



# Supporting Pharmacists with HRT decision making

**Dr Nuttan Tanna, IPP, PhD, FFRPS, FRPS.**

Pharmacist Consultant, Women's Health & Osteoporosis / Bone Health  
**London North West University NHS Healthcare Trust, Harrow, Middlesex.**  
Clinical Reference Group, NHS England  
BMS Menopause Accredited Specialist



# HRT Prescribing



- Weekly Menopause & Osteoporosis Medication Management Clinics
- Rationale HRT prescribing
- Patient
  - Full medical history
  - Hormone Replacement Therapy Risks and Benefits
    - Individualised for patient
    - Patient's views
    - Holistic management plan important
  - Alternative options - Prescribed / Non-Pharmacological .....
- Pharmaceutical Care model [1] / Medicines Optimisation [2]
  - Indication, Safety, Efficacy, Compliance & Persistence (Adherence), and Cost effectiveness

[1]. Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. Am J Hosp Pharm. 1990 Mar;47(3):533-43. PMID: 2316538.

[2]. Medicines Optimization: the safe and effective use of medicines to enable the best possible outcomes. NICE guideline [NG5]Published: 04 March 2015

# Rationale HRT Prescribing

- Terminology

- Menopause.....Greek language.....
  - Climacteric....the phase

- Perimenopause

- Some endogenous cycling

- Postmenopause

- LNMP one year or more

- Hormone Replacement Therapy - HRT

- SCT .....sequential .....mimics menstrual cycle
- CCT .....continuous combined oestrogen + progestogen/progesterone
- Unopposed oestrogen.....when?
- Vaginal ERT.....for local relief.....uro-genital syndrome symptomology

# The Menopause....

- Average age menopause / UK
  - 50/51 years > **Climacteric** phase: 45-55
- ~ 1% women > **Premature Ovarian Insufficiency** [POI]
  - Menopause before age 40 > **Young** menopause / 40-45 - **Early** menopause
- With **longevity**, millions of women - now live 30-40% of their life after menopause
- 8 / 10 women > > > peri-menopausal symptoms
  - Hot flushes and night sweats
  - ~ last about 4 years
  - QoL severely affected
- 25% women with severe menopausal symptoms
- SWAN study arms – symptomatic average 7 years, but up to 12 years....

1. World Health Organization. Research on the menopause in the 1990's. Report of a WHO Scientific Group. World Health Organ Tech Rep Ser. 1996;866,12–14.
2. Menopause Terminology. International Menopause Society 1999. [https://www.imsociety.org/menopause\\_terminology.php](https://www.imsociety.org/menopause_terminology.php)
3. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3185240/>
4. <https://www.everydayhealth.com/menopause/things-weve-learned-about-menopausal-symptoms-from-menopause-research/>

# Rationale HRT Prescribing

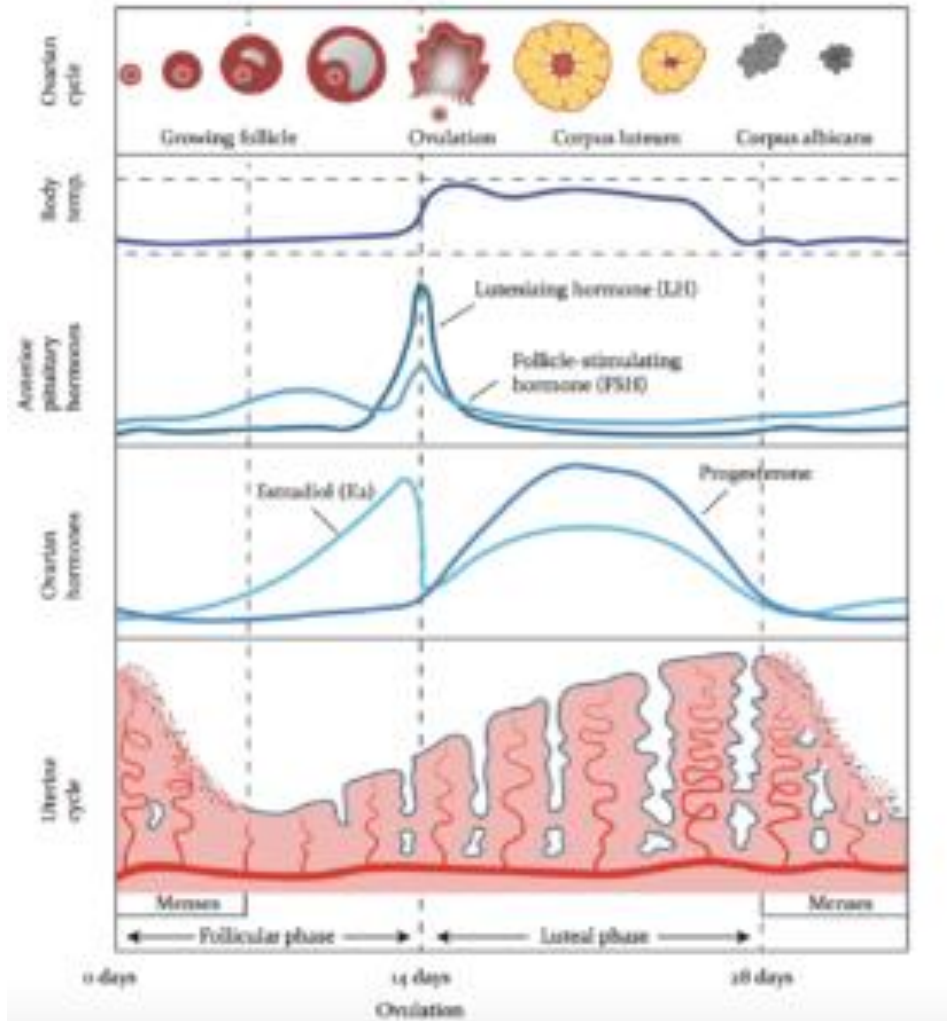
- HRT Risks and benefits
  - NICE NG23 menopause guidance
  - Benefits
    - Vasomotor symptom control
    - Bone protection / osteoporosis and fracture prevention
    - Sleep
    - Low moods / anxiety
    - Sexual health .....role of testosterone [off license; NICE NG23]
  - Risks
    - Breast cancer
    - Strokes / Thrombosis
      - Other ... based on patient's medical history eg unstable diabetes; thyroid dysfunction; POI.....
- CHD?

# Hormone Replacement Therapy

- HRT Risks and Benefits

- National Institute of Health & Care Excellence [NICE] Menopause Guidelines NG23 Nov. 2015 <https://www.nice.org.uk/guidance/ng23>
  - For women between 50-60.....?65
  - Data for added risk calculated over 7.5 years HRT use...
    - Breast cancer
    - CVD – thrombosis and strokes
    - Osteoporosis\* [\* 3-5 years]
- Menopause Patient Information Leaflet: Selfcare Forum endorsed by NHSE Clinical Reference Group <https://www.selfcareforum.org/menopause/>

# The Menstrual Cycle



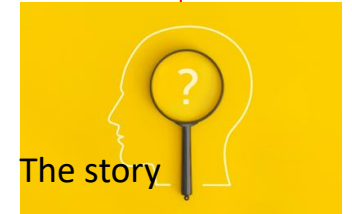
Premature Ovarian Insufficiency [POI]  
 Measure FSH levels 4-6 weeks apart; if  
 levels over 30 > Premature Ovarian Failure  
 [NICE NG23]

Systemic cyclical circulation

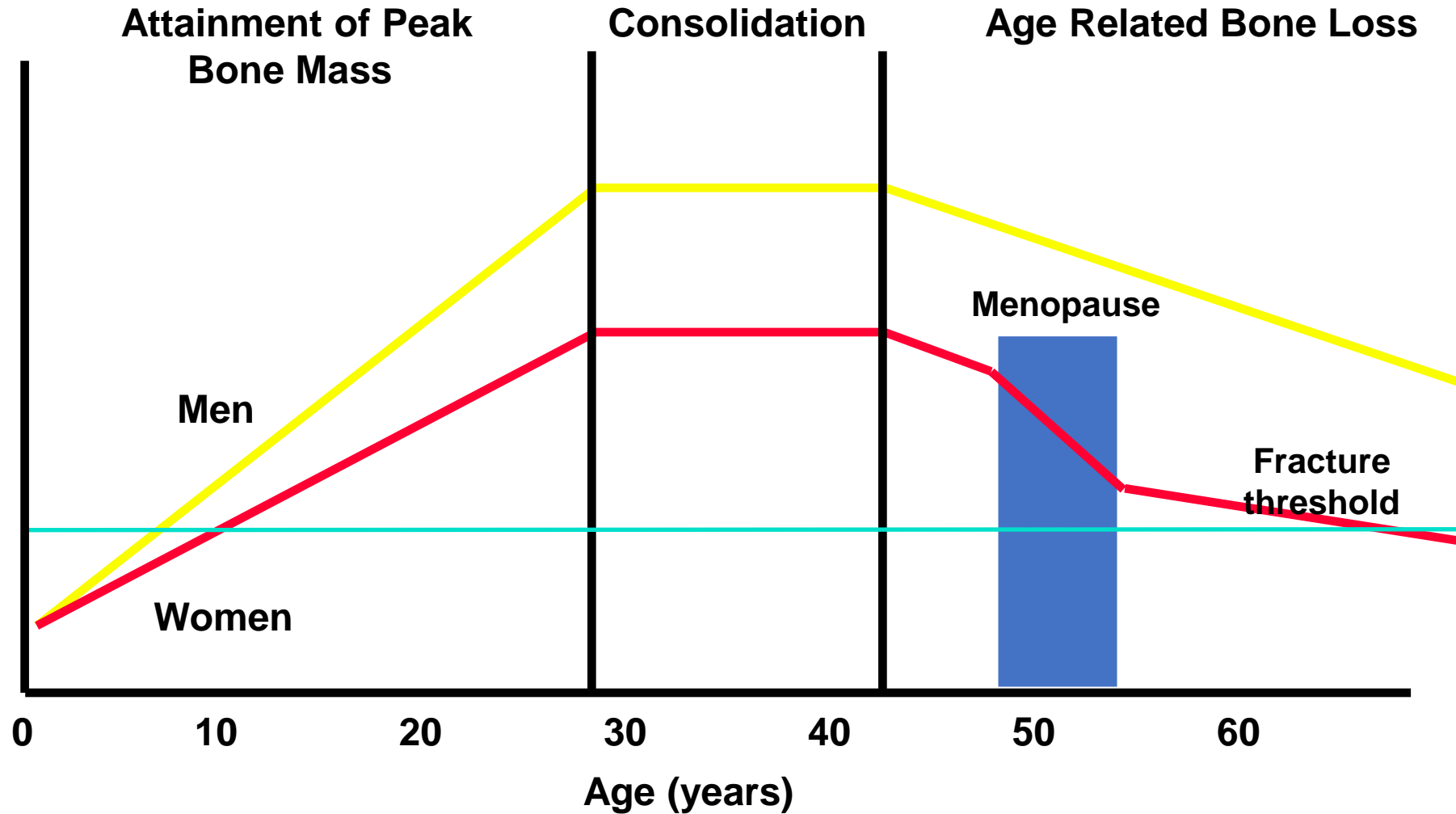
- Estradiol [17 $\beta$  estradiol]
- Natural progesterone

## HRT

- physiological replacement
- 17 $\beta$  estradiol / estradiol salts
- Natural progesterone..... →
  - Progestogens
    - C19 testosterone analogues
    - C21 progesterone analogues
      - Natural progesterone



# Age Related Changes in Bone Mass<sup>1</sup>

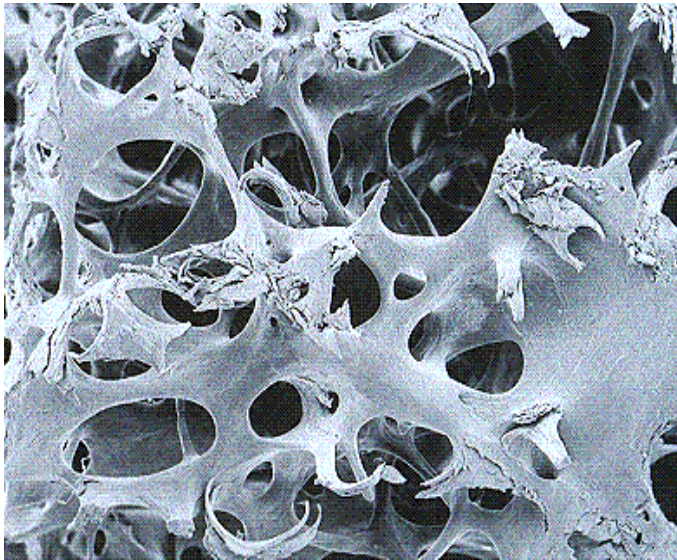


1. Compston JE. Clinical Endocrinology 1990; 33: 653-682.

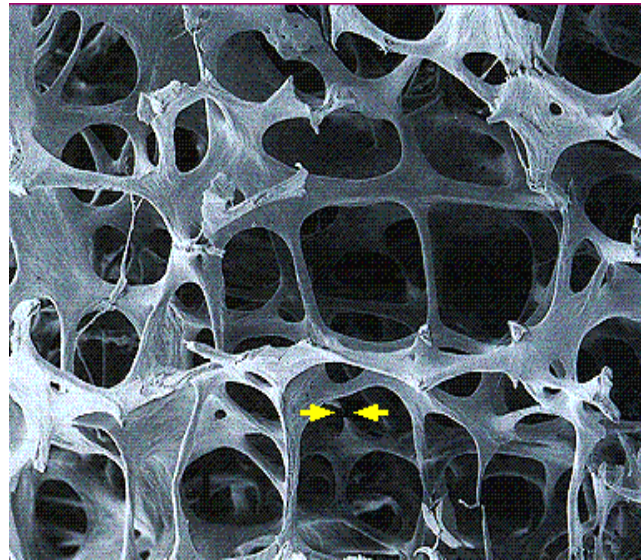


# Osteoporosis = loss of bone density?

“Osteoporosis is a skeletal disorder characterized by compromised **bone strength** predisposing a person to an **increased risk of fracture.**”<sup>1</sup>



**Normal<sup>2</sup>**



**Osteoporosis<sup>2</sup>**

## FRAX / Qfracture

- for fragility fracture assessment
- Prediction algorithms

1. Consensus Development Conference, JAMA 2001; 285: 785-95

2. Dempster DW et al, JBMR 1986; 1: 15-21.

# The LNWUHT Mid-life Womens Health - Symptom Assessment Chart



With permission

QUESTIONS	ANSWERS				Office Use Only
	0	1	2	3	
<b>General Problems:</b>					
Daytime Sweats & Flushes				X	
Night-time Sweats & Flushes			X	X	
Unable to sleep				X	
Headaches		X			
Tiredness				X	
Loss of energy			X	X	
General aches & pains <i>Variable</i>		X	X		
General Itchiness		X			
Formication (feeling of something crawling over you)	X				
<b>Emotional Problems:</b>					
Tearfulness			X	X	
Depression			X	X	
Feeling of unworthiness			X	X	
Irritability			X	X	
Anger			X	X	
Bitterness			X		
Panic Attacks		X			
+ / - Palpitations		X			
Aggression		X			
<b>Bladder Problems:</b>					
Daytime Frequency		X			
Urgency		X			
Urge Incontinence (leakage if you do not get there in time)		X			
Stress Incontinence (Leakage if cough, sneeze or laugh)	X				
Night-time Frequency		X			
<b>Sexual Problems:</b>					
Bed Wetting	X				
Vaginal dryness/soreness			X	X	
Vaginal Itching			X	X	
Soreness / pain with intercourse	*?				
Bleeding with intercourse	*?				
Loss of Libido (sex drive)	*?		X		
Difficulty achieving orgasm	*?				
<b>Memory Problems:</b>					
Loss of Memory			X	X	
Loss of concentration			X	X	
Inability to cope		X			
Feelings of personality disintegration			X		
<b>Period Problems:</b>					
Periods increasingly erratic	?				
Periods much lighter	?				
Periods much heavier	?				
Irregular Bleeding between periods	?				
New bleed over 1 year after periods have stopped	?				

\* Not in a relationship  
\*\* No periods for well over a year.

# Table: Hormone Replacement Therapy (HRT)

MIMS : 1 April 2020

Last updated 1st April 2020: added Lenzetto

Hormone replacement therapy (HRT)							
SYSTEMIC							
Type	Brand	Oestrogen	Progestogen	Formulation	Bleed	RX*	Cost
Sequential combined therapy	<a href="#">Clinorette</a>	Estradiol (2mg, 2mg)	Norethisterone (1mg)	Tabs	M	2	£3.08
	<a href="#">Elleste Duet</a>	Estradiol (1mg, 2mg)	Norethisterone (1mg)	Tabs	M	2	£3.07
	<a href="#">Evorel Sequi</a>	Estradiol (50mcg)	Norethisterone (170mcg)	Patches	M	2	£11.09
	<a href="#">Femoston</a>	Estradiol (1mg, 2mg)	Dydrogesterone (10mg)	Tabs	M	2	£5.39
	<a href="#">FemSeven Sequi</a>	Estradiol (50mcg)	Levonorgestrel (10mcg)	Patches	M	2	£13.18
	<a href="#">Novofem</a>	Estradiol (1mg)	Norethisterone (1mg)	Tabs	M	2	£3.81
	<a href="#">Tridestra</a>	Estradiol (2mg)	Medroxyprogesterone (20mg)	Tabs	Q	2	£6.83
	<a href="#">Trisequens</a>	Estradiol (2mg, 2mg, 1mg)	Norethisterone (1mg)	Tabs	M	2	£3.70

## Progestogens:

### C19 Testosterone analogues

Norethisterone

Levonorgestrel

- Androgenic side effects
- Libido and energy affect?
- Bones?
- Better choice for bleed control

### C21 Progesterone analogues

Dydrogesterone

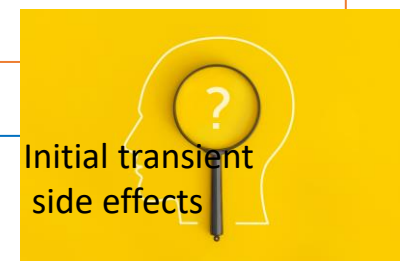
Medroxyprogesterone

- Dydrogesterone – Insulin Resistance; lipid markers?; no affinity for androgen receptors
- MPA – some affinity for androgen receptors

Natural progesterone / Utrogestan<sup>Rx</sup> or Gepretix<sup>Rx</sup>



Estrogen throughout month  
with Progesterone for half the month



Initial transient side effects

Type	Brand	Oestrogen	Progestogen	Formulation	Bleed	RX*	Cost
Continuous combined therapy	<a href="#">Elleste Duet Conti</a>	Estradiol (2mg)	Norethisterone (1mg)	Tabs	X	1	£5.67
	<a href="#">Evorel Conti</a>	Estradiol (50mcg)	Norethisterone (170mcg)	Patches	X	1	£13.00
	<a href="#">Femoston Conti</a>	Estradiol (500mcg, 1mg)	Dydrogesterone (2.5mg, 5mg)	Tabs	X	1	£8.14
	<a href="#">FemSeven Conti</a>	Estradiol (50mcg)	Levonorgestrel (7mcg)	Patches	X	1	£15.48
	<a href="#">Indivina</a>	Estradiol (1mg, 2mg)	Medroxyprogesterone (2.5mg, 5mg)	Tabs	X	1	£6.86
	<a href="#">Kliofem</a>	Estradiol (2mg)	Norethisterone (1mg)	Tabs	X	1	£3.81
	<a href="#">Kliovance</a>	Estradiol (1mg)	Norethisterone (500mcg)	Tabs	X	1	£4.40
	<a href="#">Premique Low Dose</a>	Conj. oestr (300mcg)	Medroxyprogesterone (1.5mg)	Tabs	X	1	£2.17

LNMP = 1 year or more > Postmenopausal > can be prescribed CCT HRT .....can take upto 4-6 months to settle....

Type	Brand	Oestrogen	Progestogen	Formulation	Bleed	RX*	Cost
Gonadomimetic	<a href="#">Livial</a>	Tibolone (2.5mg)		Tabs	X	1	£10.36
Selective oestrogen receptor modulator	<a href="#">Senshio</a>	Ospemifene (60mg)		Tabs	X	1	£39.50

**Tibolone** > breaks up into 3 isomers – estrogen, progesterone and androgen receptor affinity  
- Licensed for PM women ...> alternative ‘no-bleed’ HRT option

**Ospemifene** – new product; licensed for moderate to severe symptomatic vulvar and vaginal atrophy / PM women / ? tried vaginal ERT



Type	Brand	Oestrogen	Progestogen	Formulation	Bleed	RX*	Cost
<b>Unopposed oestrogen</b> (if uterus is intact an adjunctive progestogen must be used)	<a href="#">Bedol</a>	Estradiol (2mg)		Tabs		1	£1.69
	<a href="#">Elleste Solo</a>	Estradiol (1mg, 2mg)		Tabs		1	£1.69
	<a href="#">Elleste Solo MX</a>	Estradiol (40mcg, 80mcg)		Patches		1	£5.19, £5.99
	<a href="#">Estraderm MX</a>	Estradiol (25mcg, 50mcg, 75mcg, 100mcg)		Patches		1	£5.50, £5.51, £6.42, £6.66
	<a href="#">Estradot</a>	Estradiol (25mcg, 37.5mcg, 50mcg, 75mcg, 100mcg)		Patches		1	£5.99, £6.00, £6.02, £7.00, £7.27
	<a href="#">Evorel</a>	Estradiol (25mcg, 50mcg, 75mcg, 100mcg)		Patches		1	£3.42, £3.88, £4.12, £4.28
	<a href="#">FemSeven</a>	Estradiol (50mcg, 75mcg, 100mcg)		Patches		1	£6.04, £6.98, £7.28
	<a href="#">Lenzetto</a>	Estradiol (1.53mg per actuation)		Spray		1	£3.45-£6.90
	<a href="#">Oestrogel</a>	Estradiol (0.06%)		Gel		1	£4.20
	<a href="#">Premarin</a>	Conj. oestr (300mcg, 625mcg, 1.25mg)		Tabs		1	£2.02, £1.34, £1.19
	<a href="#">Progynova</a>	Estradiol (1mg, 2mg)		Tabs		1	£2.43
	<a href="#">Progynova TS</a>	Estradiol (50mcg, 100mcg)		Patches		1	£6.30, £6.90
	<a href="#">Sandrena</a>	Estradiol (500mcg, 1mg)		Gel		1	£5.08, £5.85
<a href="#">Zumenon</a>	Estradiol (1mg, 2mg)		Tabs		1	£2.30	

# HRT in women with subtotal hysterectomy

- Limited evidence to guide practice.
- **Common practice**
  - consider sequential progestogens for up to 3 months
  - if no bleeding is noted with this regimen, then it is unlikely that any residual endometrium is present
    - then.....oestrogen only HRT can be considered as sufficient.
- **Ongoing progestogen intake should be considered**
  - **With** any concerns that the remnant cervical stump may contain residual endometrial tissue in women who experience cyclical bleeding with sequential HRT.

**Reference:** BMS tools for clinicians: Progestogens and endometrial protection. H Hamoda on behalf of the BMS medical advisory council. *Post Reproductive Health* 2022(28)1: 40-46

# HRT in women with endometriosis:

- CCT should be considered in women following hysterectomy for severe endometriosis
  - to prevent reactivation of residual disease and potentially prevent malignant transformation of residual deposits.
- Limited evidence to guide practice.

**Reference:** BMS tools for clinicians: Progestogens and endometrial protection. H Hamoda on behalf of the BMS medical advisory council. *Post Reproductive Health* 2022(28)1: 40-46



# HRT in women with endometrial ablation:

- Combined HRT regimens (SCT or CCT as appropriate] in women with endometrial ablation wishing to take HRT

**Reference:** BMS tools for clinicians: Progestogens and endometrial protection. H Hamoda on behalf of the BMS medical advisory council. *Post Reproductive Health* 2022(28)1: 40-46

Type	Brand	Oestrogen	Progestogen	Formulation	Bleed	RX*	Cost
Adjunctive progestogen	<a href="#">Climanor</a>		Medroxyprogesterone (5mg)	Tab		1	£3.27
	<a href="#">Mirena</a>		Levonorgestrel (20mcg/24hrs)	IUS		1	£1.69
	<a href="#">Utrogestan</a>		Progesterone (100mg, 200mg)	Caps		1	£4.28, £4.10

**Noriday POP 350mcg**

(i) 3 daily = 1050 mcg / Norethisterone 1 mg effective for endometrial protection

(ii) FRS guidelines > SCT HRT with POP [eg Noriday 350mcg daily] = HRT plus contraception

**Mirena IUS** – licensed for menorrhagia, contraception and the progestogen component of HRT

**Utrogestan** – natural progesterone / SPC queries

Type	Brand	Oestrogen	Progestogen	Formulation	Bleed	RX*	Cost
<b>LOCAL</b>							
<b>Oestrogen only</b>	<a href="#">Blissel</a>	Estriol (50mcg)		Vaginal gel		1	
	<a href="#">Estring</a>	Estradiol (7.5mcg)		Vaginal ring		1	
	<a href="#">Generic prep</a>	Estriol (0.01%)		Vaginal cream		1	
	<a href="#">Imvaggis</a>	Estriol (30mcg)		Pessary		1	
	<a href="#">Ovestin Cream</a>	Estriol (1mg)		Vaginal cream		1	
	<a href="#">Vagifem</a>	Estradiol (10mcg)		Vaginal tabs		1	
<b>Non-oestrogen</b>	<a href="#">Intrarosa</a>	Prasterone (6.5mg)		Pessary		1	15.94

**Prasterone** pessary - licensed for vulvar and vaginal atrophy

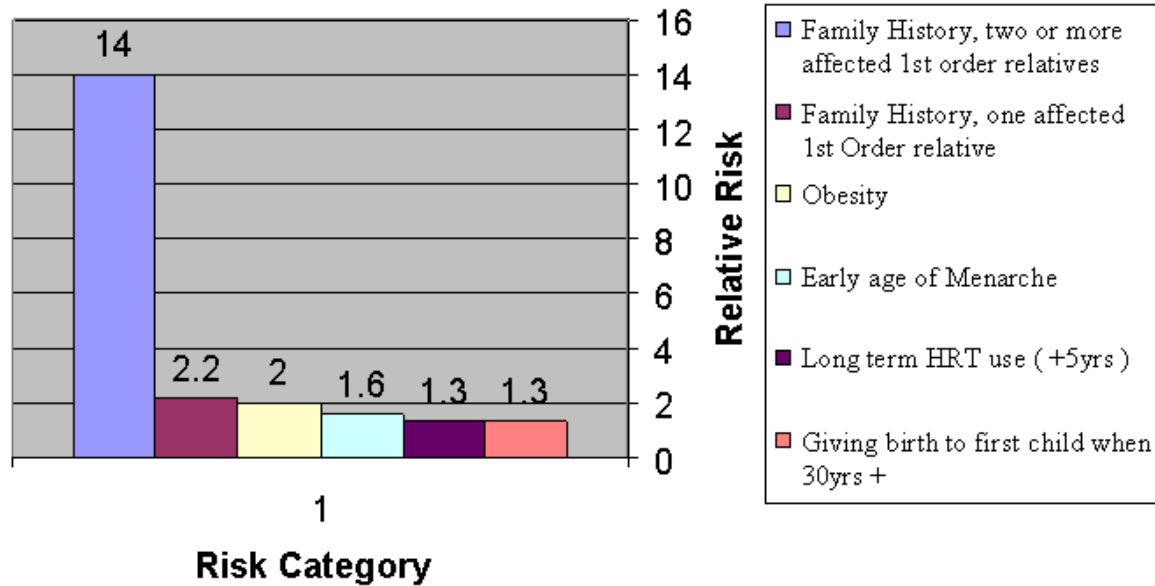
- biochemically and biologically identical to endogenous DHEA [dehydroepiandrosterone]
- converted to oestrogens and androgens....

# Prescribing and Supply Issues

- **Serious Shortage Protocols** [Feb 2019 - 2023] > .....> **Community Pharmacy** [nhsbsa.nhs.uk]
- **Oestrogen<sub>Rx</sub> Plus Utrogestan<sub>Rx</sub> .....**
- **Transdermal estrogen**
  - Thrombosis risk lower
  - NICE NG23 > with BMI over 30 or some thrombosis risk element ...
- **Natural progesterone**
  - Maybe more breast safe [IMS; BMS guidance]
    - Background ageing related breast cancer risk
      - NHS mammography screening program plus advise self breast exams
      - FH / genetic risk eg with young women with BRCA gene mutation
      - Bleed control issues?
- **Patients need to know**
  1. With use of HRT there is increased exposure to female hormones
  2. We can consider safer options with an individualised risk benefit evaluation
  3. Holistic management plan very important [exercise; weight control; diet; stress relief ....]

Review Fig 4

### Canadian Consensus on HRT



**Relative risks of breast cancer placed in perspective:** The greatest single risk factor, after sex and advancing age, is the presence of two or more affected first-order relatives. Several commonly experienced risks include being 20% overweight, delaying childbirth until 30 or older, consuming three glasses of alcohol daily, and lack of regular exercise. Long-term use of combined continuous HRT is of comparable magnitude to this group of risk factors. Risks do not appear to be additive. In the WHI, the Gael model for computing and predicting risk of breast cancer did not identify women who were at higher risk for a diagnosis of invasive breast cancer.

- The SOGC Statement on the WHI Report on
- Estrogen & Progestin Use in Post Menopausal Women
  
- Oct 2002 Volume 24 Number 10 JOGC

# Clinical practice paper

Kennedy B et al. Post Reproductive Health 2023;29(3):143-147

- FAQs
  - **Testosterone prescribing [NICE NG23 off-label prescribing]**
    - **Clinician Tool – BMS website**
    - **PIL – Women’s Health Concern Website**
  - HRT post-breast cancer diagnosis
  - HRT with FH of breast cancer or cardiovascular risk
  - HRT and Migraine
  - Perimenopausal contraception
  - **Oestradiol approximate equivalent doses**
    - **BMS website; NHSE Menopause side effects section**
  - HRT and gall bladder disease / and epilepsy
  - Local vaginal oestrogen options
  - Premature Ovarian Insufficiency POI

# Utrogestan<sup>Rx</sup> case study

## Summary Product Characteristics

- **License:** For adjunctive use with estrogen in post-menopausal women with intact uterus, as HRT regimen
  - Postmenopausal: 6 months bleed free
- Gestagenic, antiestrogenic, slightly anti-androgenic, anti-aldosterone effects
- Elimination half-life 16.8+/- 2.3 hrs; higher systemic levels if taken with food; Cause drowsiness and dizziness
  - > Take at bedtime, not with food
- Dosage recommendation
  - 200mg at bedtime daily D15-D26 of cycle, bleed expected following week
    - If breakthrough bleed persists [after settling in period of few months]
      - 100mg at bedtime D1-D25, withdrawal bleed less

# Utrogestan<sup>Rx</sup> case study

## Best practice

- Perimenopausal
  - Daily Estradiol with Utrogestan 200mg D15-26 of each cycle
  - .....or with Utrogestan 100mg D1- D25 of cycle?
- Postmenopausal
  - LNMP of 1 year ; atrophic static endometrium
    - Daily Estradiol with Utrogestan 100mg daily at bedtime
      - Qs
        - Should we advise Utrogestan 200mg for endometrial protection with higher estradiol dose
        - For h/o menorrhagia – should we advise change to C19 progestogens options / Mirena IUS?
        - Dealing with patient requests for bio-identical hormones [Use BMS consensus leaflet]; wanting same combination being used by a well-known journalist; etc....





Acknowledgement:

My thanks to Miss Joan Pitkin,  
Consultant Gynaecologist and Lead  
for the Menopause Service at  
LNWH [now retired ....]

For

- Academic clinical supervisor
- Superb mentorship whilst we were developing the Menopause MMC service

# Practical HRT Prescribing

- Questions?

- Thank you!

**Dr Nuttan Tanna**

[nuttantanna@nhs.net](mailto:nuttantanna@nhs.net)

# Case study 1

**31 year old patient with LNMP of 2 years; since starting menarche always had infrequent cycling. Has had investigations and had been diagnosed with premature ovarian failure.**

For discussion:

- Undertake HRT risk benefit evaluation for this patient and describe your management plan
- What HRT regimens would you recommend to this patient
- List lifestyle interventions for patient

# Case study 2

**51 year old patient with vasomotor symptoms and erratic bleeding profile. DEXA reports osteopenia at spine site (T score -2.1)**

For discussion:

- Undertake HRT risk benefit evaluation for this patient and describe your management plan
- What HRT regimens would you recommend to this patient
- List lifestyle interventions for patient

# Clinical risk factors for fragility fracture

The image shows a screenshot of the FRAX WHO Fracture Risk Assessment Tool. The page has a red header with the FRAX logo and the text 'WHO Fracture Risk Assessment Tool'. Below the header is a navigation bar with links for 'Home', 'Calculation Tool', 'Paper Charts', 'FAQ', and 'Ref'. The main content area is titled 'Calculation Tool' and contains a questionnaire for calculating the ten-year probability of fracture with BMD. The questionnaire includes fields for age, sex, weight, height, and various clinical risk factors. A summary box on the right displays the BMI (19.5) and the ten-year probability of fracture without BMD for major osteoporotic (11%) and hip (2.9%) fractures. A 'View NOGG Guidance' button is also present.

Country: UK Name/ID:  [About the risk factors](#)

### Questionnaire:

- Age (between 40 and 90 years) or Date of Birth  
Age:  Date of Birth: Y:  M:  D:
- Sex  Male  Female
- Weight (kg)
- Height (cm)
- Previous Fracture  No  Yes
- Parent Fractured Hip  No  Yes
- Current Smoking  No  Yes
- Glucocorticoids  No  Yes
- Rheumatoid arthritis  No  Yes
- Secondary osteoporosis  No  Yes
- Alcohol 3 or more units/day  No  Yes
- Femoral neck BMD (g/cm<sup>2</sup>)  
Select BMD

**BMI: 19.5**

The ten year probability of fracture (%)

without BMD

Major osteoporotic	11
Hip Fracture	2.9

# Another important Q.....or 2....

- How long can you carry on, on vaginal ERT?
  - GINA 10 mcg? - Product license
- What alternative prescribed options can you recommend for vasomotor symptom control?
  - Is there a non-pharmacological option for patients to consider that is evidence based? – NICE NG23 2015, to be updated 2024