Menopause

DR CLARE SPENCER

GPWSI IN THE MENOPAUSE AND GYNAECOLOGY

THE MEANWOOD GROUP PRACTICE

Menopause

- Recognition of symptoms of the perimenopause and menopause
- Risks and benefits of HRT
- Practical prescribing

POI – sequelae……

- **Life expectancy is reduced – all causes**
  - Post oophorectomy <45yrs, HR for death 1.67 (Mayo clinic >2000 women – higher rates when risk factors for CVD) WHI HR 1.41 all cause mortality (25000 women oophorectomy under 50yrs)
  - CVD, osteoporosis and fractures
- **Cardiovascular disease**
  - Earlier onset of CVD and increase in mortality (no difference whether iatrogenic or not)
- **Bone mineral density**
  - 26-46% lower than controls
- **Psychological and mental health**
  - Increase risk of mental illness and increase lifetime risk of major depression
- **Neurological**
  - Accelerated cognitive decline, increase rates dementia and Parkinson's Disease

Age – the perimenopause

- **Perimenopause** – 4-5 years before the menopause
  - Declining oestrogen levels
  - Anovulatory cycles
  - Ovaries resistant to FSH so levels rise – levels fluctuate
  - Can have fluctuating symptoms of oestrogen deficiency
  - Fluctuations can cause symptoms (eg migraine worse)
  - Bleeding regular or irregular – patterns can change – may get referred for Ix (encourage Mirena if referring)

Symptoms of oestrogen deficiency/menopause

Physical

- Hot flushes and night sweats (90% all; 54% persisted >10yrs; 20% severe)
- Heat intolerance
- Palpitations
- Infertility
- Dry skin and hair thinning
- Headaches
- Breast tenderness
- Fat redistribution
- Urinary frequency and dysuria
- Recurrent UTIs
- Joint pains – collagen loss

Psychological

- Mood changes and irritability
- Lethargy
- Difficulty concentrating, brain fog
- Anxiety and panic
- Depression
- Sleep disturbance
- Low self esteem
- Difficulty finding words

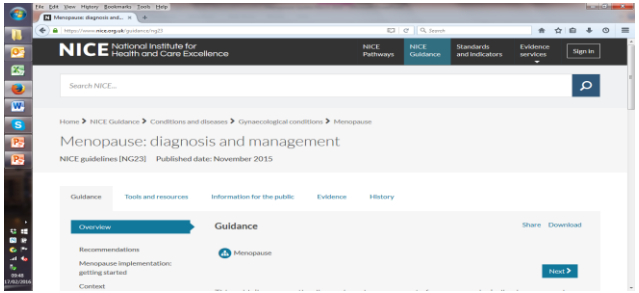
Sexual

- Reduced sex drive
- Dyspareunia (vaginal dryness)

To blood test or not to blood test?

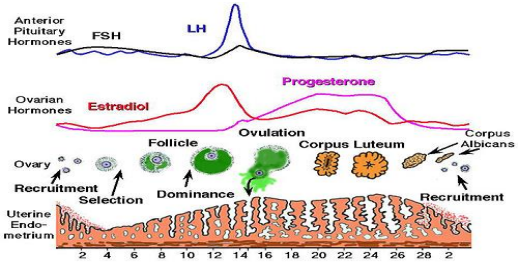
NICE (2015)

- Blood tests useful if under 40yrs - 2 FSH 4-6 weeks apart – result >30iu/L to diagnose POI
  - Can be useful 40-45 years
  - *Not useful* over 45 years



FSRH (2017)

- Contraception needs use FSH in women over 50 with amenorrhea on POC.
  - If >30iU/L, continue for 1 yr.
  - If FSH <30iU/L measure again in 1 yr



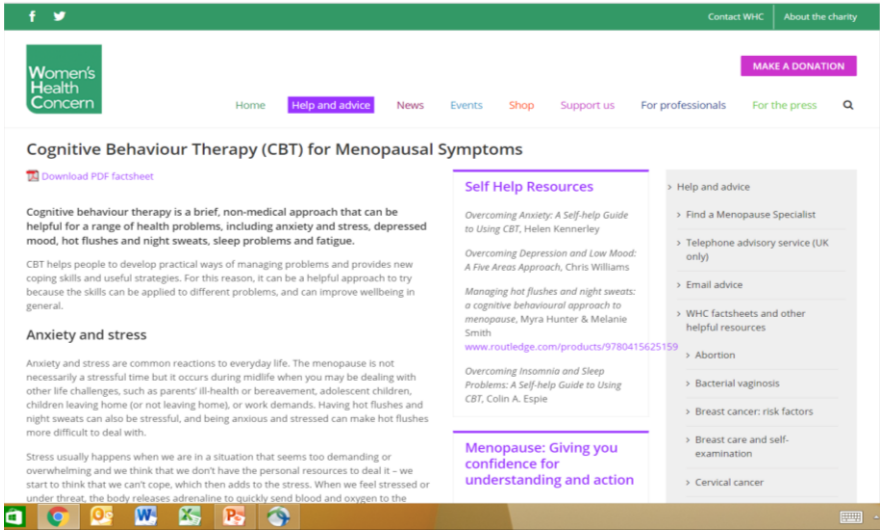
Management options

Lifestyle changes for health prevention and symptom control

- Lose weight
- Exercise
- Stop smoking
- Diet
  - vit D, Ca, phytoestrogens
  - Low carb diet??
- Avoid caffeine
- Avoid alcohol
- Avoid spicey foods

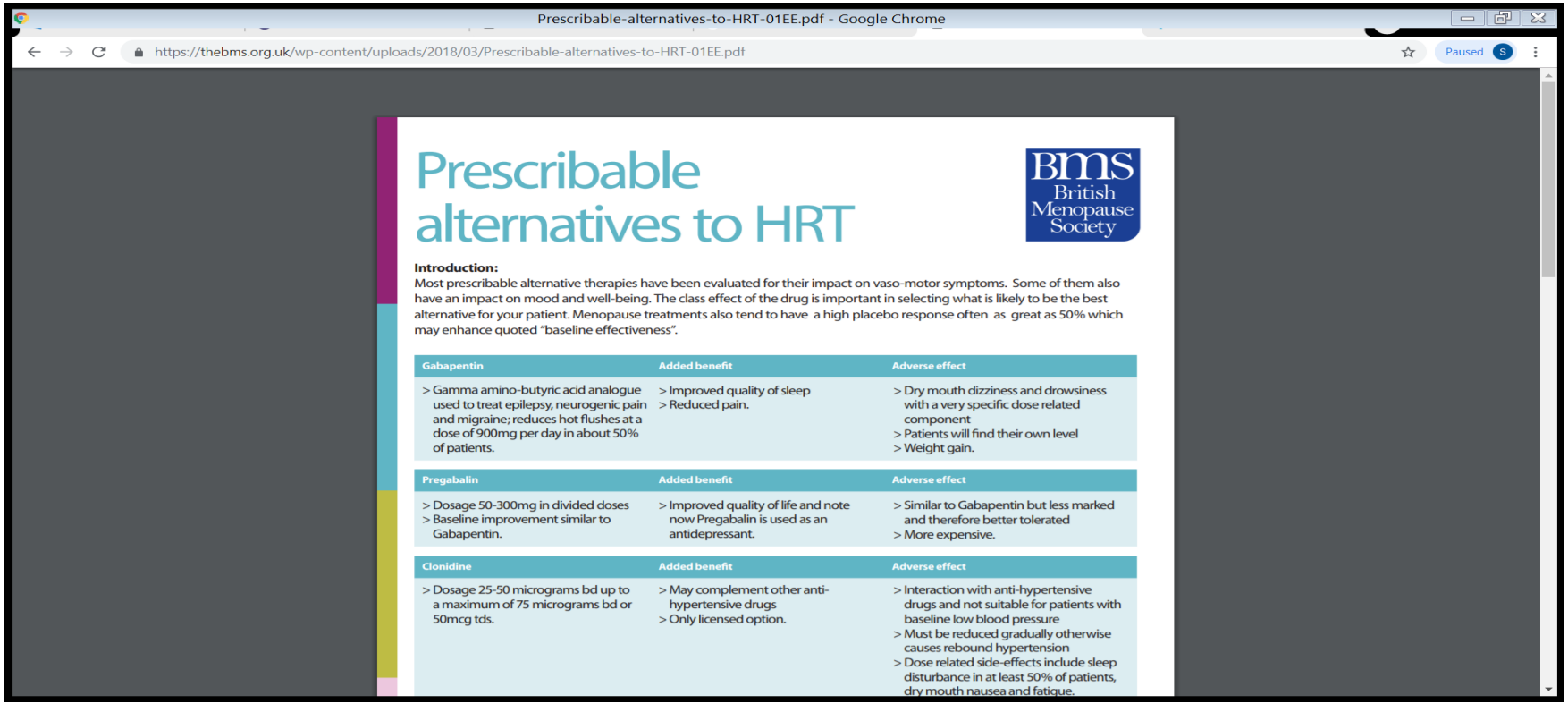
CBT (Nice 2015)

- WHC info sheet



Prescribable alternatives to HRT

‘BMS PRESCRIBABLE ALTERNATIVES TO HRT’



Prescribable alternatives to HRT

BMS British Menopause Society

Introduction:
Most prescribable alternative therapies have been evaluated for their impact on vaso-motor symptoms. Some of them also have an impact on mood and well-being. The class effect of the drug is important in selecting what is likely to be the best alternative for your patient. Menopause treatments also tend to have a high placebo response often as great as 50% which may enhance quoted "baseline effectiveness".

Gabapentin	Added benefit	Adverse effect
> Gamma amino-butyric acid analogue used to treat epilepsy, neurogenic pain and migraine; reduces hot flushes at a dose of 900mg per day in about 50% of patients.	> Improved quality of sleep > Reduced pain.	> Dry mouth dizziness and drowsiness with a very specific dose related component > Patients will find their own level > Weight gain.

Pregabalin	Added benefit	Adverse effect
> Dosage 50-300mg in divided doses > Baseline improvement similar to Gabapentin.	> Improved quality of life and note now Pregabalin is used as an antidepressant.	> Similar to Gabapentin but less marked and therefore better tolerated > More expensive.

Clonidine	Added benefit	Adverse effect
> Dosage 25-50 micrograms bd up to a maximum of 75 micrograms bd or 50mcg tds.	> May complement other anti-hypertensive drugs > Only licensed option.	> Interaction with anti-hypertensive drugs and not suitable for patients with baseline low blood pressure > Must be reduced gradually otherwise causes rebound hypertension > Dose related side-effects include sleep disturbance in at least 50% of patients, dry mouth nausea and fatigue.

Prescribable alternatives to HRT

Medication	Added benefit
Gabapentin	Improved sleep and reduced pain. Hot flushes reduced in 50% of patients
Pregabalin	Improved QOL and AD
Clonidine	Licensed for hot flushes
SSRIs	Class effect 20-50% effective – AD effect and QOL
Paroxetine	Interacts with cytochrome P450 – ci with tamoxifen
Fluoxetine	Class effect. P450 interaction
Citalopram	Class effect
Sertraline	Better for anxiety. P450 interaction
SSRI/SNRI Venlafaxine	Baseline benefit 20-66%, improved QOL and AD

HRT

Contraindications -

Listed contraindications:

- oestrogen dependent malignant tumours
- undiagnosed vaginal bleeding
- pregnancy
- active liver disease with abnormal liver function
- active thromboembolic disorder or acute phase myocardial infarction

HRT risks and benefits

Benefits of HRT

- Treat hot flushes
- Improve her psychological symptoms
- Improve her cognitive function
- Prevent osteoporosis
- Reduce risk of bowel cancer
- Reduce risk of cardiovascular disease
- Improve joint pain
- Improve control in type 2 Dm
- Improve muscle strength

Risks of HRT

- Breast cancer
- Ovarian cancer
  - Risk is doubled if HRT taken >10yrs
- Endometrial cancer
  - Oestrogen HRT only with uterus risk increases by 40%, >4-5 years of sequential HRT (CC lowers risk)
- Gall bladder disease
  - risk higher with oral oestrogens)
- CVD
  - oral oestrogens started more than 10 years after the menopause increases the risk of CVD (WHI)
- VTE and CVA
  - oral oestrogens

Benefits vs risks and age

- <50 benefits >> risks
  - all women should be offered HRT
- 50-60 benefits > risks for symptomatic women
- 60-70 benefits = risks
  - individualise and consider changing to transdermal therapy, decrease dose of oestrogen
- >70 risks>benefits
  - individualise

Prescribing HRT

Prescribing HRT

Has she got a uterus?

- If YES – needs a progestogen
- If NO – can have oestrogen only (BUT subtotal hysterectomy and ?endometriosis)

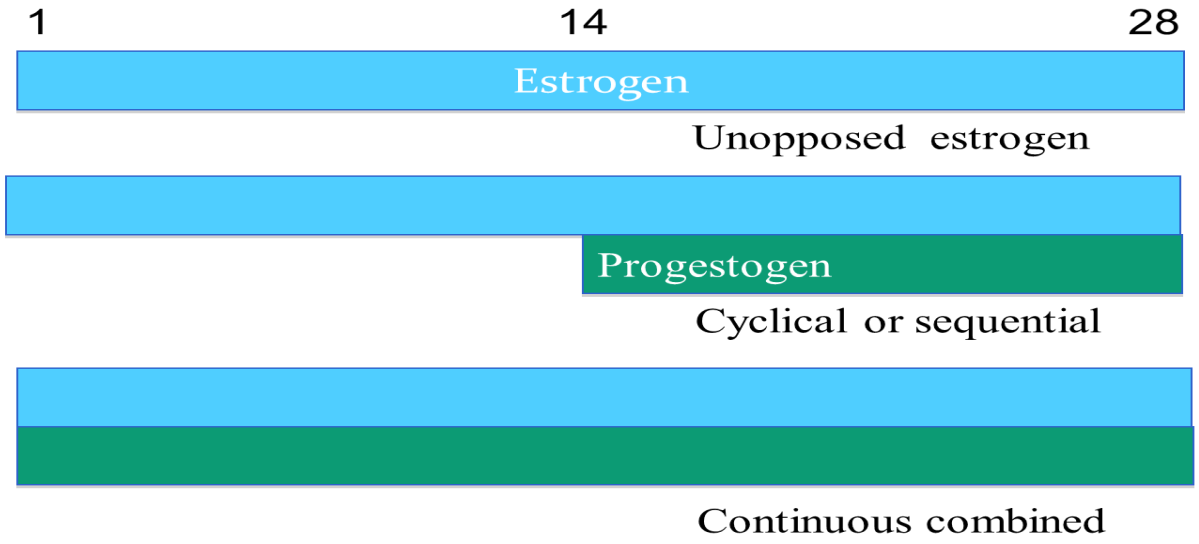
Is it within 1 year of her LMP?

- If YES – better to have sequential
- If NO – can have continuous combined

Does she have any risk factors for VTE/CVD?

- If YES – transdermal better
- If NO – can choose

Regimens


1
14
28
Estrogen
Unopposed estrogen
Progestogen
Cyclical or sequential
Continuous combined

Transdermal HRT

Transdermal continuous combined combinations

Oestrogen	Progestogen
Evorel conti = Estradiol 50mcg	Norethisterone 170mcg
Evorel/Elleste = Estradiol patch 25mcg, 50cmg, 75mcg, 100mcg twice weekly **Estraderm MX** 40mcg, 80mcg twice weekly **Estradot** 25mcg, 37.5mcg, 50mcg, 75mcg, 100mcg **Femseven** 50mcg, 75mcg, 100mcg weekly **Progynova TS** 50mcg, 100mcg weekly	100mg micronized progesterone capsule at night 5mg medoxyprogesterone acetate Mirena IUS – better if increasing beyond standard estradiol doses
Oestrogel = Estradiol 0.06% gel – 1 pump, 2 pumps, 3 pumps, 4 pumps	
Sandrena = Estradiol gel sachets – 0.5mg, 1 mg	

Oral HRT

Oral HRT combinations

- See MIMS HRT TABLE
- Start low dose
- Not all progestogens are equal

Hormone replacement therapy (HRT)							
SYSTEMIC							
Type	Brand	Oestrogen	Progestogen	Formulation	Bleed	RX*	Cost
Sequential combined therapy	Clinorette	Estradiol (2mg, 2mg)	Norethisterone (1mg)	Tabs	M	2	£3.08
	Cyclo-progynova	Estradiol (2mg)	Norgestrel (500mcg)	Tabs	M	2	£3.11
	Elleste Duet	Estradiol (1mg, 2mg)	Norethisterone (1mg)	Tabs	M	2	£3.07
	Evorel Sequi	Estradiol (50mcg)	Norethisterone (170mcg)	Patches	M	2	£11.09
	Femoston	Estradiol (1mg, 2mg)	Dydrogesterone (10mg)	Tabs	M	2	£5.39
	Novofem	Estradiol (1mg)	Norethisterone (1mg)	Tabs	M	2	£3.81
	Tridestra	Estradiol (2mg)	Medroxyprogesterone (20mg)	Tabs	Q	2	£6.83
	Trisequens	Estradiol (2mg, 2mg, 1mg)	Norethisterone (1mg)	Tabs	M	2	£3.70
Type	Brand	Oestrogen	Progestogen	Formulation	Bleed	RX*	Cost
Continuous combined therapy	Elleste Duet Conti	Estradiol (2mg)	Norethisterone (1mg)	Tabs	X	1	£5.67
	Evorel Conti	Estradiol (50mcg)	Norethisterone (170mcg)	Patches	X	1	£13.00
	Femoston Conti	Estradiol (500mcg, 1mg)	Dydrogesterone (2.5mg, 5mg)	Tabs	X	1	£8.14
	Indivina	Estradiol (1mg, 2mg)	Medroxyprogesterone (2.5mg, 5mg)	Tabs	X	1	£6.86
	Kliofem	Estradiol (2mg)	Norethisterone (1mg)	Tabs	X	1	£3.81
	Kliovance	Estradiol (1mg)	Norethisterone (500mcg)	Tabs	X	1	£4.40
	Premique Low Dose	Conj. oestr (300mcg)	Medroxyprogesterone (1.5mg)	Tabs	X	1	£2.17

Progestogens

Synthetic

C19 structurally related to testosterone

(Norethisterone, Norgestrel, Levonorgestrel)

C21 structurally related to progesterone

(Dydrogesterone, Medroxyprogesterone acetate)

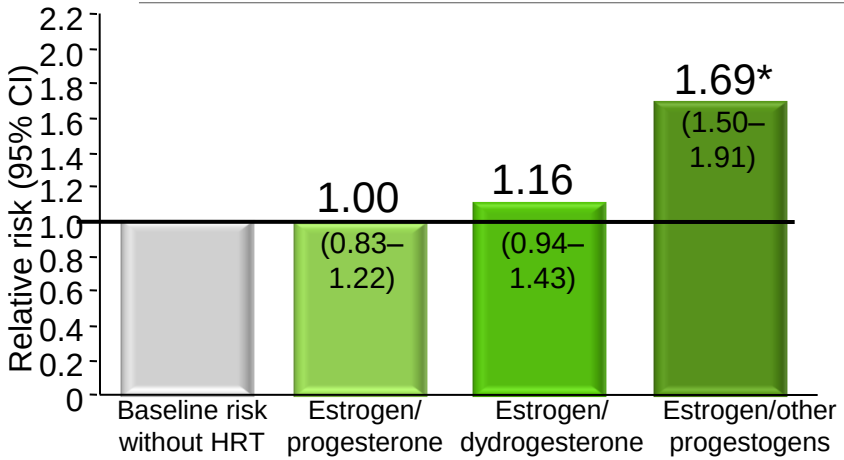
Spirolactone derived progesterone (Drospirinone)

Natural ('bioidentical')

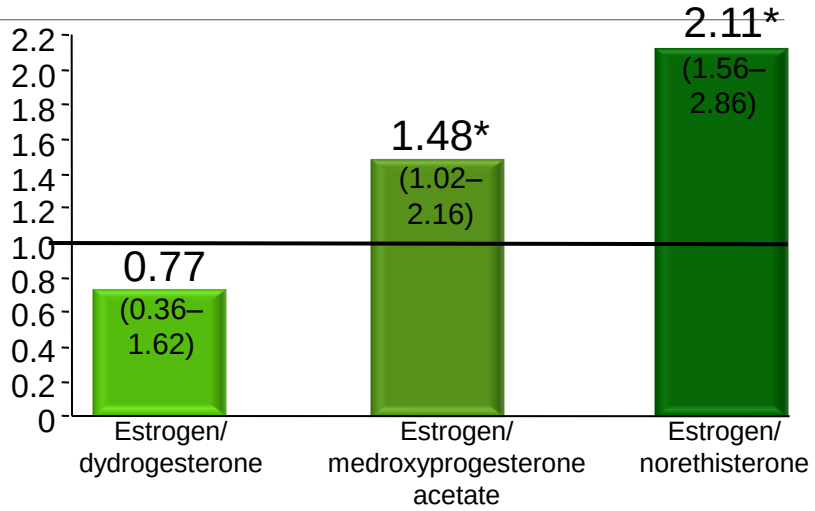
Micronised progesterone (Utrogestan)

Progestogens and breast cancer risk – E3PN study 2008.

Risk of breast cancer (all HRT routes)



Risk of breast cancer (oral HRT only)

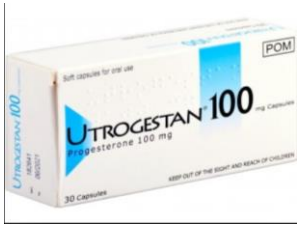


*significant increased risk

N = 80,377 women, for an average treatment duration of 8.1 years

Utrogestan = Micronised progesterone

- Micronised progesterone
- Oral capsule
- Mildly sedative
- Take 2 hours after eating
- Only comes as 100mg capsules
- PROs
  - Better tolerated
  - Fewer s/e – less androgenic
  - Off license – used vaginally
  - No risk of VTE/CVD
  - Lowest risk of breast cancer
- CONS
  - Potentially not as good for endometrial protection
  - Not as good bleeding control



Case 1

- 46 yr old
- Periods have changed – some months normal, sometimes late
- Some months hot flushes, sometimes not.
- More anxious, unusual for her – doesn't like driving on motorways; used to juggling jobs and children – now struggling to remember who needs to be where when
- Tired
- Just doesn't feel like herself
- Worried about her thyroid function – wants bloods.

Case 1 continued….

- Her grandmother had breast cancer aged 64 yrs. Died aged 89 yrs.
- Drinking 2 bottles of wine a week to help cope with symptoms and life.
- She is really worried about the recent newspaper reports on HRT and the risk of breast cancer

- She thinks she wants to take HRT, but worried about it

Contraception and HRT

- Mirena useful +++
- Combined oral contraceptive can be used if no ci up to 50yrs (Zoelly = estradiol)
- If menopause (ie greater than 1 year amenorrhoea) < 50 years, advise continue for 2 years
- If menopause > 50 years advise continue for 1 year
- Which methods? All progestogen only can be used alongside HRT

Refer to breast unit if…… (NICE 2013)

- One relative

  - Female 1st degree with breast ca <40
  - Male 1st degree with breast ca at any age
  - Female 1st degree with bilateral breast ca <50
  - 1st degree with breast and ovarian ca

- Two relatives

  - 1st/2nd degree with breast ca at any age
  - 1st/2nd degree with breast and ovarian cancer
  - With breast and/or ovarian cancer on paternal side

- Three relatives:

  - 1st or 2nd degree with breast cancer at any age

Breast cancer studies

1997 Collaborative Group on Hormonal Factors in Breast Cancer (CGHFBC)

- re-analysis of fifty-one world-wide observational studies

2002 Women's Health Initiative Study

- RCT – women aged 50-79yrs – combined arm (CEE +MPA) 16,608 post menopausal women

2003 Million Women's Study

- observational study - 1 084 110 women aged 50-64 years attending NHSBSP = quarter of British women between 50-64

WHI Results (CEE/MPA Arm)

Overall Relative and Attributable Risk for Women 50 to 80 Years of Age

Health Event	Overall Hazard Ratio	Confidence Interval Nominal 95%	Confidence Interval Adjusted 95%	Attributable Risk per 10,000 Women/Year	Benefit per 10,000 Women/Year
CHD	1.29	1.02–1.63	0.85–1.97	7	
Breast cancer	1.26	1.00–1.59	0.83–1.92	8	
Stroke	1.41	1.07–1.85	0.86–2.31	8	
VTE	2.11	1.58–2.82	1.26–3.55	18	
DVT	2.07	1.47–2.87	1.14–3.74	13	
PE	2.13	1.39–3.25	0.99–4.56	8	
Colorectal cancer	0.63	0.43–0.92	0.32–1.24		6
Hip fractures	0.66	0.45–0.98	0.33–1.33		5
Total fractures	0.76	0.69–0.85	0.63–0.92		44

DVT = deep vein thrombosis; PE = pulmonary embolism.

Writing Group for the Women's Health Initiative Investigators. *JAMA.* 2002;288:321-33.

Table 1: Adaptation of NICE menopause guidance reference table 3 with insertion of negative and positive framing of absolute risk [11]

	Absolute excess risk of breast cancer diagnosis per 1000 women aged 45 to 79*					
	Observational studies			Randomised studies		
	Excess	Diagnosed	Not diagnosed	Excess	Diagnosed	Not diagnosed
No HRT	–	23	977	–	23	977
Oestrogen only						
Past use	–	23	977	–	–	–
Current use	+6	29	971	-4	19	981
Duration of use < 5 years	+4	27	973	–	–	–
Duration of use 5 to 10 years	+5	28	972	–	–	–
Time since last use > 5 years	-5	18	982	-5	18	982
Combined HRT						
Past use	-3	20	980	–	–	–
Current use	+17	40	960	+5	28	972
Duration of use < 5 years	+12	35	965	–	–	–
Duration of use 5 to 10 years	+21	44	956	–	–	–
Time since last use > 5 years	-9	14	986	+8	31	969

* The absolute number of events has been calculated using a baseline risk population risk of 23/1000 women aged 45 to 79 years with 7.5 years of follow-up as estimated by NICE from 2010 Office of National Statistics data.[11] The duration of use selected (i.e. up to 5 years) reflects the average duration of HRT exposure in women in the UK prior to publication of the MWS.[6]

Table 2: The impact of lifestyle risk factors on the absolute risk of breast cancer diagnosis in women at population risk; comparison of HRT with other lifestyle risk factors with negative and positive framing[9]

	Absolute risk of diagnosis per 1000 women aged 45 to 79*		
	Cancers diagnosed	Cancers not diagnosed	Excess risk
No exposure	23	977	–
Risk Increased			
Postmenopausal obesity or overweight	27-40	960-973	+4 to +17
Combined HRT (NICE observational studies)	40	960	+17
Alcohol (regular intake ≥ 6 g/day)	29	971	+6
Unopposed HRT (NICE observational studies)	29	971	+6
Combined HRT (NICE randomised studies)	29	971	+6
Smoking (current smoker)	26	974	+3
Risk reduced			
Unopposed HRT (NICE randomised studies)	17	983	-6
Physical activity (> 9 MET-h/wk)	13	987	-10

* The absolute number of events has been calculated using a baseline risk population risk of 23/1000 women aged 45 to 79 years with 7.5 years of follow-up as estimated by NICE from 2010 Office of National Statistics data.[11]

Understanding the risks of breast cancer

Women's Health Concern

A comparison of lifestyle risk factors versus Hormone Replacement Therapy (HRT) treatment.

Difference in breast cancer incidence per 1,000 women aged 50-59.
Approximate number of women developing breast cancer over the next five years.

NICE Guideline, Menopause: Diagnosis and management November 2015

23 cases of breast cancer diagnosed in the UK general population

An additional four cases in women on combined hormone replacement therapy (HRT)

Four fewer cases in women on oestrogen only Hormone Replacement Therapy (HRT)

An additional four cases in women on combined hormonal contraceptives (the pill)

An additional five cases in women who drink 2 or more units of alcohol per day

Three additional cases in women who are current smokers

An additional 24 cases in women who are overweight or obese (BMI equal or greater than 30)

Seven fewer cases in women who take at least2½ hours moderate exercise per week

Women's Health Concern
www.womens-health-concern.org
Reg Charity No: 279851
Company Reg No: 1453523

Women's Health Concern is the patient arm of the BMS.
We provide an independent service to advise, reassure and educate women of all ages about their health, wellbeing and lifestyle concerns.

Go to **www.womens-health-concern.org**

BMS British Menopause Society
www.thebms.org.uk
Reg Charity No: 1051344
Company Reg No: 02759439

March 2017

Breast cancer – NICE 2015

(observational and RCT data)

- HRT with oestrogen alone is associated with no or little change in risk.
- HRT with oestrogen and progestogen 'can be associated with an increase in the risk.'
- Risk of diagnosis is not elevated in past users of HRT.
- Any increase in risk 'is related to treatment duration and reduces after stopping HRT.'
- No significant increase in breast cancer mortality was found
  - confirmed subsequently with long-term follow-up of the WHI study

Lancet paper findings

- 58 studies, 108647 post menopausal women who developed breast cancer
- Increase in the risk of breast cancer Dx with HRT intake.
- Risk of breast cancer was noted to be higher with combined oestrogen / progesterone compounds, but also increased to a lesser extent, with oestrogen only systemic HRT.
- The risk of breast cancer remained elevated for more than 10 years after discontinuing HRT and this appeared dependant on the duration of HRT use.
- Starting HRT between the age of 40 and 50 was also associated with an increased risk of breast cancer, but the number of women in this sub-group was relatively small.

BUT…..

- Heterogeneous data spanning 1990 into 2007
- No assessment of mortality – no significant increase in WHI. Eurostat data shows decline in breast cancer mortality predating HRT decline in use.
- MHRA recommendations that followed re lowest dose oestrogen, lowest time – no evidence for dose and doesn't take into account risk/benefits
- Consider the benefits, particularly younger women – did not compare those with ovarian function.

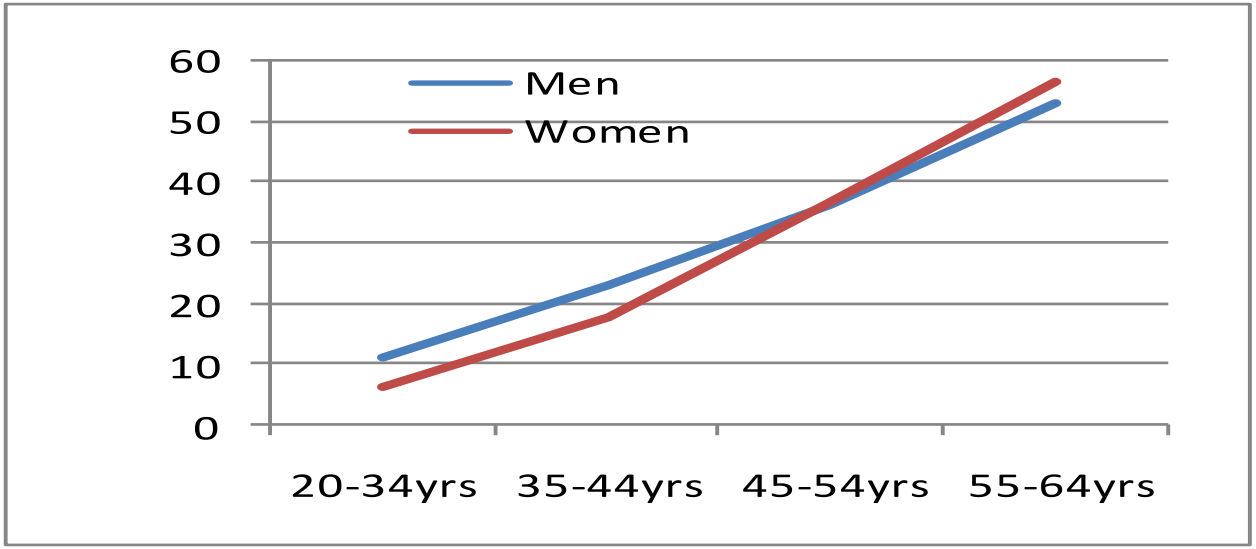
Case 1

- More risk from drinking than HRT
- Lifestyle counselling – reducing alcohol may help her symptoms
- Additional risk of breast cancer from combined HRT is low
- HRT may help her to feel better, but she needs to understands the benefits and risks to make her own decision.

Case 2

- 55 yr old
- Hot flushes, brain fog. No period for 2 years. Completely fed up.
- PMH – treated hypertension, type 2 Dm
- FH – father MI, mother CVA
- Smoker
- BP – 150/80
- BMI – 38 kg/m2

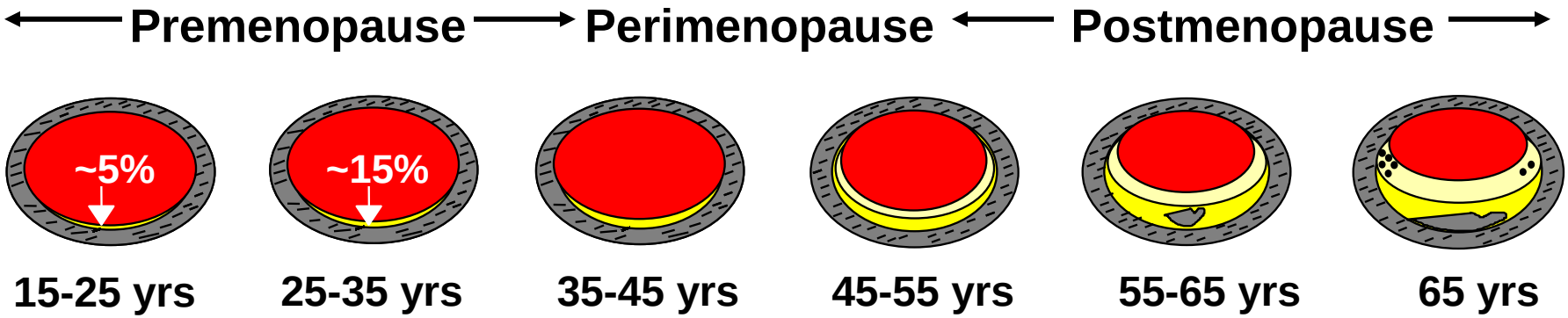
Risk of cardiovascular disease



Metabolic changes resulting from the menopause

Lipids/ Lipoproteins	Glucose/ Insulin	Haemostasis	Body composition	Vascular function
LDL chol ↑	Pancreatic insulin secretion ↓	Fibrinogen ↑	Android fat ↑	Arterial waveform pulsatility index ↑
HDL chol ↓	Insulin elimination ↓	Factor VII ↑	Gynoid fat ↓	Endothelial-dependant vasodilation ↓
TGs ↑	Insulin resistance ↑	Anti-thrombin ↑		BP ↑
LDL particle size ↓		PAI-1 (plasminogen activator inhibitor) ↑		

CVS - progressive plaque formation



Benefits of Endogenous E_2 **Primary Benefits of HT** **No Benefits of HT**

Mikkola TS, et al. *Ann Med*. 2004;36:402-13.

WHI Results (CEE/MPA Arm)

Overall Relative and Attributable Risk for Women 50 to 80 Years of Age

Health Event	Overall Hazard Ratio	Confidence Interval Nominal 95%	Confidence Interval Adjusted 95%	Attributable Risk per 10,000 Women/Year	Benefit per 10,000 Women/Year
CHD	1.29	1.02–1.63	0.85–1.97	7	
Breast cancer	1.26	1.00–1.59	0.83–1.92	8	
Stroke	1.41	1.07–1.85	0.86–2.31	8	
VTE	2.11	1.58–2.82	1.26–3.55	18	
DVT	2.07	1.47–2.87	1.14–3.74	13	
PE	2.13	1.39–3.25	0.99–4.56	8	
Colorectal cancer	0.63	0.43–0.92	0.32–1.24		6
Hip fractures	0.66	0.45–0.98	0.33–1.33		5
Total fractures	0.76	0.69–0.85	0.63–0.92		44

DVT = deep vein thrombosis; PE = pulmonary embolism.

Writing Group for the Women's Health Initiative Investigators. *JAMA.* 2002;288:321-33.

Further analysis of WHI

Starting HT within 10 years of menopause
- 24 % reduction in CHD
- 30 % reduction in overall deaths

Slight increase in ischaemic stroke risk at all ages
- Other studies, no change in baseline risk with transdermal HRT

Coronary artery calcium
- Mild-to-moderate 40% reduced
- Severe 60 % reduced

VTE and CVA

Oral estrogen—

- ↑ prothrombin fragment 1+2,
- ↓ antithrombin,
- acquired resistance to activated protein C
- DVT/PE 2—3 background risk
- Greatest risk is in the first 12 months

Transdermal estrogen—

- no effect at low and standard doses (50mcg estradiol patch, 2 pumps 0.06% estradiol gel, 1g Sandrena gel)

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Stroke

Renoux et al BMJ 2010;340:c2519

Type of HRT	HR (95% CI)
None	1.00
Oral E only	1.35 (1.16 to 1.58)
Oral E+P	1.24 (1.08 to 1.41)
Transdermal E only	1.02 (0.78 to 1.34)
Transdermal E+P	0.76 (0.47 to 1.22)

GPRD case control study 15,710 cases matched to 59,958 controls

Adjusted for: age, body mass index, smoking status, alcohol misuse, diabetes, hyperlipidaemia, hypertension, atrial fibrillation, cardiovascular disease, transient ischaemic attack, aspirin or other NSAID use, and history of hysterectomy or oophorectomy

VTE

Renoux C, DellAniello S, Suissa S. J Thromb Haemost 2010; 8: 979-86.

Regimen	Risk relative to non-use	Comment
Current use oral E alone	RR **1.49**; 95% CI, 1.37–1.63	Dose effect lost in 4/12
Current use oral E+P	RR **1.54**; 95%CI, 1.44–1.65	Dose effect lost in 4/12
Current use TD E alone	RR 1.01; 95% CI, 0.89–1.16	
Current use TD E+P	RR 0.96; 95% CI, 0.77–1.20	
Current use Tibolone	RR 0.92; 95% CI: 0.77–1.10	

- GPRD study
- Nested case control study 955 582 women aged 50-79 Jan 1987 – March 2008
- 23 505 VTE with 231562 controls

Case 2

- Lifestyle advice
- Transdermal HRT
  - Weight up the risks and benefits
  - What does she want?
  - Consider the endometrium if bleeds – risk of endometrial Ca

Case 3

50 yr old accountant

Brain fog, hot sweats, low self esteem. No period for 9 months

Migraine with aura

Worse in the last 1-2 years

Did not think she could have hormones

BP 140/85; BMI 27 kg/m2

Needs help fast – work impacted

Migraine .....

Not a contraindication to HRT

HRT may improve migraine (can be triggered by fluctuations of oestrogen)

Migraine associated with small increased risk of CVA

HRT is not the same as the COP

- Oral (and transdermal) Ethinyl estradiol in COP thrombogenic
- Oral estradiol thrombogenic and blood levels can fluctuate
- Transdermal estradiol at low or standard doses is not thrombogenic = better

Transdermal sequential combined combinations

Oestrogen	Progestogen
Evorel sequi = Estradiol 50mcg	Norethisterone 170mcg
Evorel/Elleste = Estradiol patch 25mcg, 50cmg, 75mcg, 100mcg twice weekly **Estraderm MX** 40mcg, 80mcg twice weekly **Estradot** 25mcg, 37.5mcg, 50mcg, 75mcg, 100mcg **Femseven** 50mcg, 75mcg, 100mcg weekly **Progynova TS** 50mcg, 100mcg weekly	200mg micronized progesterone capsule (2x100mg) 12/28 10mg medoxyprogesterone acetate 12/28 Mirena IUS – better if increasing beyond standard estradiol doses.
Oestrogel = Estradiol 0.06% gel – 1 pump, 2 pumps, 3 pumps, 4 pumps	
Sandrena = Estradiol gel sachets – 0.5mg, 1 mg	

Case 4

- 55 yr old
- Happy on Evorel Conti
  - Found in small independent pharmacy
- Loss of libido
- When asked, volunteers vaginal dryness and uncomfortable intercourse
- Otherwise well

Prescribing HRT – vaginal symptoms

Vaginal moisturisers - use daily as needed – can use with vaginal oestrogen

- Replens
- Regelle
- Hyalofemme

Vaginal lubricants – during intercourse

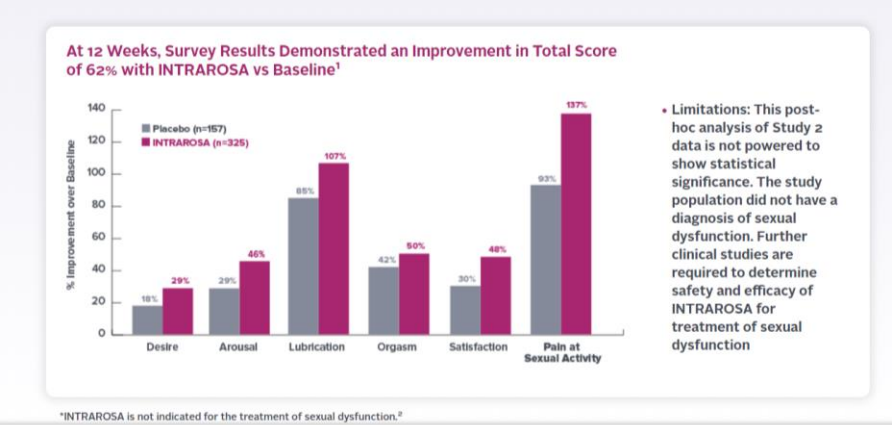
- Water based – KY Gel
- Oil based – Yes
- Silicone based – Durex Play Perfect Glide
- Plant based – Sylk

Prescribing HRT – vaginal symptoms

- Can have vaginal oestrogen for as long as she needs (NICE ‘15). No need for endometrial protection (blood oestrogen levels remain post menopausal)
- Can have and may need as well as systemic HRT
- Vagifem 10mcg every night for 2 weeks then twice a week
- Estriol 0.1% or 0.01% as above
- Estring - Estradiol Hemihydrate 2.0 mg,
  - Each ring releases estradiol at an average amount of 7.5 microgram per 24 hours, over a period of 90 days.

Prasterone - Intrarosa (dehydroepiandrosterone)

Designed to treat moderate to severe pain during sexual intercourse in menopausal women.



Case 4

- 55 yr old
- Adding Vagifem has helped, along with soap substitute and hyalofemme
- Enjoying sex again
- Using oil based lubricant
- Doesn’t want to stop vagifem

Case 6

- 58 yr old
- On Oestrogel 0.06% 2 pumps a day with Utrogestan 100mg at night
- No vaginal symptoms after using Vagifem
- Still getting some hot flushes, but improved
- Still no libido
- Has read about testosterone

Case 6

- 58 yr old
- Is she using Oestrogel correctly?
- Options
  - could increase the dose to 3 and then 4 pumps of Oestrogel
  - Could change to a patch – 1 measure of 0.06% gel equivalent to 25mcg twice weekly patch

Testosterone

- Serum levels gradually decline from age 30yrs – derived from ovaries – adrenal also
- Replacement therapy is not licensed for women in the UK
- NICE 2015 recommend that it can be used in women on HRT who still suffer loss of libido. Exclude physical causes.
- Some of the effects are direct and some due to peripheral conversion to oestrogen by aromatase
- Contributes to libido, sexual arousal and orgasm by increasing dopamine levels in the central nervous system

Testosterone

Women with hyposexual desire disorder (HSDD) – approx 2/3 respond (cf placebo)

Tostran 2% - max every other day

Testogel 1% - 5g sachet to last 10-14 days

Androfem (Australian – private prescription) Implants (privately)

Potential adverse effects –

- Increased body hair at site of application (occasional problem) – spread more thinly, vary site of application, reduce dosage.
- Generalised Hirsutism (uncommon)
- Alopecia, male pattern hair loss (uncommon)
- Acne and greasy skin (uncommon)
- Deepening of voice (rare)
- Enlarged clitoris (rare)

BMS guideline 2019 – Nick Panay

Effects on oestrogen on bone

- Inhibits bone resorption, Interleukin 6
- Osteoclast apoptosis regulated by oestrogen
  - Oestrogen deficiency—osteoclasts live longer—increased bone resorption
- Enhances intestinal calcium absorption
- Protects bone from resorptive effects of PTH

HRT and osteoporosis

- While taking HRT, incidence of fragility fracture is reduced – hip and spine
- 23 fewer fragility fractures per 1000 (NICE 2015)
- Maintained during treatment
- May continue longer when HRT taken longer
- Bone sparing doses – standard doses (50mcg estradiol patch, 2mg estradiol orally, 2 pumps 0.06% estradiol gel, 1g Sandrena gel), though there is benefit at low doses.

Thank you for listening…

www.menopausematters.co.uk

www.BMS.org.uk

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