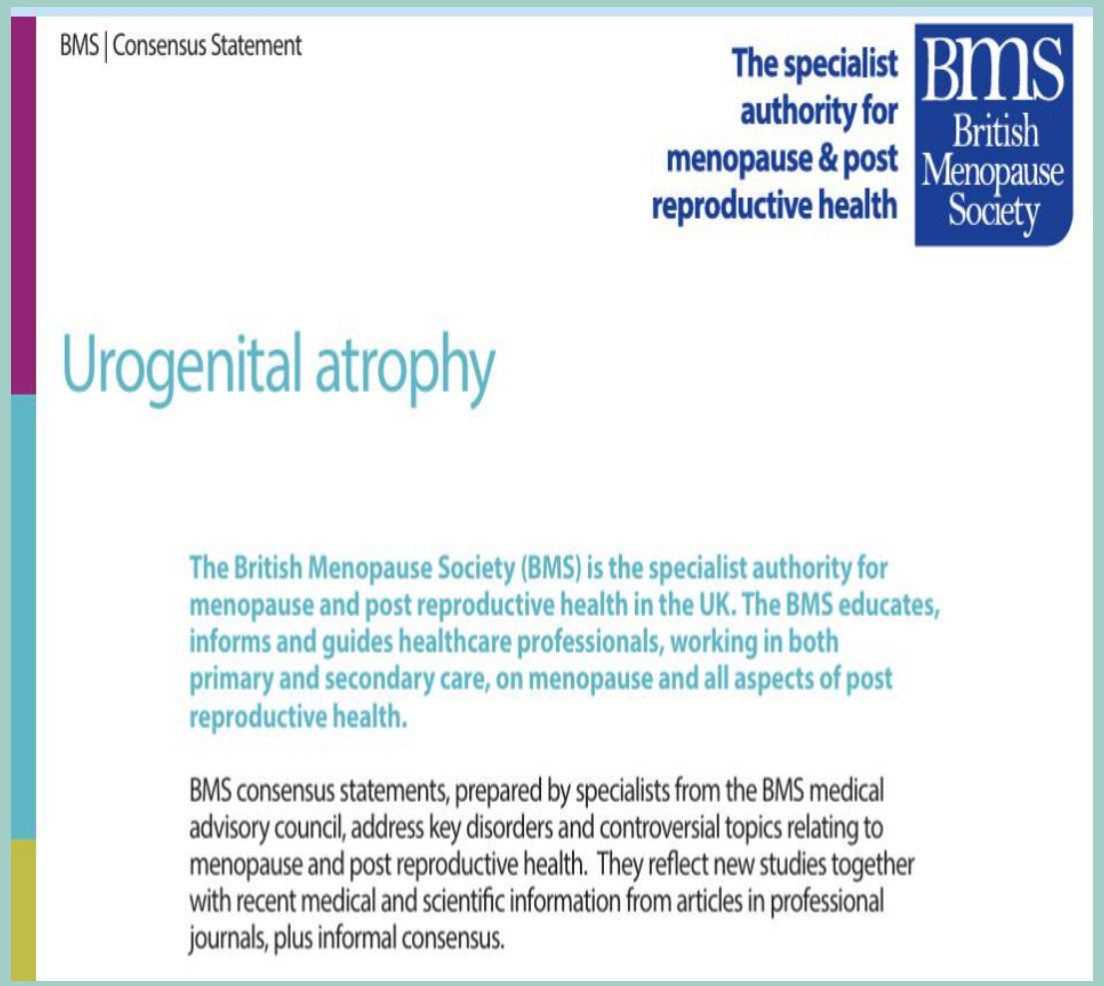
There should be a holistic and individualised approach in assessing and advising people , with particular reference to lifestyle advice and dietary modification

The decision whether to take HRT, the dose of HRT used and the duration of its use should be made on an individualised basis after discussing the benefits and risks with each patient

Arbitrary limits should not be placed on the duration of usage of HRT

MANAGEMENT OF GENITO – URINARY SYNDROME OF THE MENOPAUSE (GSM)





thebms.org.uk/wp-content/uploads/2024/04/09-BMS-ConsensusStatement-Urogenital-atrophy-MARCH2024-A.pdf

Health Promotion & sensible choices might help deal with Menopause w or w/out HRT !

Nutrition (diet) www.womens-health-concern.org/wp-content/uploads/2023/07/28-WHC-FACTSHEET-Nutrition-in-Menopause-JULY2023-A.pdf

Movement www.womens-health-concern.org/wp-content/uploads/2023/06/29-WHC-FACTSHEET-Exercise-in-menopause-JUNE2023-A.pdf

Weight management www.womens-health-concern.org/wp-content/uploads/2023/06/31-WHC-FACTSHEET-Weight-Gain-and-menopause-JUNE2023-A.pdf

Reduce Alcohol **www.balance-menopause.com/menopause-library/alcohol-and-the-menopause-why-cutting-down-can-improve-your-menopause-and-overall-health**

Smoking & Vaping **www.balance-menopause.com/menopause-library/menopause-and-smoking-what-you-need-to-know/ and www.quit.ie**

Talk to Friends and Colleagues and Family **https://www.arccancersupport.ie, www.hse.ie/eng/services/list/4/mental-health-services/mental-health-engagement-and-recovery/resources-information-and-publications/menopause-mental-health-report.pdf**

Breathing & Thinking differently – see CBT

Special Situations

Menopause tends to be linked to more **severe sx** and may even have **life limiting consequences** when:

- it happens **young** (esp < 40 yoa)
- It happens **abruptly** (e.g. after BSO (or sometimes even after TAH when the ovaries are left in situ), as a result of Chemotx or Radiotx)

In these circumstances not only will sx tend to be severe, the need for hormone replacement is urgent and failure to discuss the possibility of early/ severe menopause before offering a surgery or treatment goes against all gyne guidelines

THERE ARE NO ABSOLUTE CONTRAINDICATIONS TO HRT BUT THERE ARE SOME SPECIAL PRECASUTIONS AND SOME VERY SEPCIAL PREACUITONS

VERY SPECIAL PRECAUTIONS

- Breast cancer (individualise care)- get Meno expert/ Oncology opinion)
- Porphyria (individualise care- get Meno expert/Haematology opinion)
- Severe Active Liver Disease (individualise care- get Meno expert/Hepatology opinion)

<u>Special Cases</u>

- Thromboembolic disorders; avoid oral E2, pick a good Prog, start low & KEEP IT LOW
- Undiagnosed, irreg bleeding (? investigate ALL Post Meno Bleeds, examine, scan, refer)
- Hx of Endometriosis/ Fibroids/ Endometrial cancer/ Hypertriglyceridemia (just Rx wisely & monitor more often)

Consultation essentials

- History - all the basics with attention to prev pregnancies and contraceptive use (has she 'survived' estrogen in the past ?)
- Family Hx- no C/I to HRT w any FHx of anything
- Medicines - LEI meds will interact, HRT may impact lamotrigine
- Smoking & Alcohol, Diet & Movement interventions-what contraception are you using?
- BP is necessary when Rx ORAL estrogen- not TD
- HRT pro's & con's + Trial Rx is usually worthwhile if only to highlight the possibility that something ELSE may be going on?
- Signpost to support literature/ websites/ podcasts

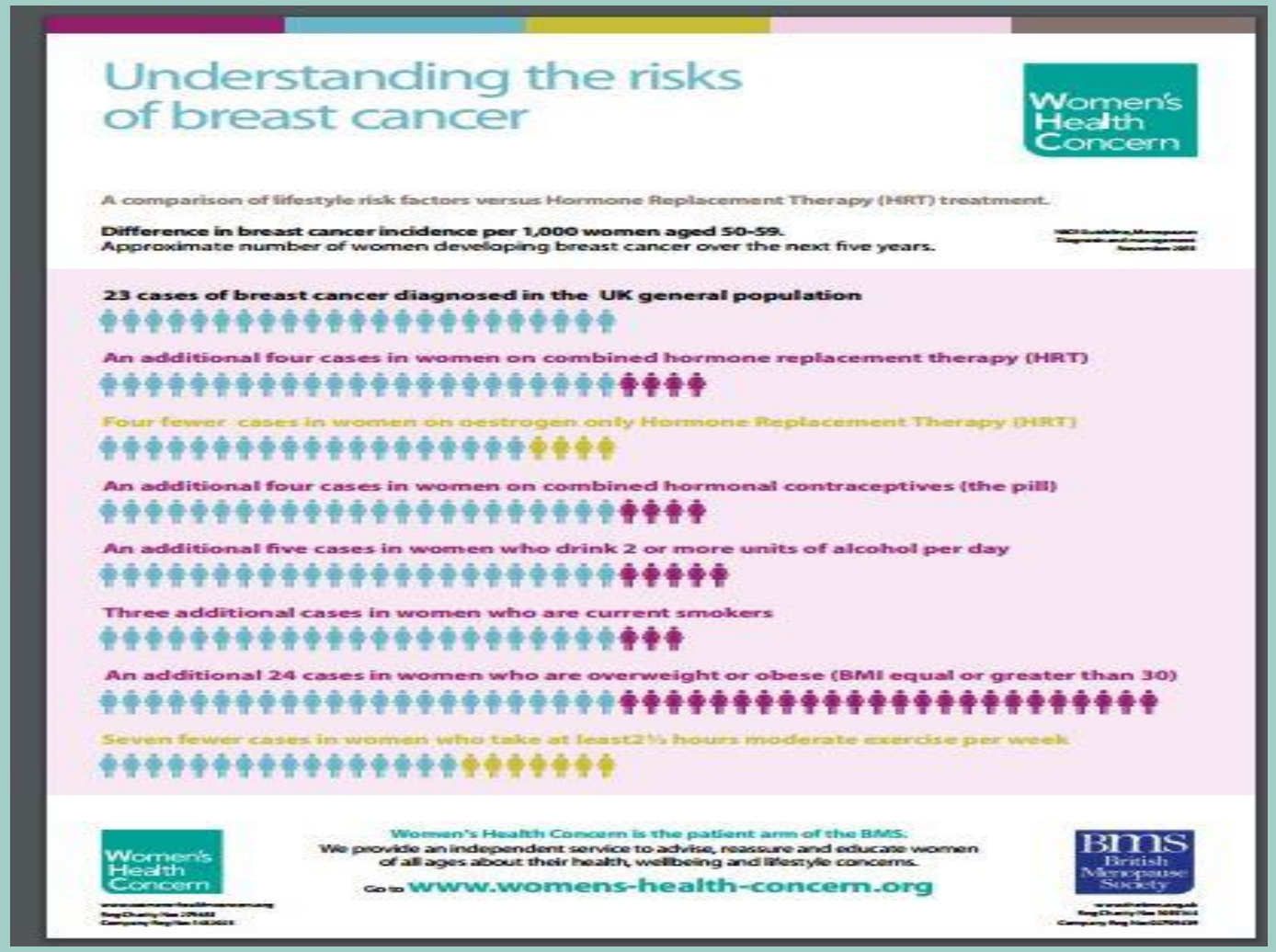
Managing patient worries by Managing OUR worries first !

Know the facts about HRT

HORMONES AND BREASTS: these are the FACTS

- HRT is not a “carcinogen”
- There is no direct evidence that HRT transforms benign breast cells into high risk, premalignant conditions but… some Hormones may have a stimulatory effect on pre-existing, quiescent premalignant lesions or not- It is Poorly understood & grossly under researched
- It takes at least 10 years for breast cells to change from the pre-malignant state to being a clinically detectable cancer
- Malignant changes cannot be reversed by stopping hormones

OLD Breast cancer & HRT Data
Where is our new data?



We are only now seeing data from Observational Studies of Older Women who stay on their E2+MP TD HRT deeper into their 60's

- A new large-scale study based on the records of 10 million senior Medicare women from 2007 to 2020 suggests that the implications of HT use beyond age 65 years vary by type, route, and dose[1].
- In this study, Baik, et al explored the initiation/continuation of HRT > 65 years plus the effects of **40 different HT preparations on 13 health outcomes**. They found important variations across different types, routes, and strengths of HT.
- The use of **Estrogen alone use** beyond age 65 years was associated with **significant risk reductions in mortality, breast cancer, lung cancer, colorectal cancer, congestive heart failure, venous thromboembolism, atrial fibrillation, acute myocardial infarction, and dementia.**
- **On average, Estrogen alone use beyond age 65 years was associated with a significant 19% reduction in mortality risk relative to non use**
- The use of a **combination Estrogen + Progestogen** therapy was found to increase the risk of breast cancer - but such risk can be mitigated using **low doses of transdermal or vaginal progestin.**
- **Progestin** usage resulted in significant risk reductions in endometrial cancer, ovarian cancer, ischemic heart disease, congestive heart failure, and venous thromboembolism.

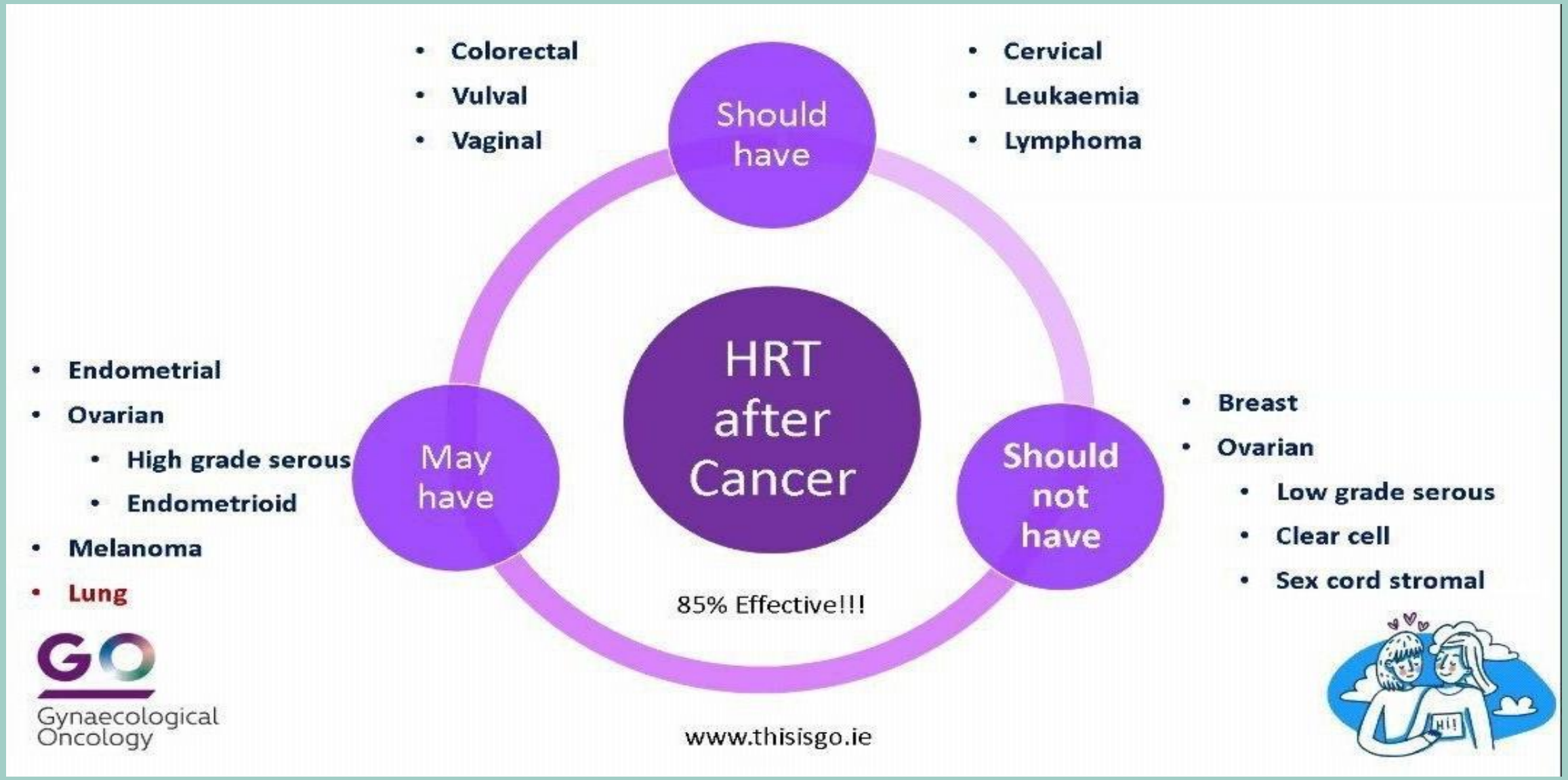
Cancers with Sex hormone links:
most Breast, some Ovary & some Endometrium cancers

People may already have (peri)menopausal symptoms before they start their cancer therapies
They may have been using MHT/HRT and now have been told to stop

Surgical Intervention to pelvis- even with ovarian preservation may precipitate ovary hormone changes

Chemotherapy and pelvic radiotherapy can result in a variable range of damage to the ovaries which can precipitate or worsen (peri)menopause symptoms
Hormone therapies that block estrogen receptors or deplete systemic estrogens can not surprisingly impact meno symptoms

Remember tho' – not ALL cancers are hormone linked!



Remember also that – not ALL gynaecological cancers are hormone linked!

Table 1: Summary of recommendations for use of systemic HRT and vaginal estrogen following treatment of gynaecological cancer

Primary Cancer	Subtype or Risk Group	Systemic HRT	Vaginal Estrogen
Ovarian Fallopian tube Primary peritoneal	High grade serous		
	Low grade serous stage 1		
	Low grade serous stage 2+		
	Endometrioid stage 1		
	Endometrioid stage 2+		
	Clear cell		
	Mucinous		
	Granulosa cell stage 1		
	Granulosa cell stage 2+		
	Germ Cell		
	Borderline tumour: No residual disease		
	Borderline tumour: Peritoneal implants, microinvasive disease, residual disease, recurrence		
Endometrial	Low and intermediate risk		
	High-intermediate risk		
	High risk: ER/PR negative		
	High risk: ER/PR positive		
	Advanced and metastatic		
Cervical	All		
Vulval	All		
Vaginal	All		
Uterine sarcoma	Leiomyosarcoma		
	Endometrial stromal sarcoma		

	Benefits usually outweigh risks. Suitable for non-specialist use.
	Refer to text of BGCS BMS guidelines. Discuss benefits and risks for the individual patient. Consider specialist advice.
	Not recommended. Refer for specialist advice if non-hormonal approaches are not effective.

www.bgcs.org.uk/wp-content/uploads/2024/09/BGCS-BMS-Guidelines-on-Management-of-Menopausal-Symptoms-after-Gynaecological-Cancer-09.09.24.pdf

"Iatrogenic Menopause"

- Evidence suggests that meno sx may be **more severe and longer lasting when caused by medical interventions** than typical, physiological menopause.
- **Following a cancer diagnosis, patients may be at an increased risk of depression and anxiety- and menopausal symptoms may exacerbate this risk[1,2]**
- Younger age at menopause may also be associated with **psychological and sexual dysfunction as well as long term risks such as cardiovascular disease, osteoporosis and, potentially, cognitive dysfunction and dementia[3]**

And what about ER-/PR-/ & HER2+ Breast Cancers?

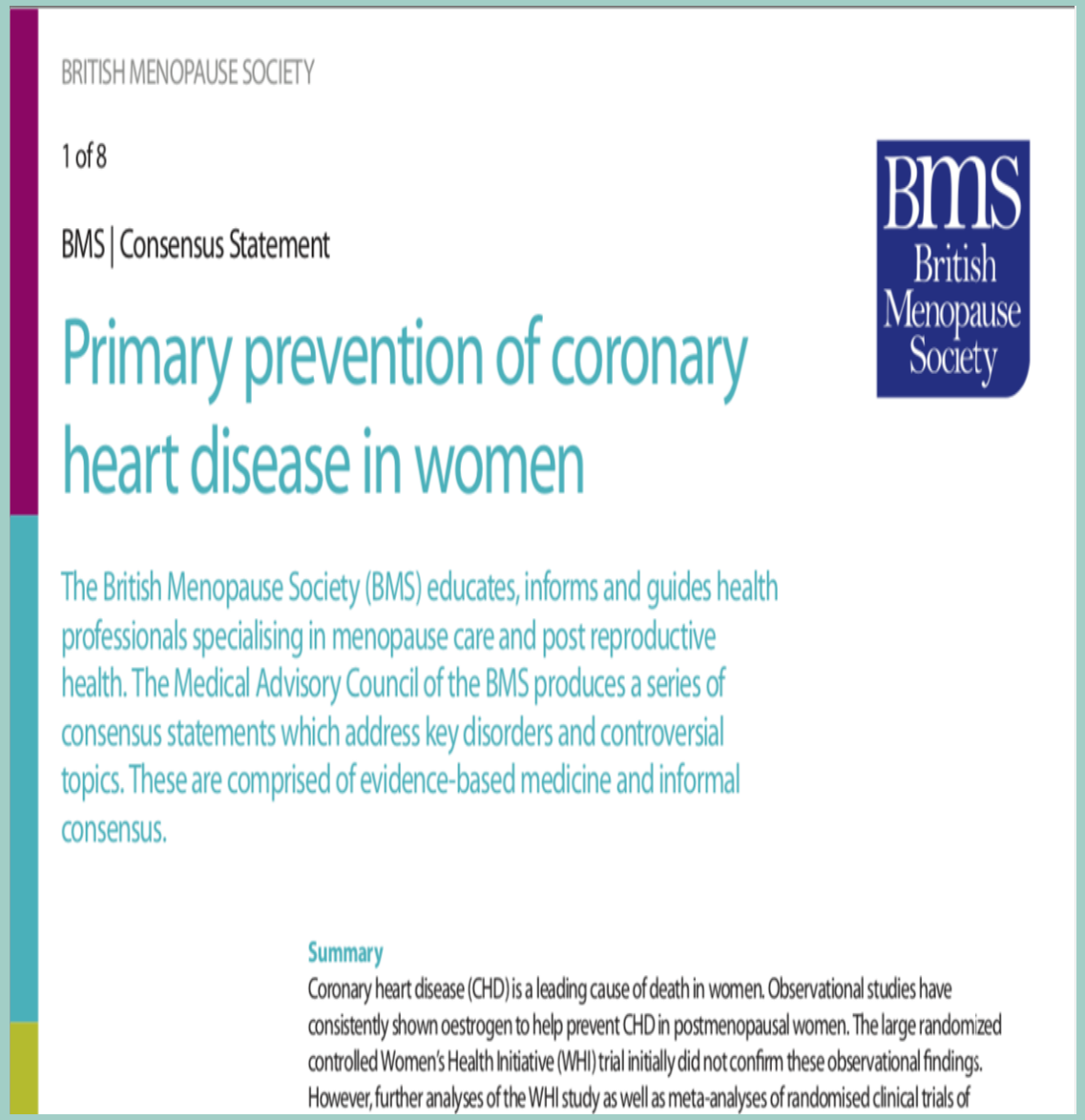
- Iatrogenic menopause symptoms are not limited to people with hormone sensitive disease
- **Chemotherapy-induced ovarian suppression** will occur irrespective of the oestrogen receptor (ER) status of the primary tumour.[1]
- **HRT may not be without risk** for those with an ER negative primary.
- Although there is high concordance in hormone receptor status between first and second primary breast cancers, **a minority with an ER negative primary may present with an ER positive contralateral cancer (up to 30%)[2] and approximately 8% may present with ER positive metastatic disease.[3]**
- **There is generally less concern about systemic absorption from low and ultra-low dose vaginal oestrogen, which is minimal and could be acceptable where systemic therapy would not be.**

What about menopause and Ischemic heart disease/ Cardiovascular Disease (CVD) ?

- **The number one cause of death in females is CVD –** we also experience more CVD morbidity when compared with males with CVD[1] but
- **Cardiovascular disease & sex hormones have a complicated relationship**
- Older observational studies suggested that HRT was associated with lower CVD incidence and all-cause mortality, comparing users and nonusers - this made sense; **we knew that there was a protective effect from HRT on cardiovascular health via lipid modulation & estrogens favourable actions on the endothelium and vascular behaviours**

but the 'Women's Health Initiative' study (2002) raised questions about that- with some MI events linked to oral CEE use- Could this have been related to their exclusive use of an oral Equine Estrogen+MPA cocktail ? Could it have been related to the fact that most of the participants were older (mean age 63) and already suffering symptomatic CVD?

Newer studies have led to the development of the "The "Timing Hypothesis" which suggest that initiating HRT within 10 years of the Final menstrual Period provides CV benefit



BRITISH MENOPAUSE SOCIETY

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BMS | Consensus Statement

Primary prevention of coronary heart disease in women

The British Menopause Society (BMS) educates, informs and guides health professionals specialising in menopause care and post reproductive health. The Medical Advisory Council of the BMS produces a series of consensus statements which address key disorders and controversial topics. These are comprised of evidence-based medicine and informal consensus.

Summary

Coronary heart disease (CHD) is a leading cause of death in women. Observational studies have consistently shown oestrogen to help prevent CHD in postmenopausal women. The large randomized controlled Women's Health Initiative (WHI) trial initially did not confirm these observational findings. However, further analyses of the WHI study as well as meta-analyses of randomised clinical trials of

BRITISH MENOPAUSE SOCIETY Tool for clinicians

Information for GPs and other health professionals

1 of 3

The specialist authority for menopause & post reproductive health

HRT after myocardial infarction

Hormone replacement therapy (HRT) comprises estrogen either alone or with progestogen addition. The primary indication for HRT use is relief of menopausal symptoms. Can it be given to postmenopausal women who have previously sustained a myocardial infarction (MI)?

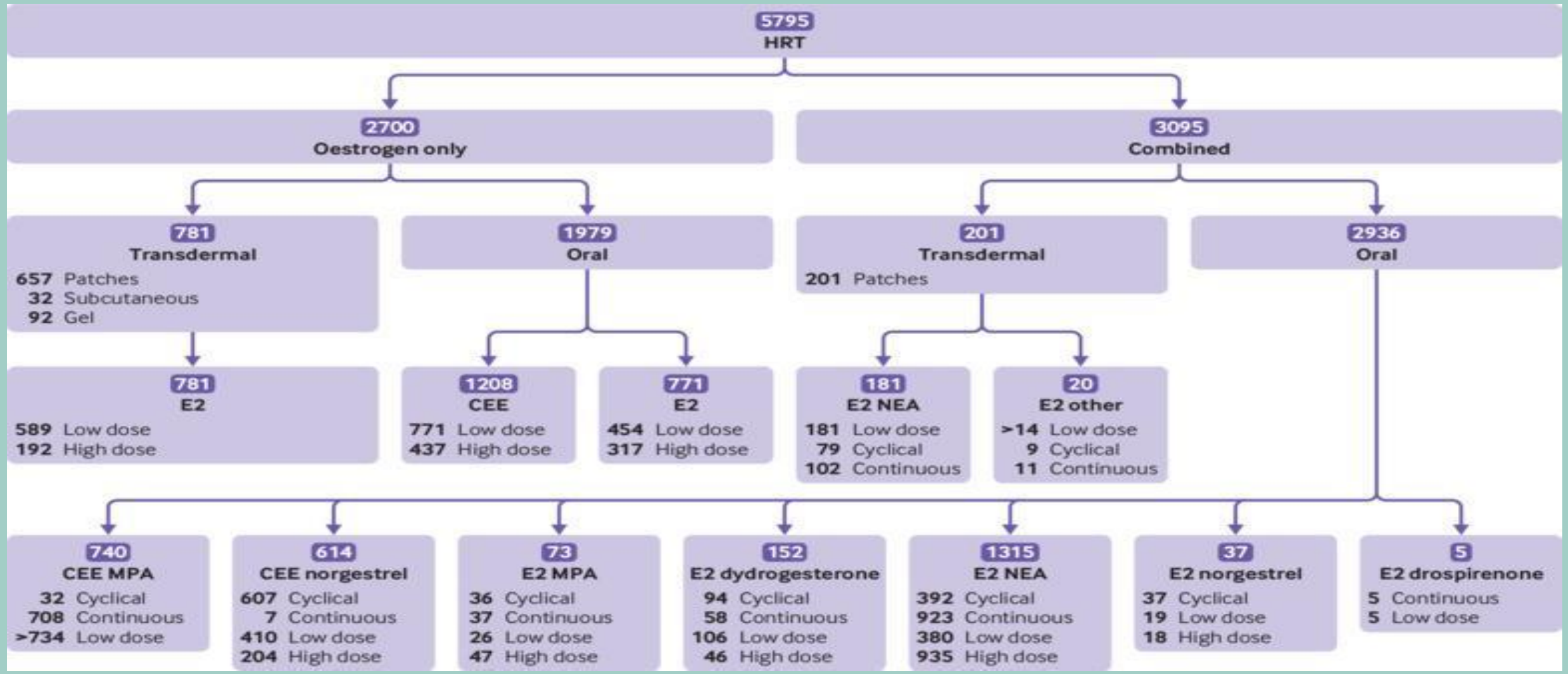
What about Menopause & Thrombosis ?

- The 20 yr. old 'WHI study' did show an **increased risk in clotting within the first 2 years of starting the Horse estrogen + strong Progestagen pills**
- Pulmonary Embolism rates were NOT increased
- Many patients are advised to **avoid HRT because they have VTE risks factors, some patients are advised they may not use HRT at all**
- **Not true, not fair and Completely depends on:**

- **Current VTE potential ? Are risks well managed ?**
- **Delivery system and dose of estrogen + type of progestagen**

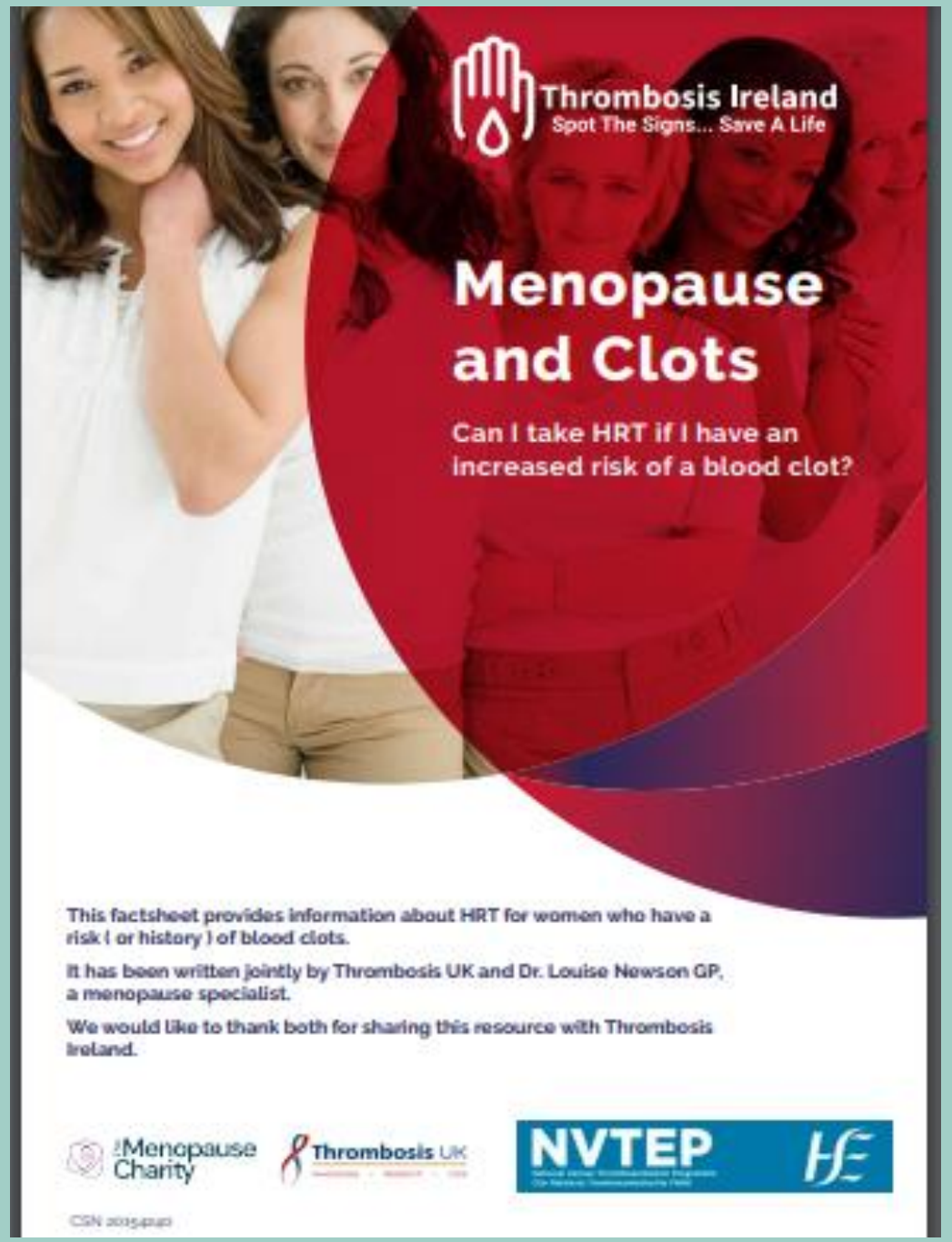
Yana Vinogradova et al. BMJ 2019;364:bmj.k4810

Hormone replacement therapy (HRT) preparations available in the UK and number of women with venous thromboembolism exposed to HRT from QResearch and Clinical Practice Research Datalink (CPRD) databases.



HRT & Thrombosis

- There is compelling evidence that **low dose, transdermal HRT does not increase the risk of VTE above that in non-users and is associated with a lower risk than oral estrogens**[1]
- With oral estrogens, the risk depends on the dose and type of estrogen, with **conjugated equine estrogens** more prothrombotic than **oral estradiol.**
- The **type of progestogen significantly affects VTE risk** with **micronised progesterone and dydrogesterone conferring a lower risk** compared to that with other **synthetic progestogens**[2]**.**
- **Mirena prob fine also**



The more recent, good quality evidence shows us:

There is a small risk of a blood clot associated with oral oestrogen tablets.[7] High levels of oestrogen in the liver (which can occur when oral oestrogen is taken) can lead to sticky blood changes that increase the risk of VTE. This does not occur with oestrogen used through the skin as a patch, gel or spray.

To understand how small this risk is, imagine a healthy woman of 50 years of age; she has a VTE risk of around 6 in 10,000 per year. If she took oral oestrogen tablets, this would double her risk to around 12 in 10,000 but it's still a small risk overall.

The good news is that estrogen absorbed through the skin is much safer and does not cause sticky blood changes and therefore does not increase the risk of clot. Transdermal oestrogen is the type of HRT that comes in a sticky skin patch, or a gel or spray that you rub into your skin.

> To be clear, transdermal oestrogen has no extra risk and is safe to take, even for those with a higher risk of getting a blood clot.[6]

Progesterone - two types with important differences and this matters.
There are two main types of progesterone - the hormone you need to protect your womb if you take replacement o

Menopause in the context of HIV

BMS Tools for Clinicians

- **Females living with HIV aged 45-60 report high levels of menopausal symptoms**[1]
- Some patients may confuse VMS with Symptoms of AIDS
- HIV infection is assoc with an increased risk of **osteoporosis and cardiovascular disease**, particularly among postmenopausal females living with HIV[2,3]

- **HRT is not contraindicated in HIV but TD HRT is preferred as there is less risk of GI side effects and CVD/ thromboembolic impact**
- **We sometimes worry about drug interactions between HRT and some ART regimens: but there is virtually NO DATA on the use of HRT with ART**
- **Most of the drug interaction concerns relate to Contraceptive hormones and ART's – not HRT & ART !**
- **Most HIV groups encourage & support the use of TD Estrogen and Progestagen for people with HIV whether they are using ART or not**

Endometriosis & HRT – in the non-hysterectomised

- There is a slight risk of Endometriosis reactivation with HRT estrogen use as well as an even more rare risk of malignant change[1] when Rx in someone w a b/g of Endometriosis
- Prescribers need to consider offering either a **potent progestagen/ Mirena/ higher dose Utrogestan if the pt still has a womb**
- If HRT is offered after hysterectomy for endometriosis, we still **add a progestagen** (esp. with a b/g of moderate to severe disease, when we know there was lots of residual Endo tissue left in at resection or if there is an Endometriotic symptom flare after we start the HRT (see next slide)
- BMS suggest we offer a **continuous regime** for at least for the first year post TAH, then can try E only[2]

Endometriosis & HRT – in the hysterectomised patient

- The BMS[1] says: 'The estrogen threshold theory suggests that add-back HRT therapy or HRT after removal of the ovaries contains a low enough dose of estrogen for maintenance of bone density and relief of hypo estrogenic and vasomotor symptoms but not enough to reactivate endometriosis'
- So, yes we **can** and often SHOULD in some cases (e.g. < 45yo) Rx HRT after TAH/BSO for endometriosis but **we must add in a progestagen** to avoid the risk of endometriotic flare (about 2% risk)[2] or malignant transformation
- If the endometriosis was mild or an incidental finding we could discuss starting with E only HRT after hysterectomy
- Pt must be informed good data is lacking and we both have to watch out for pain, pressure, haematuria, etc.

Let's talk about HRT Prescribing & Dispensing

- The 3 main ovarian hormones are the 3 estrogens, progesterone and a variety of androgens
- Estrogen is the principal hormone of HRT- it comes in many forms
- Non oral delivery of Estrogen avoids 1st pass and is considered 'superior' to other estrogens but patient preference, convenience & cost are all taken into account
- Progestogen is a requirement of HRT in a nonhysterectomised patient
- Testosterone is an optional extra at the moment

Creative Prescribing

- Estrogen will help alleviate most sx but it will cause a certain amount of endometrial thickening
- Left unopposed for any more than 3-6 mos this can allow the development of dysplasia and in some cases, increasing the risk of endometrial CA.
- In almost all cases, **estrogen needs some progestagen to prevent the development of heavy, prolonged or unpredictable PV bleeding.**

The selection of products in the MIMS is very limited so sometimes we Rx by combining an estrogen (usually 50mcg) with a progestogen but

- **which progestagen ?**
- **how much ?**
- **how often?**

ESTROGEN-ONLY products

some not in the MIMS

For use in: Hysterectomised people, Mirena wearers when Mirena in < 5 yrs. or in conjunction with one of the recommended HRT progestagens

Divigel-transdermal gel 0.1% estradiol, 1 sachet ~ 50mcg patch

Estrofem - oral 2mg.estradiol

Evorel -transdermal patch 50microg. Estradiol

Estradot-transdermal patch, estradiol 37.5, 50. 75 & 100 microg.

Fematab -oral 1 & 2 mg. estradiol

Lenzetto spray- transdermal estradiol, 3 sprays ~ 50mcg patch

Oestrogel -transdermal gel, 0.75 mg of estradiol per pump- the new pump dispenser malfunction did not affect ROI !

Premarin - oral conj. equine oestrogen .625 & 1.25 mg.

Oestrogen Dose Equivalents

Product	Low dose	Low medium	High medium	High doses
Oral	0.5mg oestradiol 0.3 mg CEE	1mg oestradiol 0.625 mg CEE	2mg oestradiol 1.25mg CEE	
Patch	25mcg	50 mcg	75mcg	100 mcg
Oestrogel	1 measure	2 measures	3 measures	4 measures
Sandrena Gel	0.5mg	1 mg	1.5mg	2mg
Lenzetto spray	1 spray	2 sprays	3 sprays	4 sprays

- Use low dose to start and increase as needed
- Younger women often require higher doses and vice versa

Which Progestagen ?

- **UTROGESTAN: Oral Micronised Progesterone 100mg- 200mg (or even 300mg prn)** Micronised progesterone has a neutral effect on BP, BMI, Glucose & HbA1c price of 100's came down recently
- **DUPHASTON : Oral Dydrogesterone 10mg- 20 mg (30mg prn)**
- **MIRENA: for 5 years – also contraceptive (no other IUS)**
- **PROVERA: Oral medroxyprogesterone acetate 5mg- 10 mg**
- **NORIDAY: Oral norethisterone acetate 1 mg ~ 350 microg (3 tabs daily) -also contraceptive- to 5mg daily (Primolut)**

BLEED-PRODUCING HRT products in the MIMS

(the SmPC may be inaccurate and contradict guidelines)

- **FEMOSTON 2/10** -Sequential Oral
- 2mg Estradiol+/-10mg.Dydrogesterone
- **Femoston 1/10-** Sequential Oral
- 1mg Estradiol+/-10mg.Dydrogesterone
- **NOVOFEM** -Sequential Oral
- 1mg Estradiol+/- 1mg.Norethisterone
- **TRISEQUENS**- Sequential Oral Estradiol 2 & 1mg +/- 1mg.Norethisterone

Or EVOREL SEQUI in NI or a "DIY" HRT cocktail……

DIY Cyclical Progestagen Options

ESTROGENs

- Patches 25-100 mcg 2/week
- Estrogen 1-4 pumps daily
- Divigel 1-2 sachets daily
- Lenzetto 1-3 sprays daily

Or Oral Estradiol 1-2mg daily

PROGESTAGENs

- Mirena
- Utrogestan 100mg daily for 21 days/ month OR 200mg for 2 weeks/month
- Utrogestan 300mg for 2 weeks/ month in v high doses
- Duphaston 10mg for 2 weeks/ month
- Duphaston 20mg for 2 weeks/ month

NON-BLEED-PRODUCING HRT in the MIMS

ACTIVELLE – Continuous Combined Oral
1mg. Estradiol + .5mg Norethisterone

ANGELIQ- Continuous Combined Oral
1mg.Estradiol + 2mg.Drospirenone

EVOREL CONTI -ContComb.Transdermal
50microg.Oestradiol + 170microg.Norethisterone
19.99

FEMOSTON-CONTI 1/5 -Cont. Comb. Oral
1mg Estradiol + 5mg.Dydrogesterone

FEMOSTON-CONTI 0.5/2.5-Cont. Comb. Oral
.5mg Estradiol + 2.5mg.Dydrogesterone

INDIVINA - Cont. Comb. Oral
1 mg. Oestradiol +
Medroxyprogesterone acetate(MPA);2.5 or 5mg

KLIOGEST- Cont. Comb. Oral
2mg.Oestradiol/ 1mg.Norethisterone

***LIVIAL- 2.5mg** Tibolone a steroid Gonadomimetic

+the DIY which is ANY transdermal estrogen + a progestagen every night OR Mirena

DIY Continuous progestagen Options

ESTROGENs

- Patches 25-100 mcg 2/week
- Estrogen 1-4 pumps daily
- Divigel 1-2 sachets daily
- Lenzetto 1-2 sprays daily

Or Oral Estradiol 1-2mg daily

PROGESTAGENs

- Mirena
- Utrogestan 100mg daily
- Utrogestan 200- 300mgdaily if bleeding
- Duphaston 10mg daily
- Duphaston 20- 30mg daily if bleeding

When is it OK to just use Estrogen?

- Mirena in for < 5 years
- Hysterectomised

Testosterone ? Why not?

- Clinical Dx- Sx mainly low libido (management of brain fog is not an indication)
- Blood levels do not equal tissue levels or action but
- Should offer bloods 3-6 mos after Rx given - Useful as baseline and to ensure they not over medicated
- Ask for Total Testosterone (FAI no longer recommended)
- Timing of blood draw ☺; between 8 and 10am & not on the day of off label application of Testogel
- Aim for total testosterone in normal physiological range < 2/2.4

What to Rx ?

- Tibolone has weak androgenic effects but is PO so not ideal for some

Licensed testosterone for women?

The only available product is

- "Androfeme1" cream 0.5ml per day – it must be imported from Australia, is not on

GMS/|DPS. Etc. so we use Unlicensed Equivalents usually:

Unlicensed equivalents include: (remember to provide a bespoke info leaflet)

- Testogel: 50mg sachet once every 7-10 days (pea sized blob daily or ½ a sachet twice a week)
- Testogel pump: 1 pump delivers 25mg so a pump every 5-7 days should do
- Tostran: 1 pump delivers 10mg so a pump every other day should do

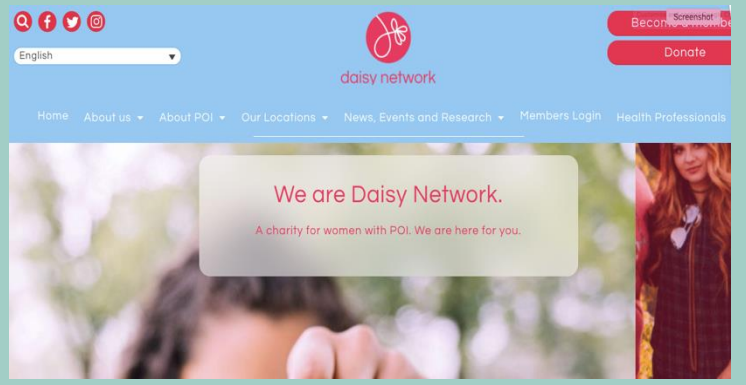
Apply to lower abdomen / upper thigh - not on genitals - it's in alcohol ☹

Might take 8-12 weeks before benefit is maximal

CONTRACEPTION & HRT

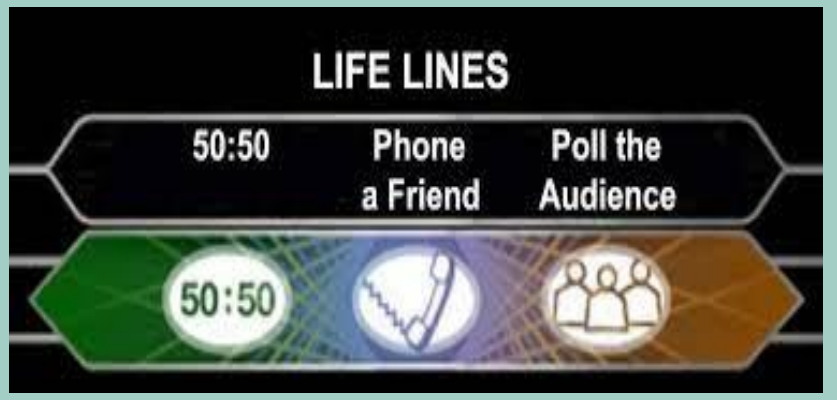
- Standard HRT is not strong enough to afford Contraception
- Mirena & Estrogen will obviously give both HRT & Contraception but once the Mirena is in place for > 5 yrs, additional progestagen will be needed
- The COCP (or ring or patch) is permitted until 50 yoa and it will also help with Meno Sx to a degree + provide contraception but may/may not be suitable (check for UKMEC 3 or 4 risks)
- Discuss and figure out what suits best

What about POI?



- Premature Ovarian Failure is a health crisis that demands hormone Rx
- Symptoms usually worse and hormone requirement higher than standard meno patient
- Fertility preservation
- Assessment for possible Underlying disorder ideally
- Testosterone more relevant here too
- HRT or COCP until 50 at least
- DAISY NETWORK

“Complex” situations & Menopause



- For most people affected by Menopause, prescribers just need to **reassure themselves that they are managing menopause according to the guidelines**

- But in some situations, the guidelines recommend **“Refer for expert advice”- usually meaning a HCP with accredited Specialist Menopause training**[1]

&

Occasionally, a situation arises for which there are no actual “guidelines”- so your HCP might need to phone a friend!

Drugs for Menopause that aren't "HRT"[1]

- **SSRI's & SNRI's** - **mood drugs** can help some people with vasomotor symptoms, mood changes and joint aches and pains. 'Paroxetine' (7.5 mg) has a license from the FDA in the US for the management of moderate to severe vasomotor flushes but most of these drugs are used in an off label capacity[2,3] Caution with ***some*** of these if using tamoxifen
- **Antihistamines –** drugs normally used for **allergies** that reduce the levels of histamine in the brain and so can make you **drowsy**- some are OTC, some on Rx[4]
- **Gabapentin & Pregabalin -** are anticonvulsants normally used for controlling partial seizures, **nerve pain** linked to fibromyalgia, diabetes or herpes and; in the case of Pregabalin, low mood. They are Rx-only, controlled drugs which are open to "misuse"- so avoid them if you are struggling with substance misuse or addiction already- they can help some people with **vasomotor symptoms, pain & poor sleep[5,6]**
- **Oxybutynin –** is an anticholinergic **anti-spasmodic** medication usually used to reduce **over active bladder** (OAB) symptoms. It was noticed that people taking oxybutynin for OAB experienced less sweating so it occurred to medics that we could use it for other problems including hyperhidrosis & **vasomotor flushes and sweats associated with the menopause[7,8]**
- **Clonidine-** is an alpha adrenergic receptor agonist medicine that is actually licenced for menopause flushing & sweating. It increases & stabilises blood vessel widths in the body which can improve high blood pressure, **migraine and vaso motor symptoms in menopause**. It was the only non-hormonal drug with a license for the control of hot flushes in the UK & Ireland until……[9,10]
- **Neurokinin 3 & 3 / 4 Receptor Antagonists -** One of the main causes of vasomotor flushes and sweats (VMS) appears to be linked to the activity of **the KNDy brain cells in the hypothalamus** & their relationship to estrogen. **Estrogen is known to suppress the activity of the KNDy neurons that control temperature**. When estrogen is lost this suppression is also lifted and temperature can fluctuate. The new NK3R antagonist **"VEOZA"(Fezolinetant)** block the NK3 Receptors like Estrogen would have and so reduces VMS, almost as effectively as HRT but N**O SAFETY DATA IN BREAST CANCER AS YET**. The 'Oasis 4' trial is helping to explore another type of these NK antagonist drugs and this drug is specifically looking at safety in people who have been diagnosed with breast cancer [11,12]

MOST OF THIS IS OFF "LABEL"[13]

Summary of what we can try; including medications that are not specifically licensed for Management of menopause

➨ **Flushes & Sweats:**

- **CBT**
- **SNRI/ SSRI (**may get benefit from v low doses)*
- **Oxybutynin** (Kentara patch or 2.5mg PO going up slowly)
- **Gabapentin** (start slow100mg nocte and work up to 300mg TID) or Pregabalin (50-300mg daily in div doses
- NK3 R antagonist, **"Veoza"**

➨ **Sleep**

- Sleepio app **(CBT)**
- Phenergan 25mg nocte/ Piriton 4mg nocte
- **Gabapentin** (start slow100mg nocte and work up to 300mg TID) or Pregabalin (50-300mg daily in div doses)

➨ **Mood**

-SNRI/ SSRI: Sertraline best for anxiety*

-CBT

➨ **Joint pains**

-Yoga/ Acupuncture

-Gaba & Pregabalin

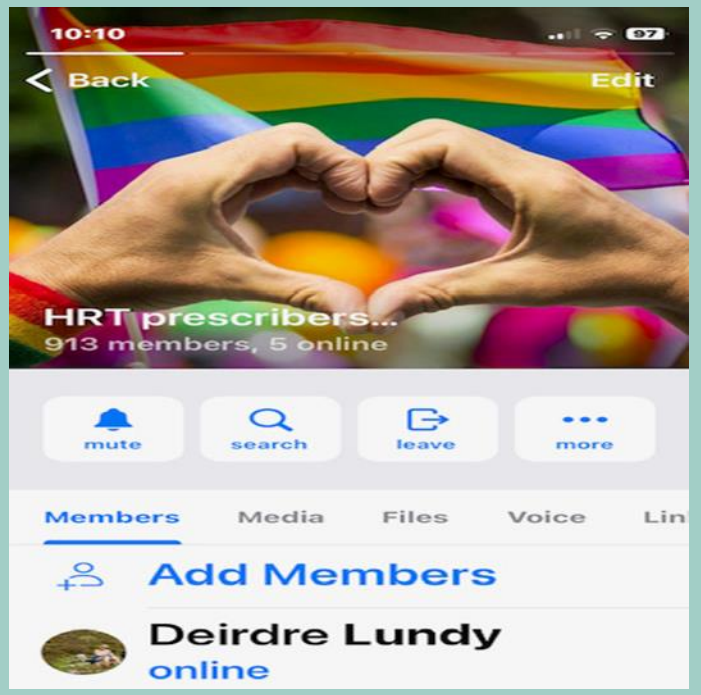
➨ **Vagina & Pelvis**

-Moisturisers/ Lubes

-Local Vag E2 or E3

-LASER

& FINALLY; be part of the conversation



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