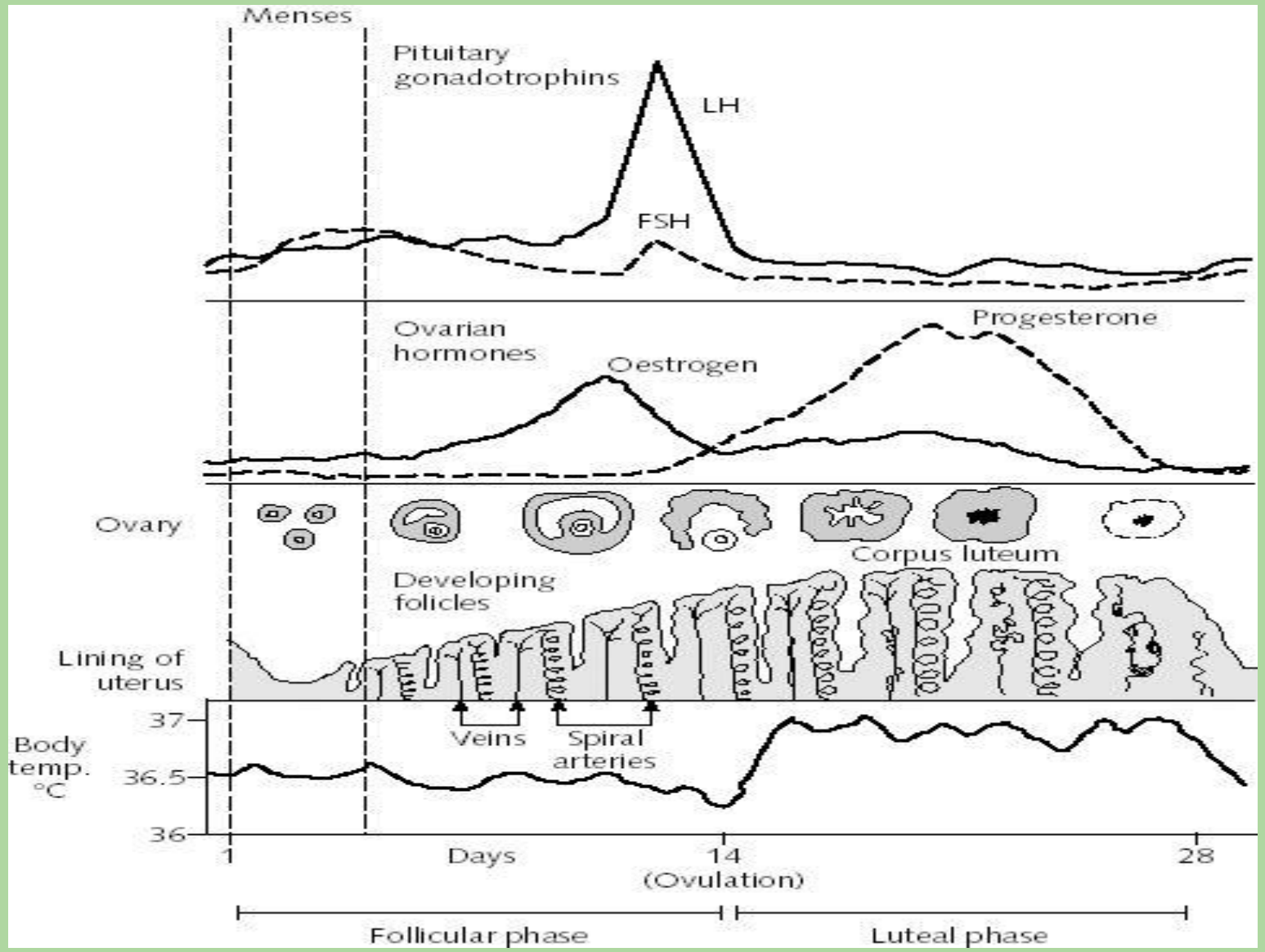
PMS / PMDD
The menstrual cycle and its effects on mental illness

[redacted]

Consultant in SRH, Tower Hamlets


Menses
Pituitary gonadotrophins
LH
FSH
Ovarian hormones
Oestrogen
Progesterone
Ovary
Corpus luteum
Developing folicles
Lining of uterus
Veins
Spiral arteries
Body temp. °C
37
36.5
36
1
Days
14
(Ovulation)
28
Follicular phase
Luteal phase

Diagnostic issues

- Catamenial disorders – similar to generally occurring disorders but timing entrained to the menstrual cycle
- Mental or physical disorders affected by the menstrual cycle
- One PMS or multiple? PMDD
- Vulnerability – trigger conceptualisation
- Attitudes to menstruation / womanhood
- Neurodiversity

Does it matter what we call it?

- Research criteria
- Treat by modulating the cycle and / or treat the symptom or underlying condition

PMS / PMDD

- symptoms occur in luteal phase and resolve in follicular phase. Must be clear for one week after menstruation
- Occur consistently for at least two cycles, on prospective charting
- Interfere with school, work or relationships

Symptoms – most common

- Depression
- Anxiety
- Iritability, anger
- Emotional lability
- Feeling out of control
- Food cravings
- Tiredness
- clumsiness

Physical symptoms

- Breast tenderness
- Bloating
- Headaches
- Joint pains
- (pelvic pain / ache)
- Almost anything!

What causes PMS?

- The menstrual cycle
- Some women more sensitive to ovarian hormone effects – end organ effect
- Effect on serotonin levels
- Individual vulnerability factors
- Not the whole story
- The place of neurodiversity in PMDD

Diagnosis

- Prospective charting
  - Daily symptom charts
  - Visual analogue scales
- Complete ovarian supression
  - Gonadotrophin releasing hormome agonists
- Psychological assessment to exclude underlying disorder

Management

- Explanation
- Lifestyle changes
- Counselling / psychotherapy
- Treat associated physical symptoms – menorrhagia, pelvic pain
- Hormonal manipulation
- SSRI

Lifestyle – symptom control

- Reduce caffeine
- Regular food intake
- Reduce alcohol
- Exercise
- Educate significant others
- Adapt commitments?
- Counselling / psychotherapy

hormonal

- Render anovulatory
  - GnRHA
  - Continuous combined pill (Yasmin / Zoely?)
  - Cerazette / drospironone
  - High dose HRT – usually IUS and transdermal oestrogen
  - ? Implanon

- ? Spironolactone / drospironone

Pschotropic therapies

- SSRIs
- most have been found to be effective
- Continuous or luteal phase only regimens

In summary and for discussion

- We need to talk about periods and cycles (apps)
- Think about contraception (and sex and STIs)
- Find a friendly gynaecologist

Morning Medical Update for Psychiatrists-ELFT

8.15am – 9am (Welcome refreshments and registration)

Costeloe Lecture Theatre, The Education Centre, Homerton University Hospital, Homerton Row, London E9 6SR

Time	Topic	Presenter
8.15-8.50:	Registration and coffee	
8.50-9.00	Welcome	[redacted] ELFT
9.00-10.00	**Menopause and an update on HRT.**	[redacted] Professor of Obstetrics and Gynaecology, Consultant in Obstetrics and Gynaecology, Unit Lead for Women's Health and Deputy Lead for the Centre of Public Health and Policy
10.15-11.15	**PMS, PMDD, diagnosis and management- The Menstrual Cycle and Its Effects on Mental Illness etc.**	[redacted] Consultant in SRH at Barts Health NHS Trust; President of the Faculty of Sexual and Reproductive Healthcare
11.15-11.45	Break	
11.45-12.45	**PCOS – Policy update on New NHS strategy and local C&H women's health update-**	[redacted] Consultant in Sexual and Reproductive Health and lead for women's health in City and Hackney, North East London. National Clinical Director for Women's Health for England
12.45-13.00	**Discussion**	All

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Menopause and an update on HRT

[redacted]

Professor of Obstetrics and Gynaecology QMUL

Research Lead Women's Health, Bart's Health

Diagnosis of menopause and peri-menopause

Average age of menopause is 51 y in the UK

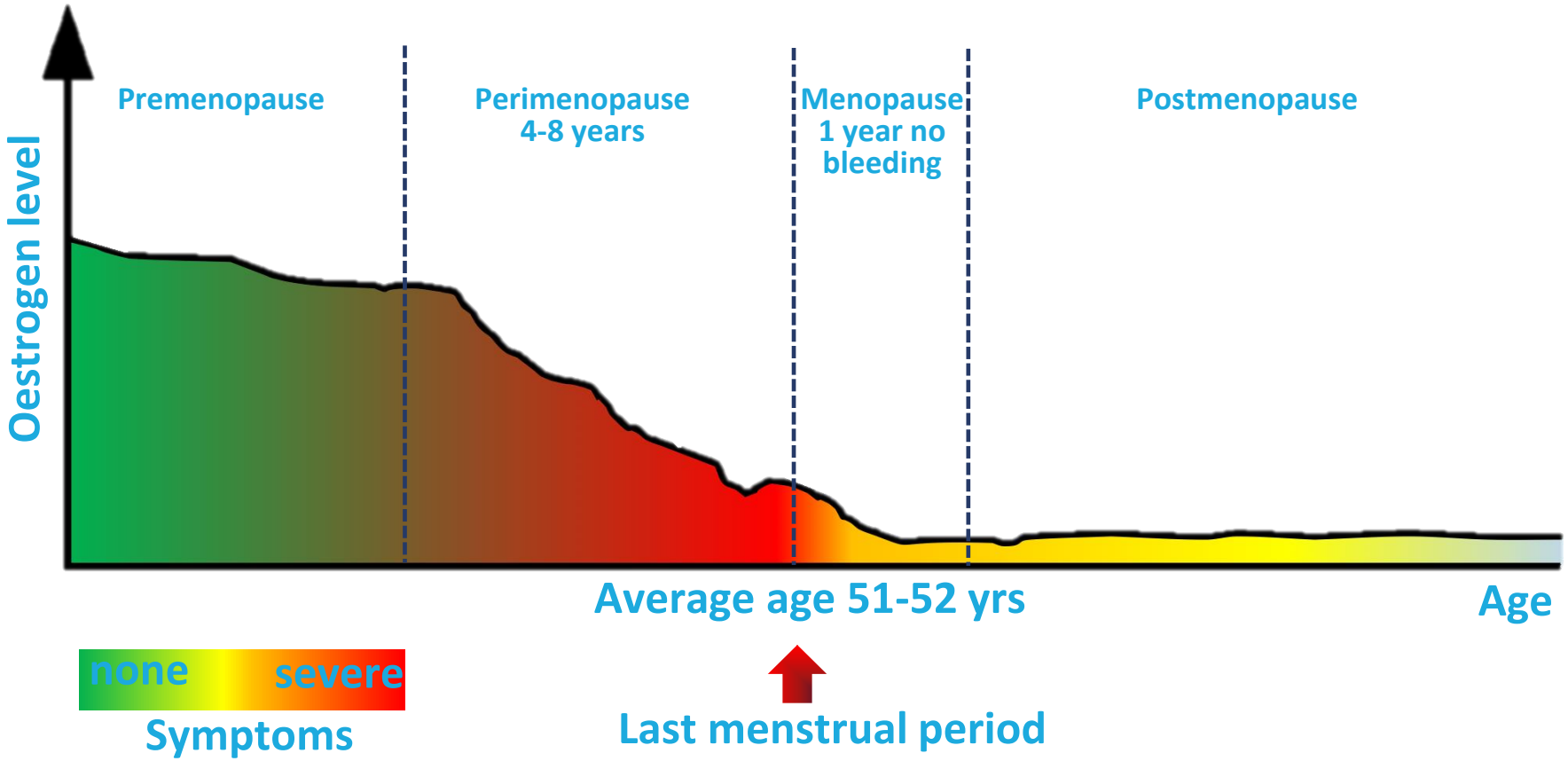
Over the age of 45

- Perimenopause: Irregular periods and vasomotor symptoms
- Menopause: No periods for 12 months
- No need for laboratory confirmation

Consider FSH (> 30 IU/L)

- > 45 years and atypical symptoms
- 40-45 and cycle irregularity +/- VMS
- < 40 years

Phases of the menopause



Diagnosis of Premature Ovarian Insufficiency (POI)

- < 40years with oligomenorrhoea or amenorrhea

- Consider medical and surgical history
- Consider family history

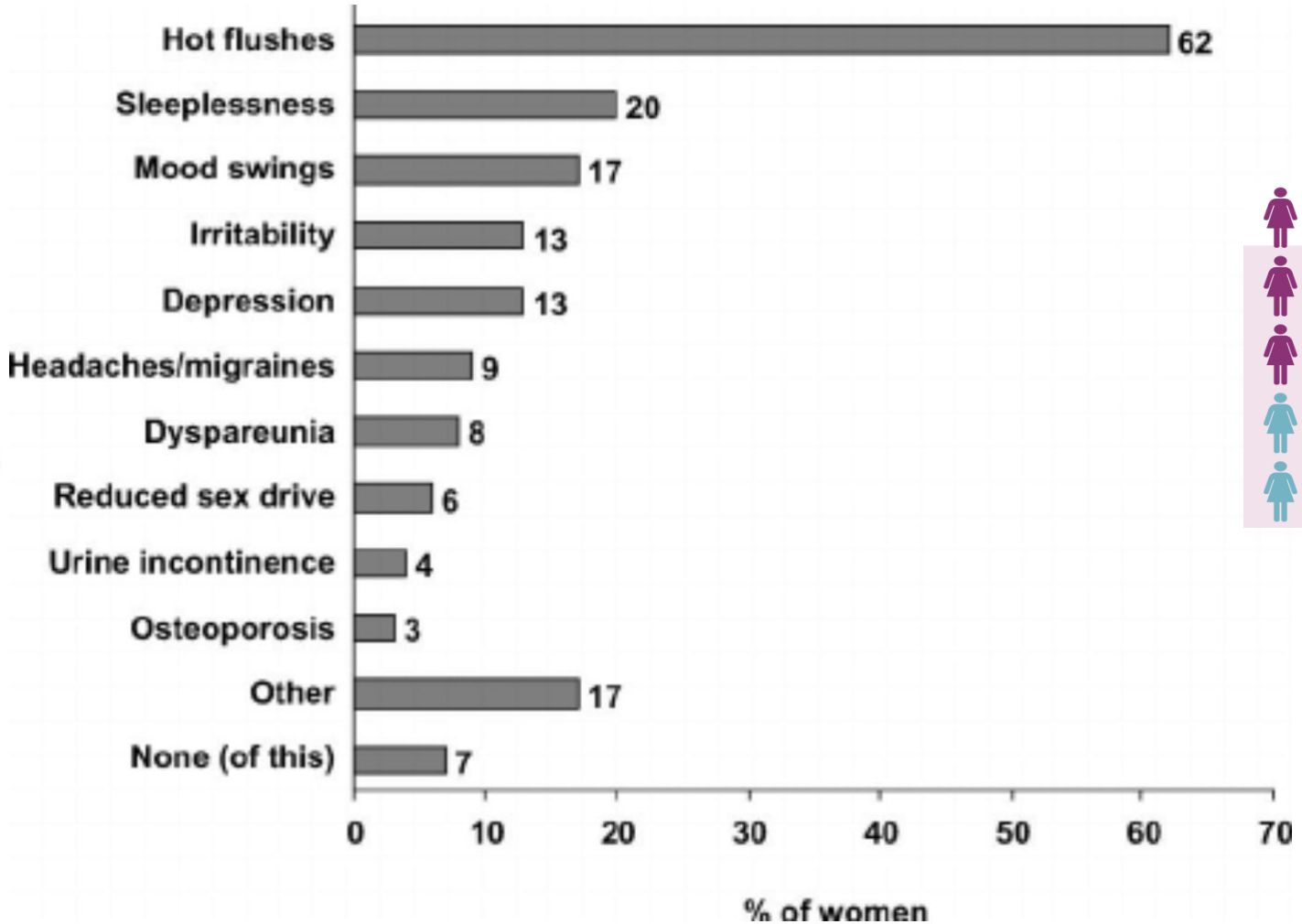
(best predictor maternal menopausal age)

- D2-D5 elevated FSH in two occasions (4-6 weeks apart)
- Exclude other causes (TSH, LH, prolactin, testosterone)
- AMH may have some value but not routinely indicated

Treatment of POI

- **Regardless of symptoms** treatment should be offered
- Increased risk of mortality (80% risk of MI and 50% of fractures- 65% osteopenia)
- Treatment as COCP or HRT
- **No greater risk** of breast cancer until the average age of menopause
- Benefits outweigh any risks until the average age of menopause

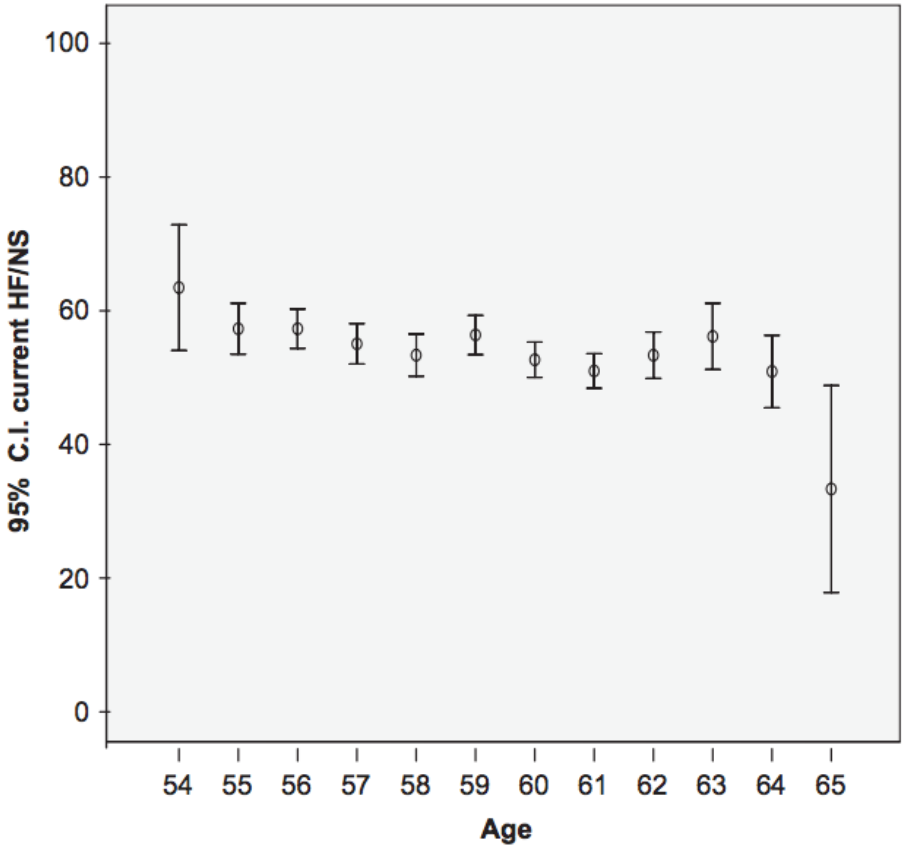
Menopausal Symptoms- Only 1 in 2 women seek treatment



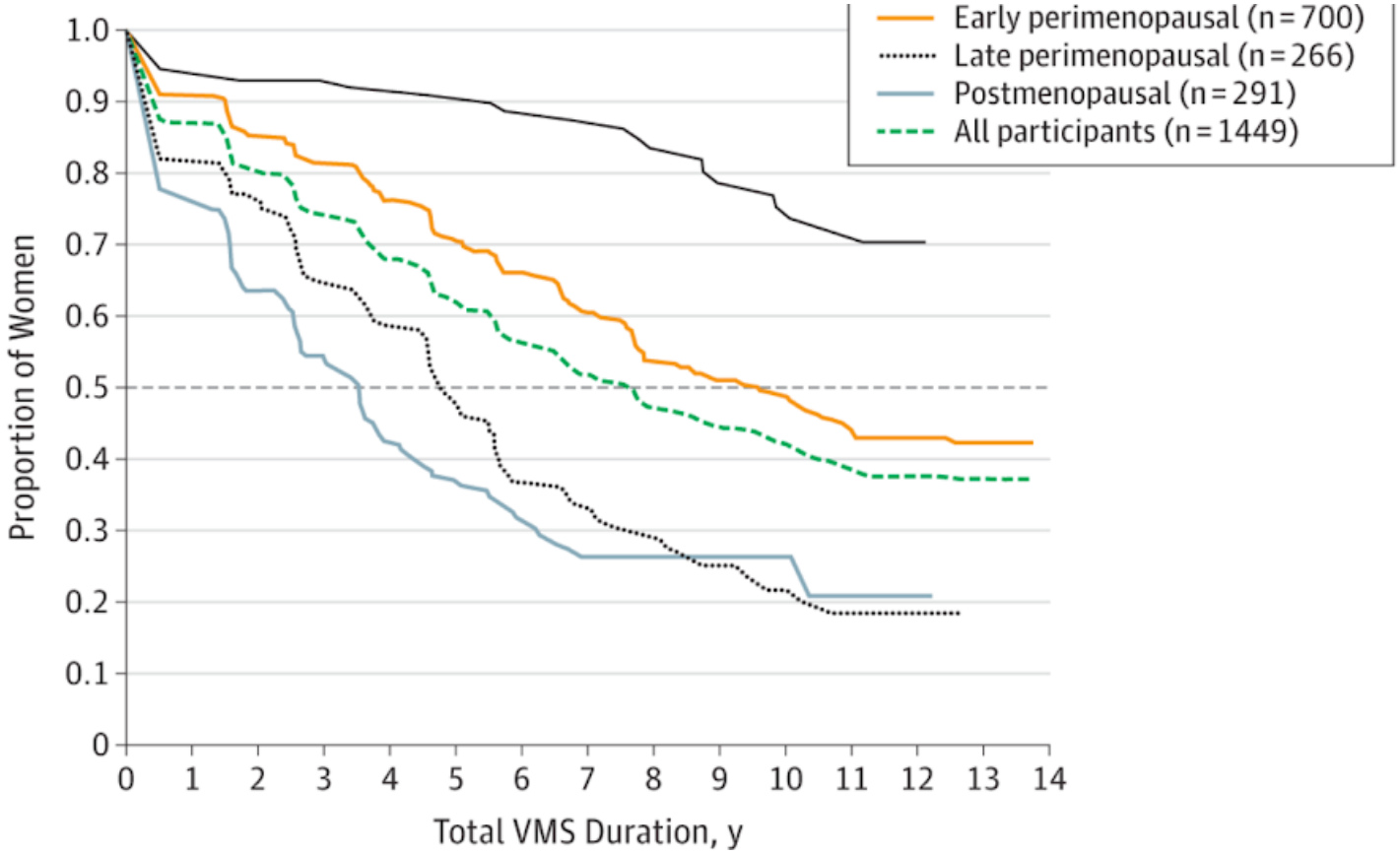
Genanazzani et al, Gyn Endocrinology 2006

Hot flushes affect 70% of women and can last for over 11 years

Prevalence of Hot flushes



Duration of Hot flushes



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Hunter et al, BJOG 2012
Avis et al, JAMA Intern Med 2015

Menopause and mental health

- Menopausal symptoms/ scales include mental wellbeing symptoms
- Anecdotal data suggest that mental health is impaired during menopausal transition and can be related with E2 fluctuation
- Contributing factors i.e. sleep disturbances/ VMS/ life role changes/ relationship challenges/ carer and career responsibilities coincide
- Anecdotal data suggest that HRT may stabilize E2 and improve mental health symptoms

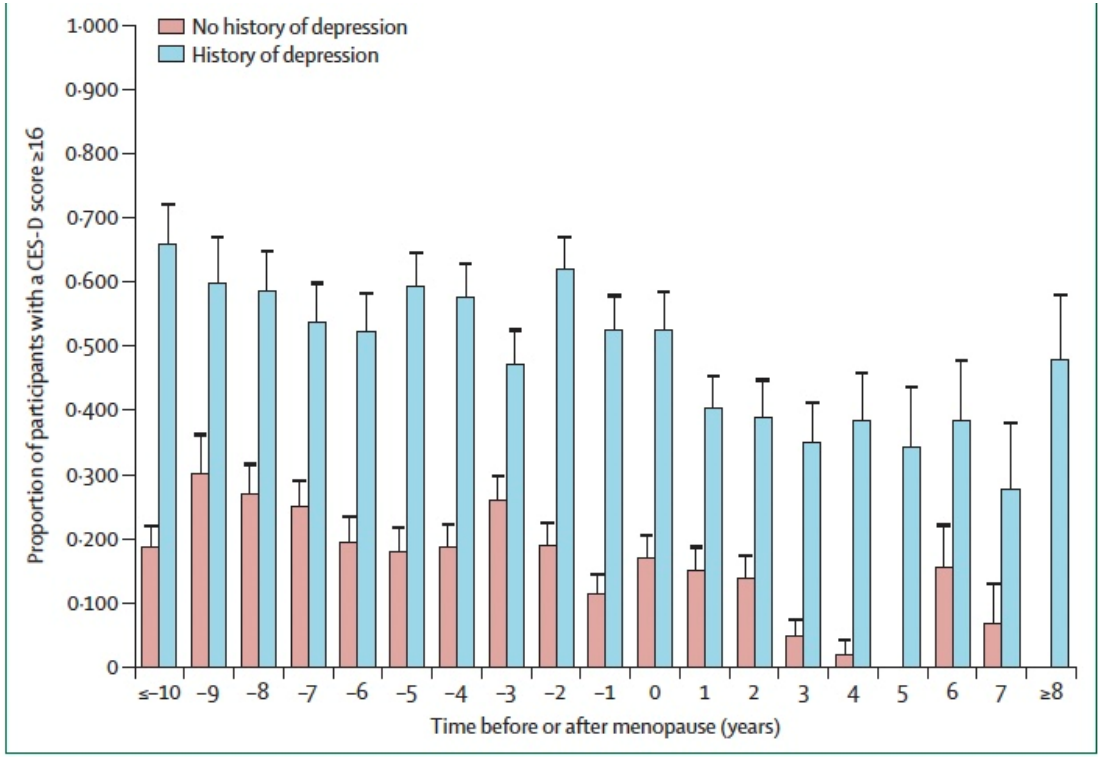
Menopause increases risk of Major depressive disorder recurrence

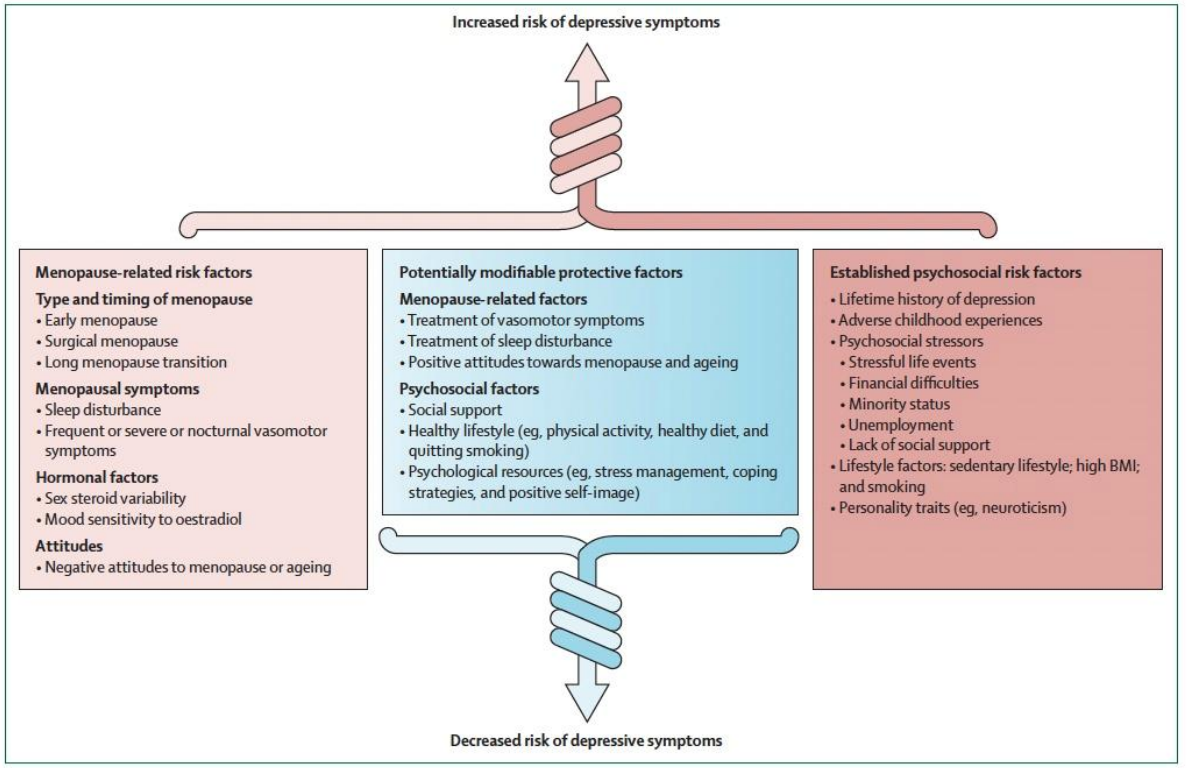
- Affects 6% globally the population
- x2 higher risk for women- unclear why sex difference

- Perimenopause increased the risk of MDD recurrence x2
- Menopause increased the risk of MDD recurrence x4
- No association when no previous history of MDD
- Contributing factors were concurrent physical and emotional conditions rather E2 levels

Bromberger JT et al. Psychol Med 2015; 45: 1653–64

Menopause and Depressive Symptoms





Freeman EW et al, JAMA Psychiatry 2014; 71: 36–43

Menopause and other mental health conditions

- Anxiety

Symptoms of anxiety may coincide with menopause symptoms i.e racing heart rate, sweating, rapid breathing

Conflicting findings- SWAN suggested increase in anxiety scores after controlling for menopausal symptoms

Women with anxiety more likely to experience VMS

- Bipolar disorders: no prospective studies
- Schizophrenia spectrum

Small increase of first psychosis event > 45 years

Small increase of hospitalization for psychosis in women > 45 years

Brown L et al, Lancet 2024

Menopause and other mental health conditions

- Suicidality

Middle aged men at higher risk of suicide than women

Cross-sectional study 7% (menopause) vs 5% (premenopause) of suicidal ideation

- ADHD

Limited research

N=36 peri/post menopause ADHD higher self reported climacteric scores

Increased rates of menopausal forgetfulness/ brain fog

May need increase on their regular medications (Atomoxetine (a SNRI), Dexamphetamines and Lisdexamfetamine)

HRT mainly for VMS

Dorani F et al, J Psychiatr Res 2021 Jan:133:10-15

HRT and mental health conditions

- HRT not an approved first line treatment for MDD or depressive symptoms during menopausal transition

- Small RCT's with conflicting results:

2 RCTs (n=84) transdermal E2 superior to placebo 3 and 12 weeks

2 RCTs (n=138) no improvement of MDD

- Improvement of depressive symptoms if concurrent VMS

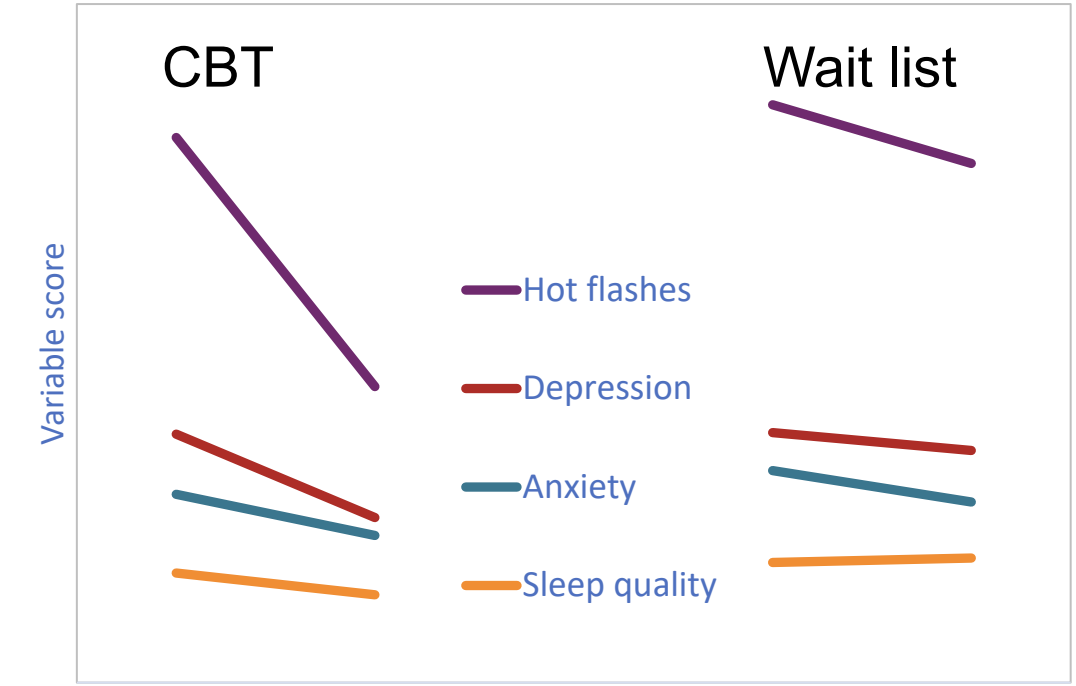
Schimdt PJ et al Am J Obstet Gynecol 2000; 183: 414–20.
Soares et al Arch Gen Psychiatry 2001; 58: 529–34
Schimdt PJ et al Menopause 2021; 28: 369–83
Joffe H et al Clin Endocrinol Metab 2011; 96: E1044–54

Management: *lifestyle*

- Regular exercise at least 30 minutes of moderate-intense exercise at least 5 times weekly
- Weight reduction
- Avoid hot drinks, caffeine, alcohol and spicy food
- Smoking cessation
- Layer clothing
- Stress management techniques

Climacteric 2007:10:181-94

Cognitive Behavioural Therapy



https://www.womens-health-concern.org/

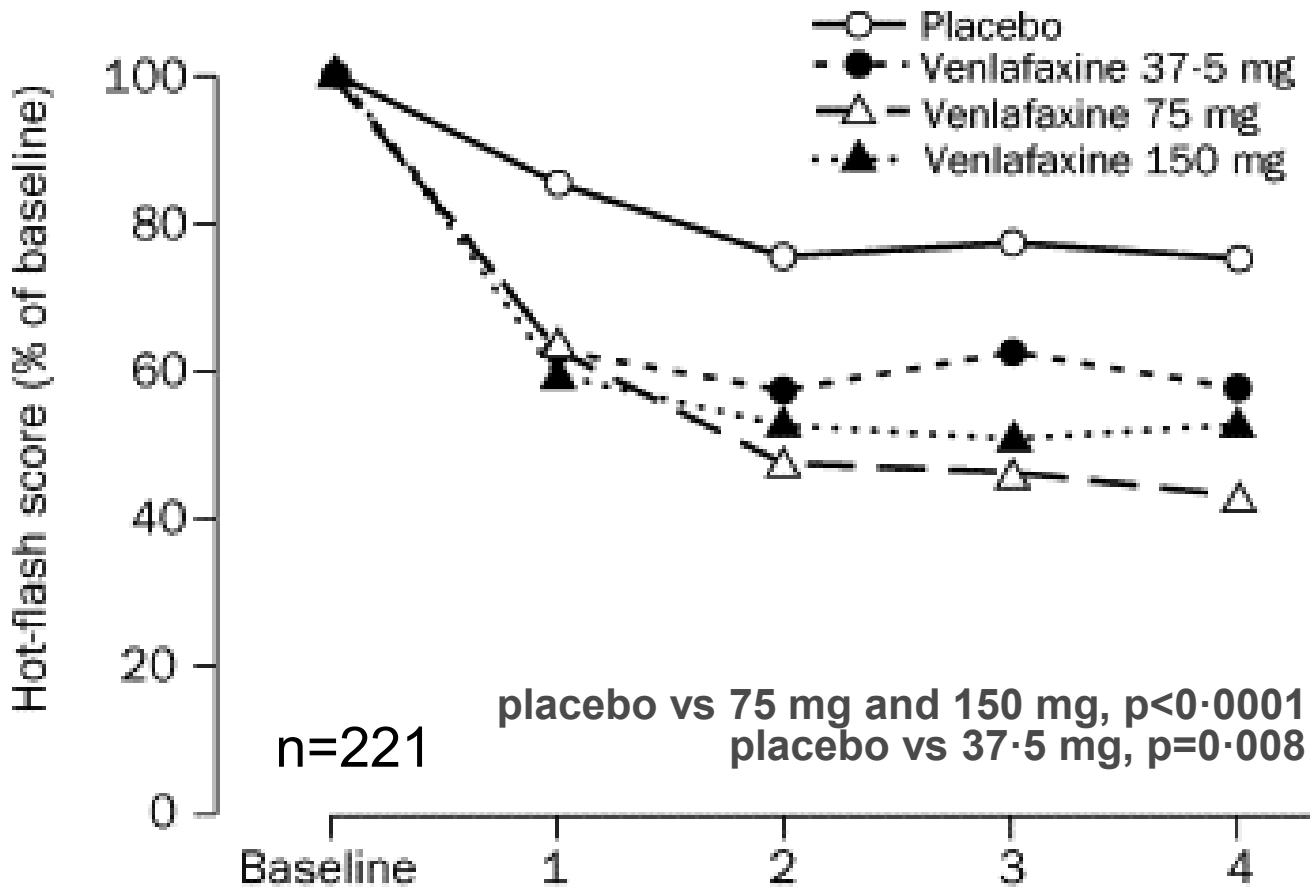
Green SM et al. Menopause 2019;26:972-80

Management: *prescription non-hormonal*

- Licensed
  - Clonidine
  - *SEs insomnia, dry mouth, dizziness, constipation, drowsiness*

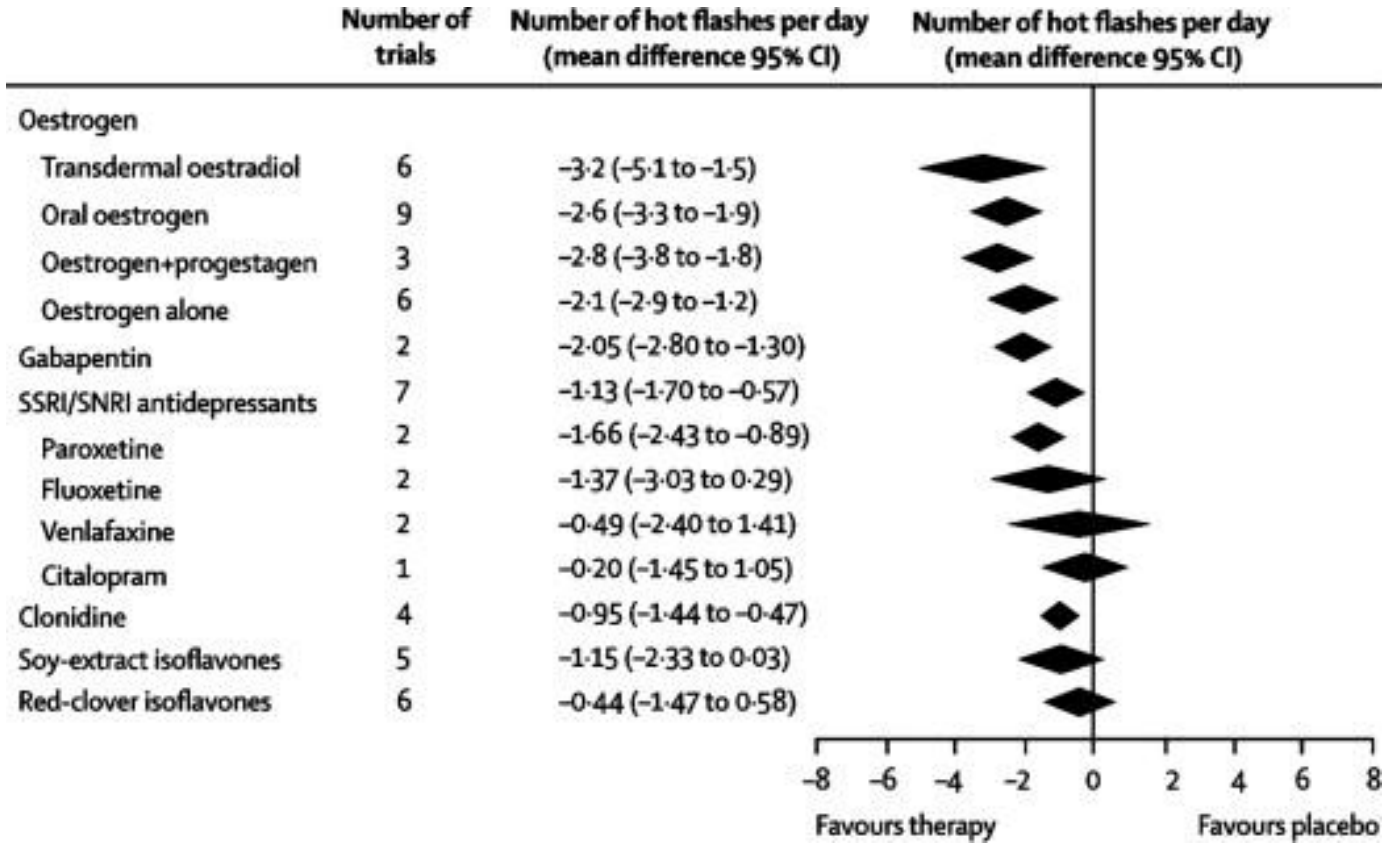
- Unlicensed
  - SSRIs/SNRI (venlafaxine)
  - Gabapentin
    - *SEs dizziness, fatigue, tremor, weight gain*

SSRIs / SNRIs



Loprinzi CL et al *Lancet* 2000;356:2059-63

HRT: the most effective treatment against VMS



Takahashi et al, Medical Clinics 2015

What is Hormone Replacement Therapy (HRT)

- Oestrogen
- Progestogen – either a synthetic version of the hormone progesterone, or a version called micronised progesterone (sometimes called body identical, or natural)

- Combined HRT- cyclical (peri-menopause/ within a year) or continuous
- Oestrogen only- when hysterectomy

- Tibolone
- “Compounded” bioidentical

Progestogen

- Oral
  - Synthetic progestogens (combined with E2)
    - dydrogesterone
    - levonorgestrel
    - medroxyprogesterone acetate
    - norethisterone
  - Micronised progesterone
- Transdermal
  - Synthetic progestogens (combined with E2)
- Intravaginal
  - Micronised progesterone
- Intrauterine
  - Levonorgestrel (contraceptive)

HRT regimes

Barts Health NHS Trust

Hysterectomy

Continuous estrogen

Perimenopause

Continuous estrogen + cyclical progestogen (monthly bleed)

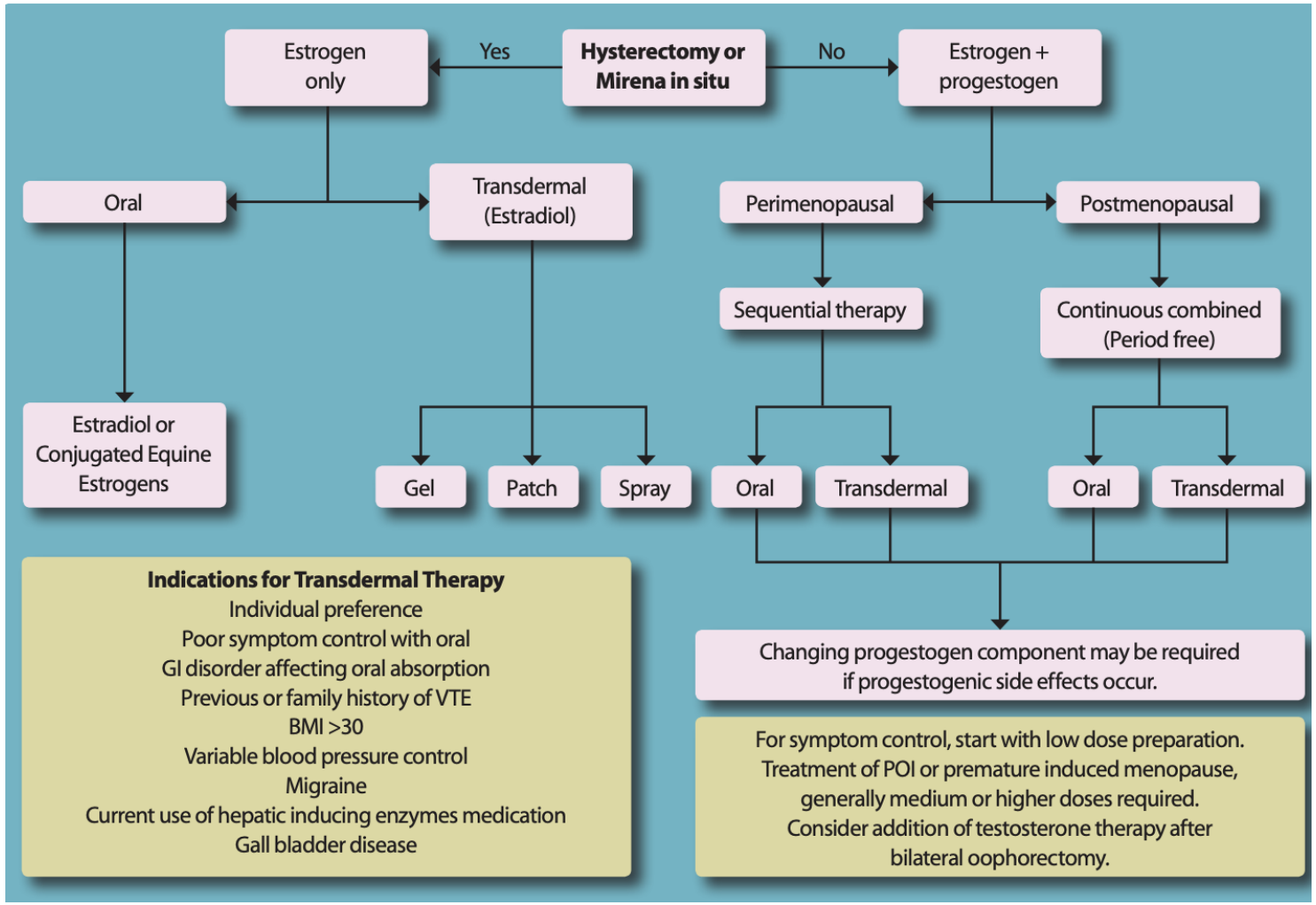
Postmenopause

Continuous estrogen + continuous progestogen (period-free)

Types of HRT

- Individualized approach
- Transdermal lower risk of blood clots

Transdermal route is preferred



- Review 3 months after initiation of treatment
- Increase dose or change preparation
- Thereafter yearly and age risk assessment
- If POI continue until at least the age of 51 years
- No absolute age to terminate HRT but discuss risks especially over the age of 60

Myth: Natural alternatives or bio-identical are safer

- Less research on natural alternatives/ bio-identical
- Interaction with other medications eg anticoagulants which is less known
- Not appropriate absorption
- Individualized approach with healthier lifestyle, weight loss, exercising (strength) and less alcohol and processed food diet

HRT CAN DOUBLE RISK OF BREAST CANCER

WOMEN today face a stark warning over links between HRT and breast cancer.

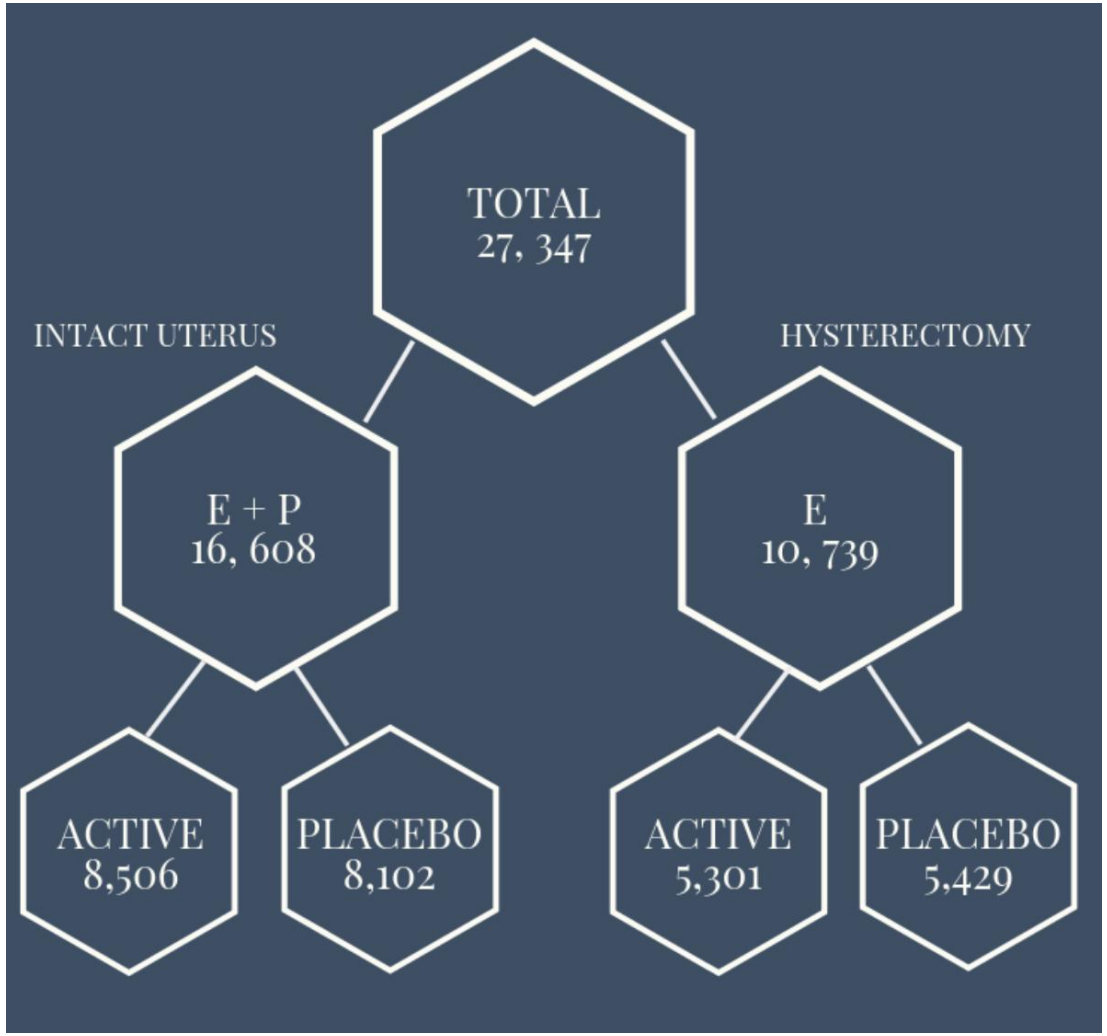
A massive British study of a million women found the risk of cancer can be twice as high for those taking the most common form of HRT for ten years.

By **Beezy Marsh**
Health Correspondent

Government experts are now issuing an alert to GPs and hospitals over the treatment, which is being blamed for 20,000 cancer cases in the past ten years. HRT, taken by 1.7million women in Britain to relieve symptoms of the menopause, was already at the centre of growing concern over cancer, heart disease and strokes.

The new study, published in the Lancet today, provides conclusive

Turn to Page 4, Col. 1



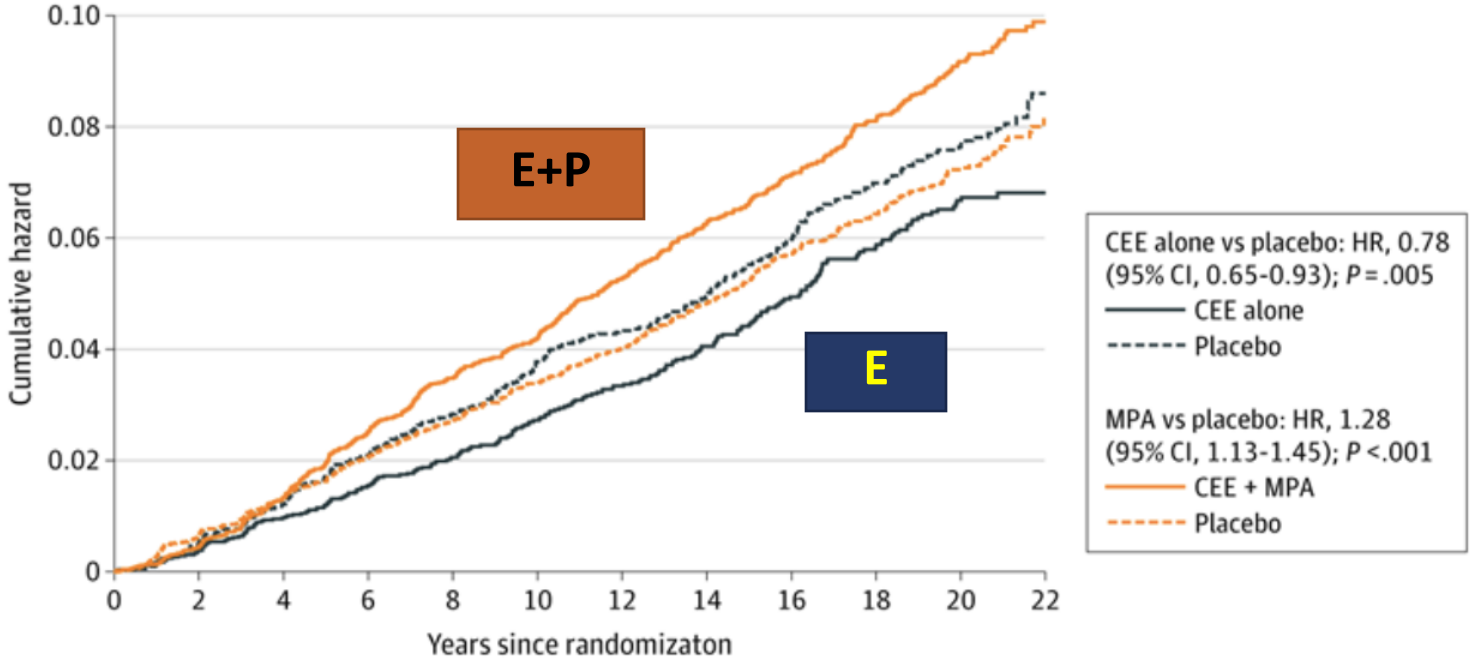
HRT: does not increase breast cancer mortality

		E + P			E-alone		
	Expected effect	HR	95% CI	AR	HR	95% CI	AR
Breast	↑	**1.24**	**1.02–1.50**	**8**	**0.8**	**0.62–1.04**	**−6**
Colorectal	↓	**0.56**	**0.38–0.81**	**−7**	**1.08**	**0.75–1.55**	**1**
Endometrial Cancer		**0.81**	**0.48–1.36**	**−1**	**NA**		

- Possible small risk of Brest Ca over the age of 50 years when combined
- No greater risk of Breast cancer mortality
- Risk is regressed to background after 5 years

Prentice and Anderson, 2008. Ann Rev Publ Health 29:131-50.

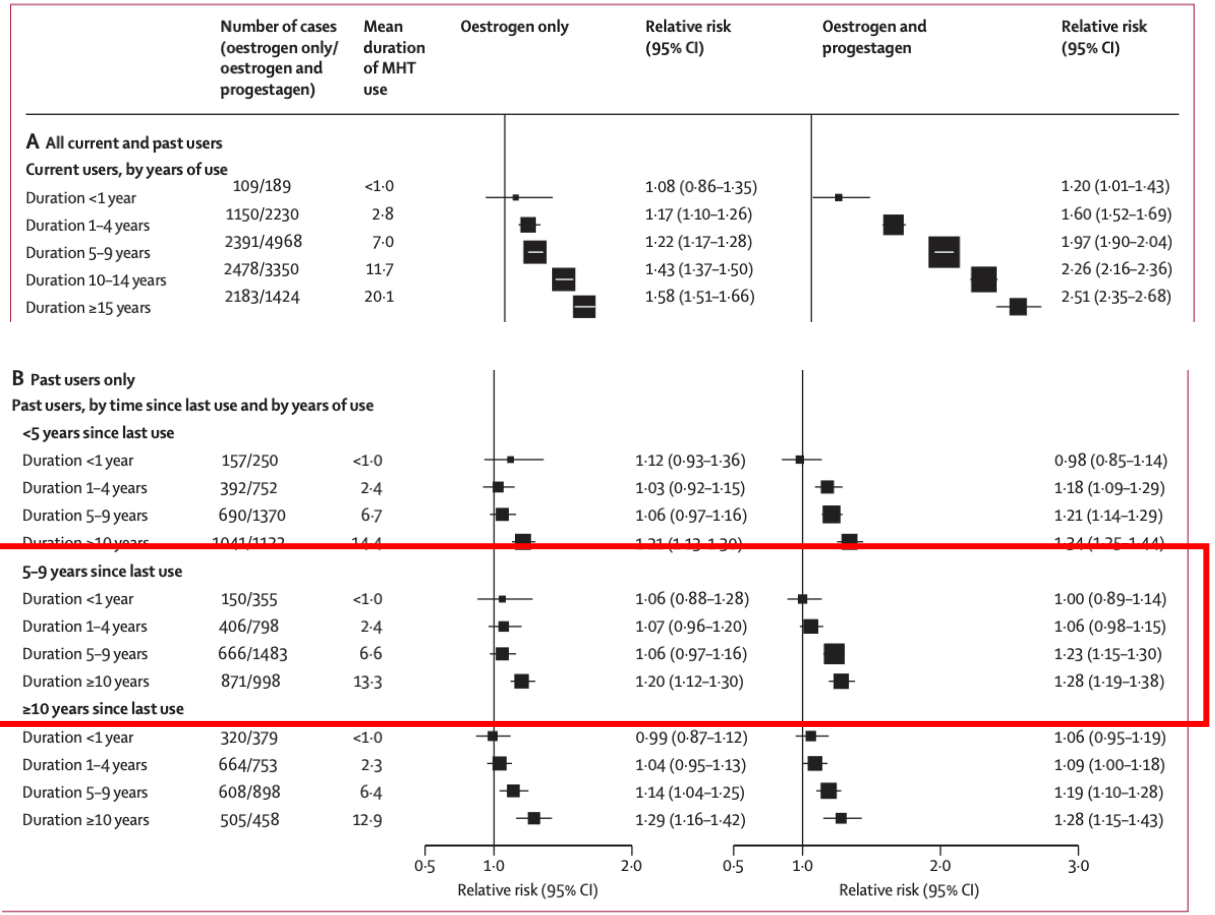
Oestrogen only HRT reduces breast cancer risk up to 10y after discontinuation

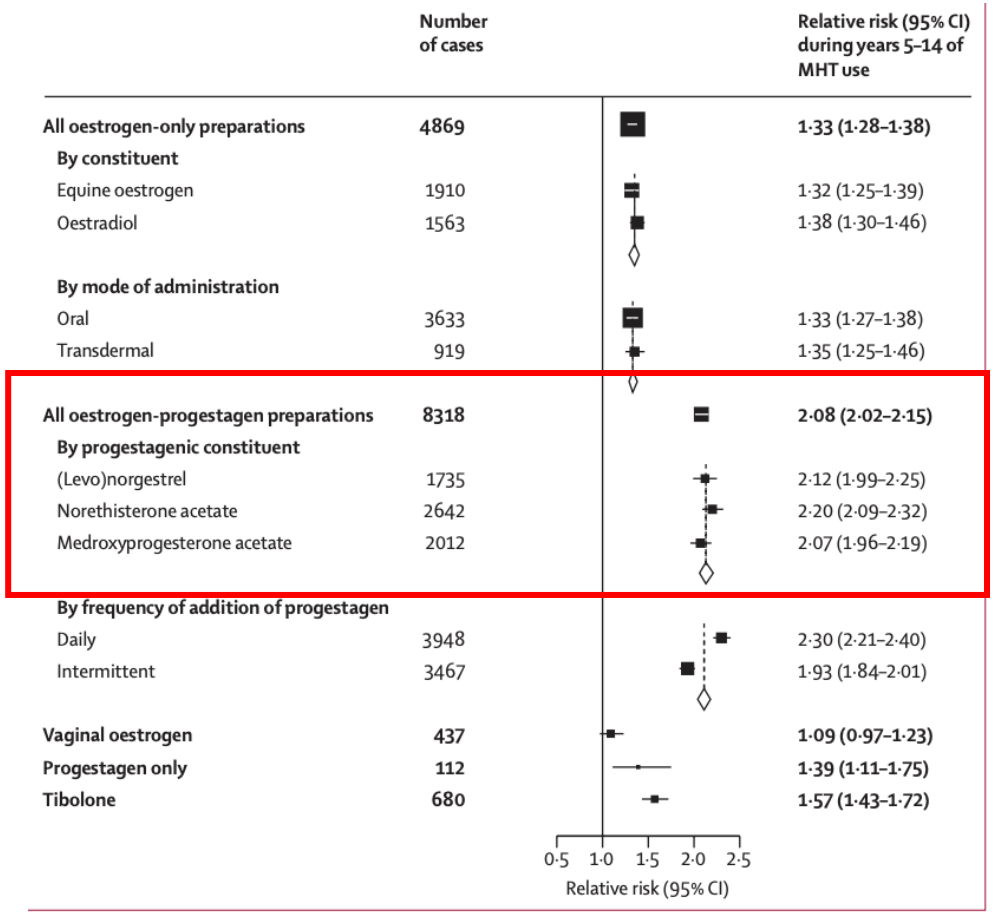


- Women on CEE group (oestrogen only) reduced risk of breast Ca morbidity and mortality vs placebo
- Women on CEE+ MPA greater risk of breast Ca but NOT mortality vs placebo
- Risk was greater > 6 years of use

Clebwoski et al, 2020. JAMA 324(4):369-380

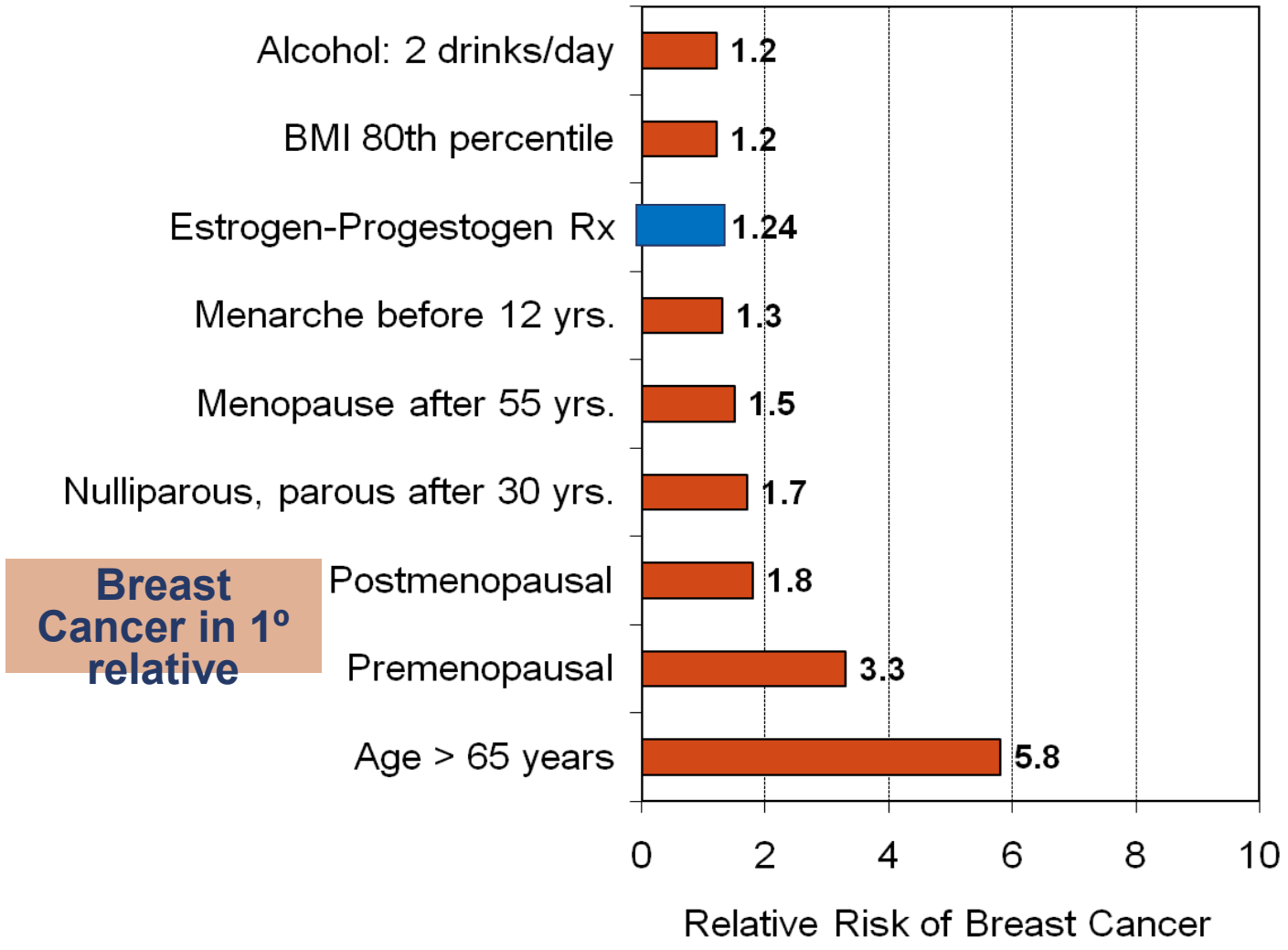
Observational data are conflicting but to be presented into context

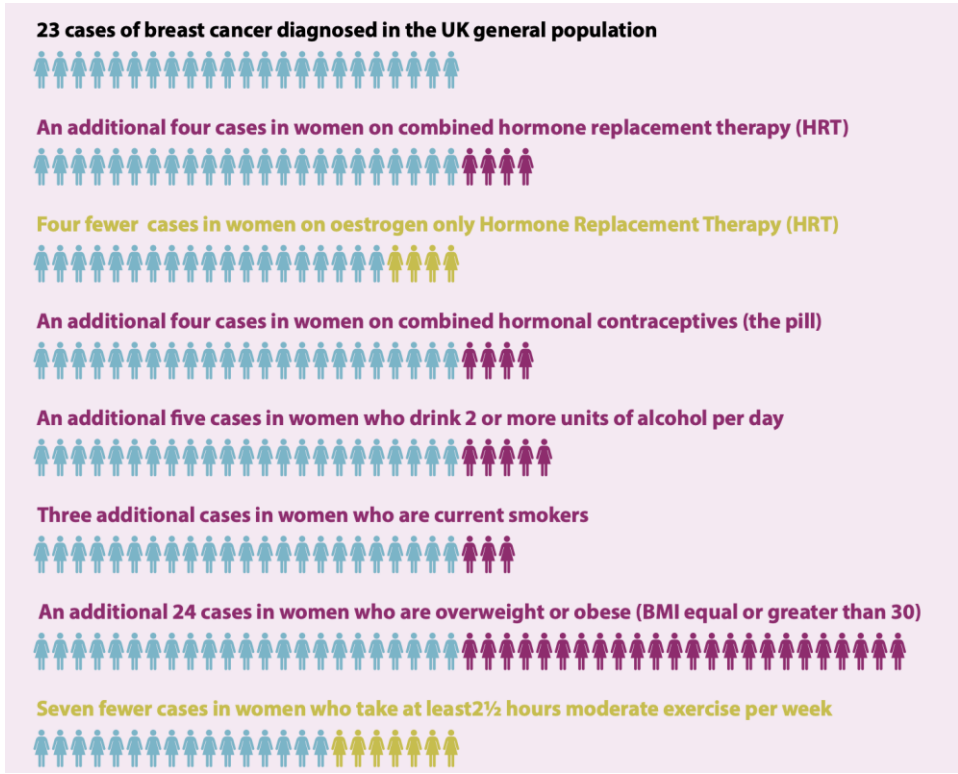




Collaborative Group on Hormonal Factors in Breast Cancer 2019. Lancet 394: 1159–68

5 year HRT is safer than drinking 2 units/ day or being obese





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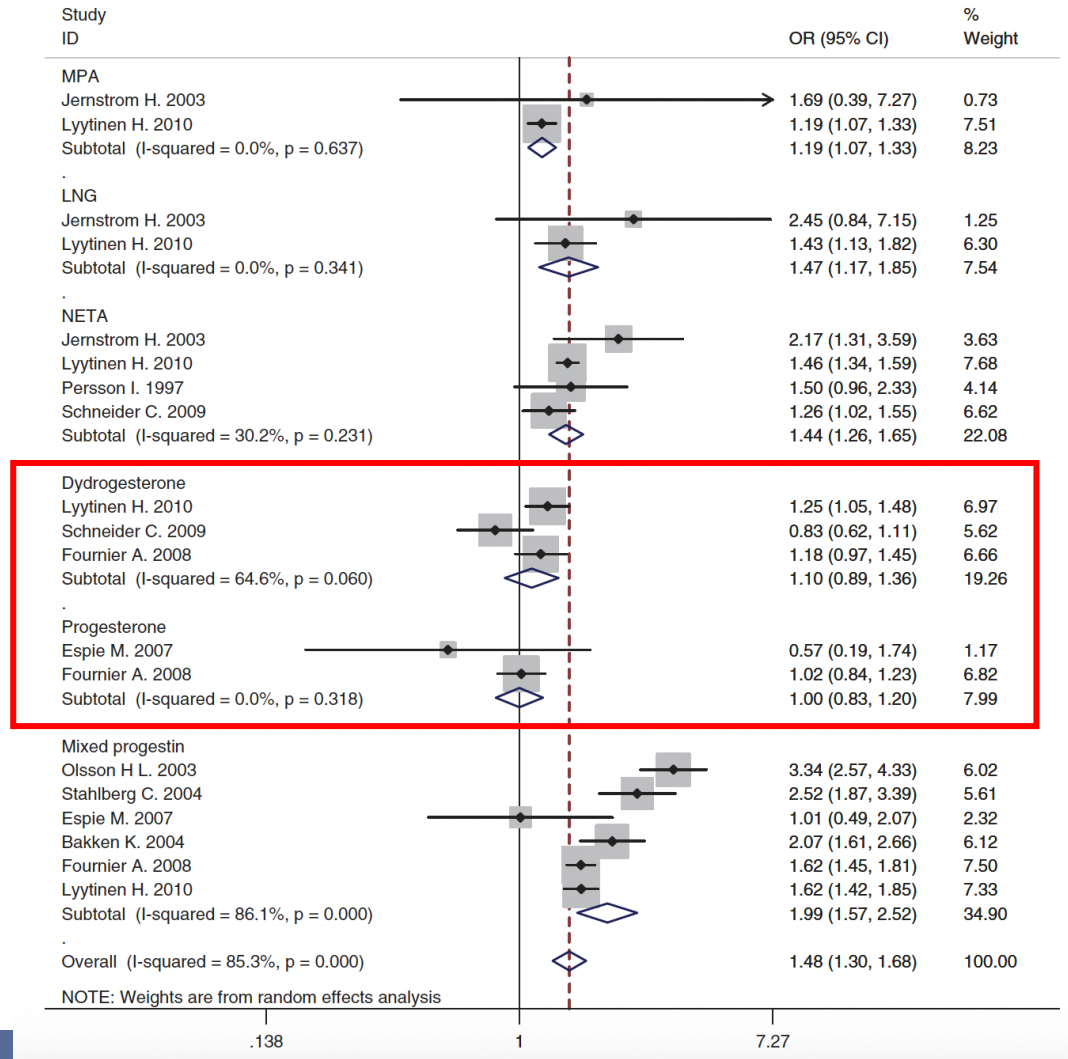
Singletary SE (2003). Annals of Surgery, 237:474-482.

Microionised progestogens seems to be the safest option

Time since last use	Estrogen-only	Estrogen + progesterone/dydrogesterone	Estrogen + other progestagen[a]
Current use			
Hazard ratio (95 % CI)[b]	1.17 (0.99–1.38)	1.22 (1.11–1.35)	1.87 (1.71–2.04)
No. of cases	169	638	931
Mean duration of use[c]	5.1	6.1	6.1
Past use			
Hazard ratio (95 % CI)[b]	1.06 (0.95–1.19)	0.96 (0.87–1.06)	1.12 (1.02–1.23)
No. of cases	374	552	708
Mean duration of use[c]	2.2	3.5	3.9
Mean time since last use[c]	7.8	5.9	5.9

Fournier et al 2014, Breast Cancer Res Treat. 145(2):535-43

Microionised progestogens seem to be the safest option



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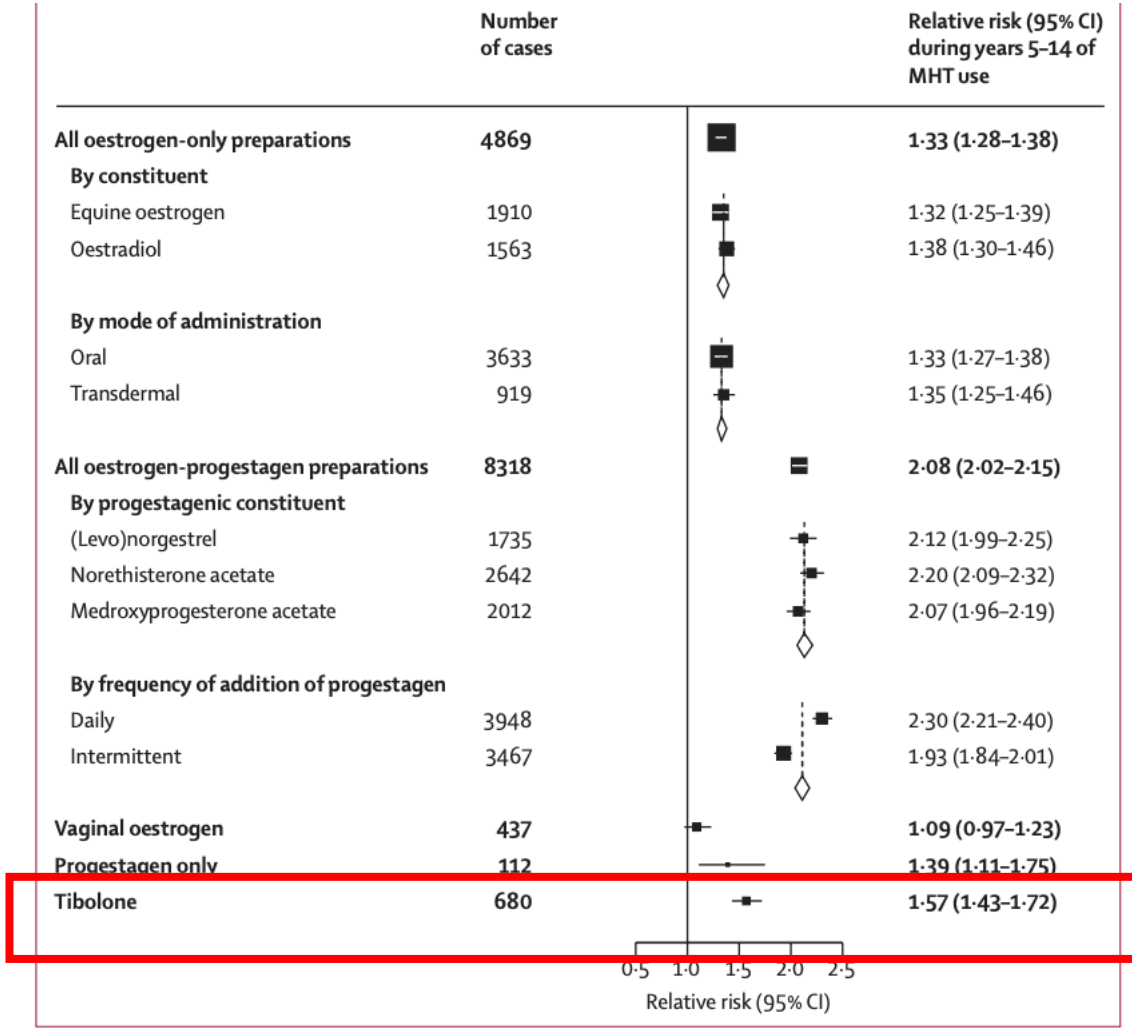
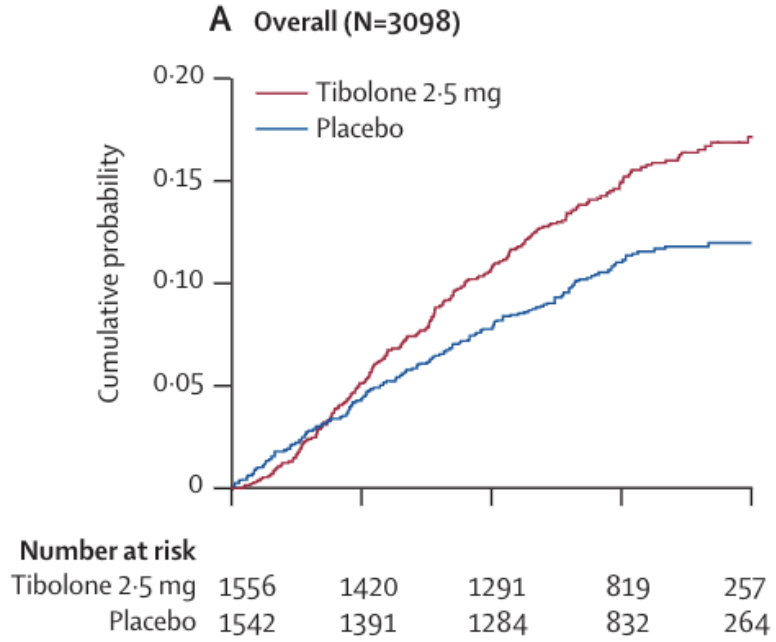
Ying et al 2017, Gynecological Endocrinology, 33:2, 87-92

Compounded Bioidentical have limited safety data

- No quality control
- Customised doses/preparations are not subjected to the same tests of safety, efficacy, or dosing consistency as regulated HRT
- Not approved regimes such as transdermal progesterone

Tibolone increases the risk of recurrence of breast cancer





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Collaborative Group on Hormonal Factors in Breast Cancer 2010. Lancet 394: 1159–68
Kenemans et al Lancet Oncol 2009; 10: 135–46

HRT in women with high background risk

- HRT do not increase further the risk in women with a family history of breast Ca or BRCA1 and 2 post oophorectomy
- The risk on women with high BMI is not additive

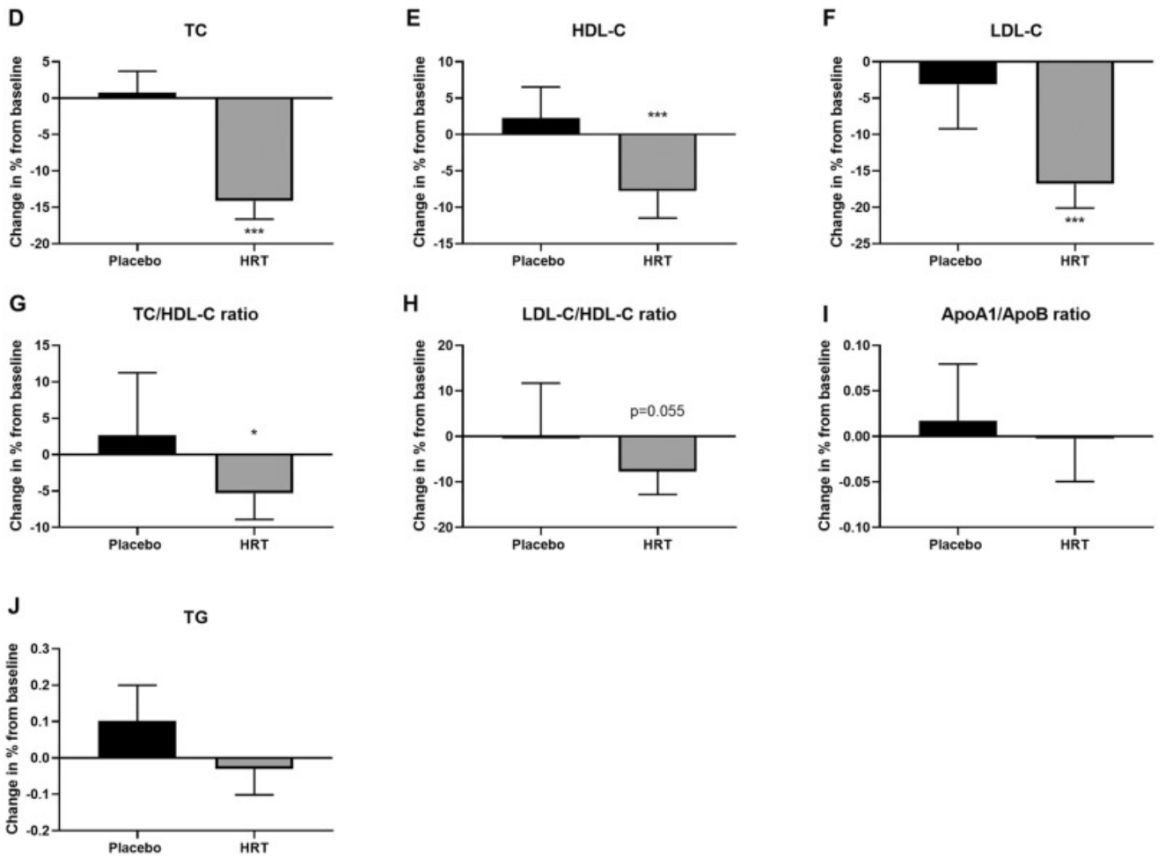
- HRT are not recommended when history of breast Ca
- Low dose vaginal oestrogen can be effective for GSM symptoms
- HRT can be considered when refractory symptoms post MDT

HRT does not increase the risk of CHD or stroke up to the age of 60 years

	CEE+MPA Trial						CEE Alone Trial					
Primary Endpoints	Active N(%*)	Placebo N(%*)	Diff per 10K pys^	HR	95%CI	P-trend	Active N(%*)	Placebo N(%*)	Diff per 10K pys^	HR	95%CI	P-trend
Coronary heart disease												
50-59	38(0.23)	22(0.13)	+5	1.74	(0.82, 2.19)	0.81	21(0.17)	35(0.28)	-11	0.60	(0.35, 1.04)	0.08
60-69	79(0.37)	73(0.37)	0	1.01	(0.73, 1.39)		100(0.61)	108(0.63)	-3	0.95	(0.72, 1.24)	
70-79	79(0.82)	59(0.63)	+19	1.31	(0.93, 1.84)		83(0.97)	79(0.90)	+7	1.09	(0.80, 1.49)	
Stroke												
50-59	26(0.15)	16(0.10)	+5	1.51	(0.81, 2.82)	0.50	19(0.16)	21(0.17)	-1	0.99	(0.53, 1.85)	0.77
60-69	72(0.34)	46(0.23)	+11	1.45	(1.00, 2.11)		84(0.51)	57(0.33)	+18	1.55	(1.10, 2.16)	
70-79	61(0.63)	47(0.50)	+13	1.22	(0.84, 1.79)		66(0.77)	52(0.59)	+17	1.29	(0.90, 1.86)	

Manson et al, JAMA 2013

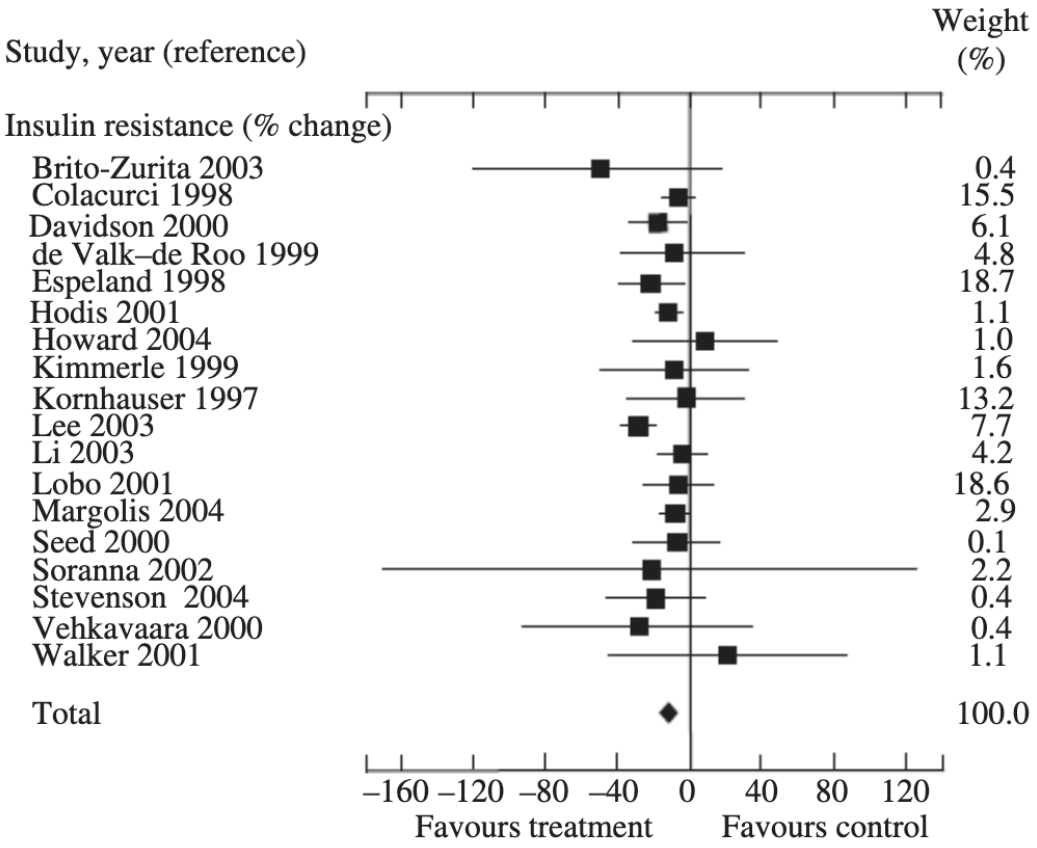
HRT-not contraindicated in dyslipidaemia or hypertension

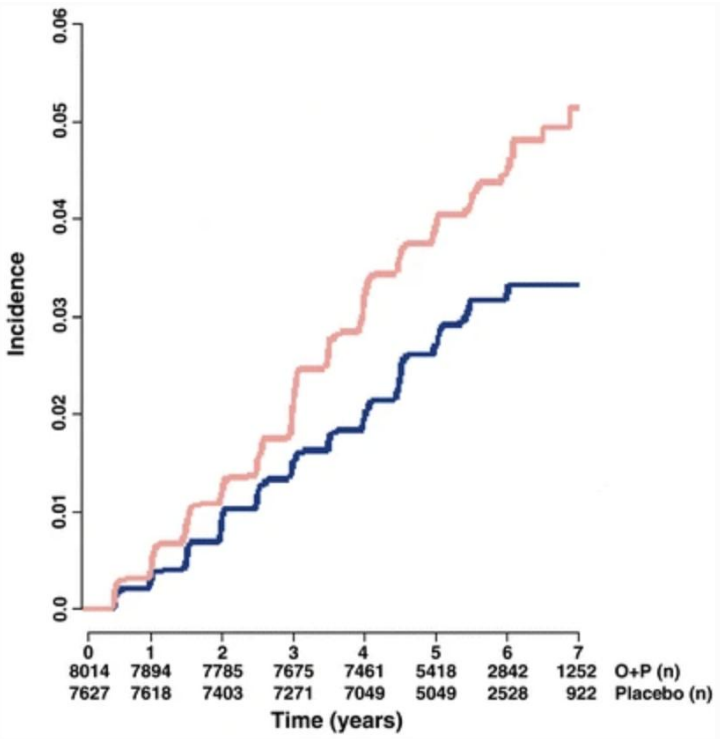


- No evidence that HRT adverse impact on lipid profile –prefer transdermal
- Hypertension is not a contraindication for HRT- optimize and monitor- prefer transdermal
- Obesity is not a contraindication for HRT- opportunity for lifestyle modification advice- prefer transdermal

Gregensen et al, Thrombosis Research 2019

HRT delays T2DM and improves insulin resistance





Diabetes incidence by treatment arm (Oestrogen Plus Progestin [O+P] versus Placebo). Hazard ratio (95% CI), 0.79 (0.67–0.93). Blue line: Oestrogen Plus Progestin; red line: Placebo

Salpeter et al, 2006
Margolis et al, Diabetologia 2004

Key points

- Mental health problems may flare up during menopausal transition due to contributing factors that coincide the same period
- Cannot assume that psychological symptoms are attributed to hormonal changes
- Menopausal symptoms such as VMS and sleep disturbances may contribute to depressive symptoms
- Avoid stopping treatment during menopausal transition
- HRT especially transdermal is a safe and effective option (most cases) to improve VMS/ sleep quality and thereafter depressive symptoms

THANK YOU

When in doubt.. Refer Out or Ask for advice
In most cases, HRT benefits outweigh risks when for symptom relief

Queen Mary
University of London

[redacted]

NHS
Homerton
University Hospital
NHS Foundation Trust

PCOS and Mental Health

Integrating physical and mental health needs

[redacted]

Consultant and Lead for Women's Health in C&H

PCO and PCOS

NHS
Homerton
University Hospital
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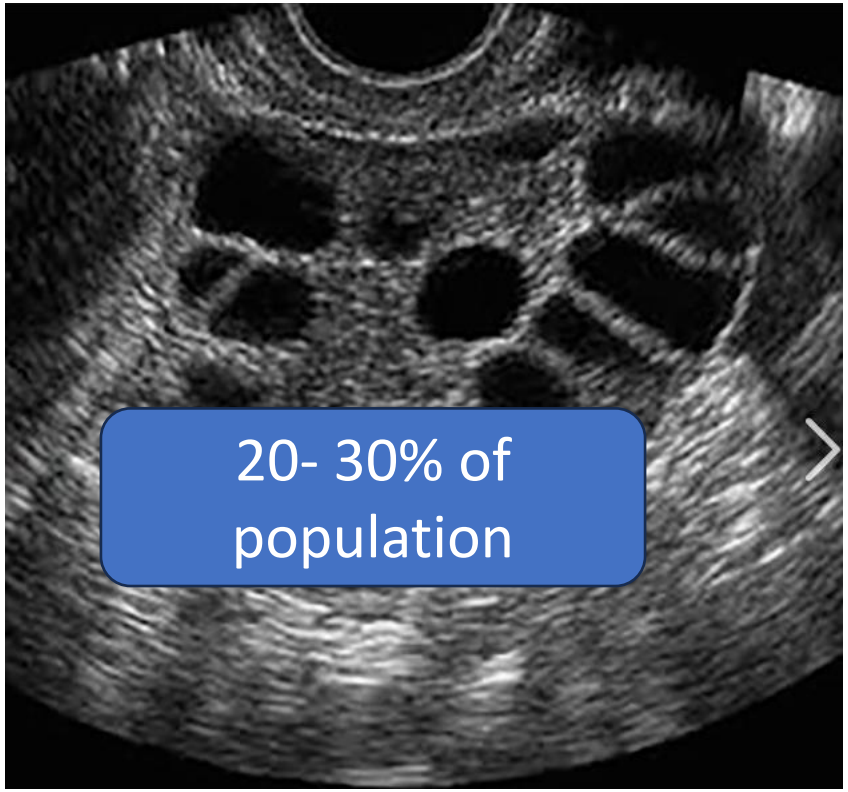
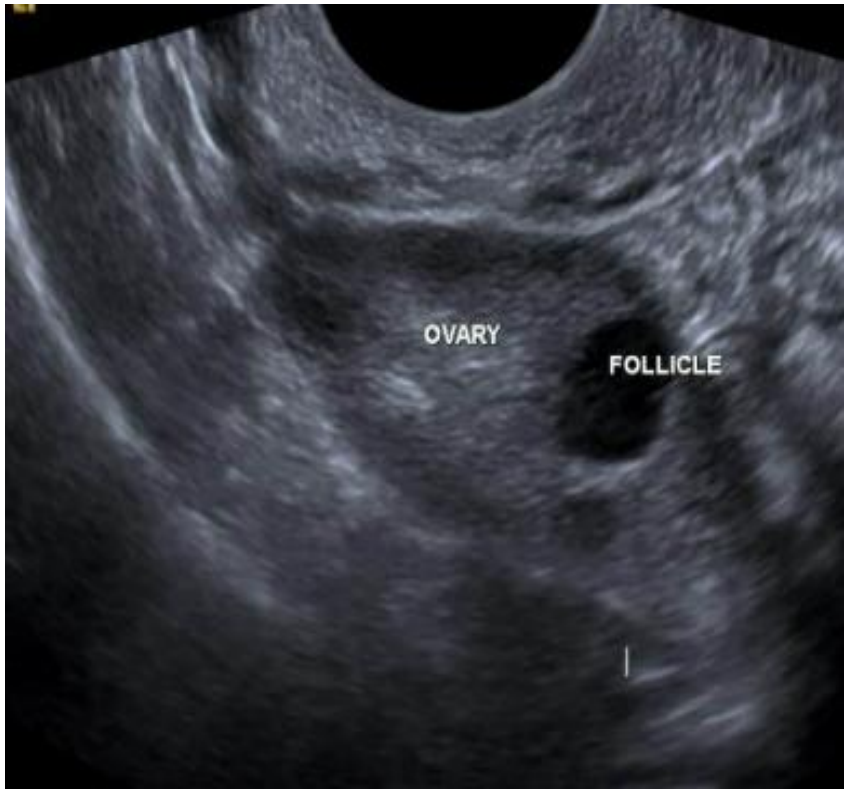
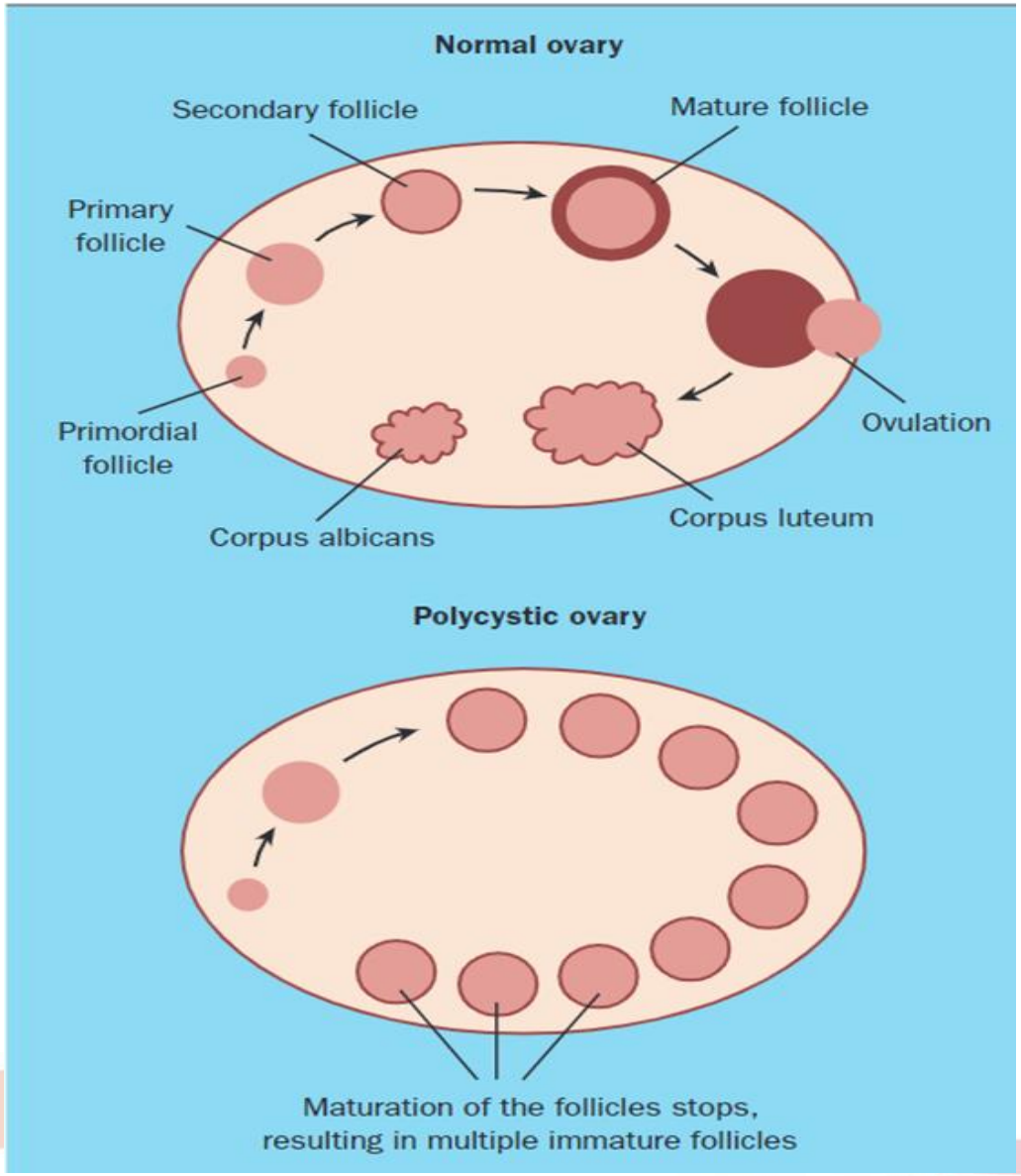




Prevalence of polycystic ovarian syndrome 5-15% worldwide

Normal vs PC ovary



Case Ms LM

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- 21 year old Turkish patient - student
- 1 year amenorrhoea after stopping combined pill
- Started periods age 13
- Always irregular
- Started combined pill for contraception age 16
- Periods regular since then
- Stopped pill 1 year previously as no relationship

On further questioning……

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- P0+0 – no immediate plans for pregnancy
- Worried about periods
- Not sexually active – not confident in relationships
- Struggling with acne – which had been better on pill
- Unwanted hair on chin and chest
- SH – student, low confidence and mood, few friends, social anxiety, embarrassed to go to gym
- Non smoker,
- BMI 32 – rapid increase in weight in the last year

Rotterdam criteria for PCOS

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- 2 out of 3 required

✓Oligo/anovulation (cycles >35/7 or amenorrhoea >6/12)

✓Hyperandrogenism Clinical (hirsutism or less commonly male pattern alopecia) OR biochemical

- Polycystic ovaries on USS 12 or more follicles (measuring 2–9 mm in diameter) in one or both ovaries and/or increased ovarian volume (more than 10 cm^3)

What is PCOS? – Endocrinopathy

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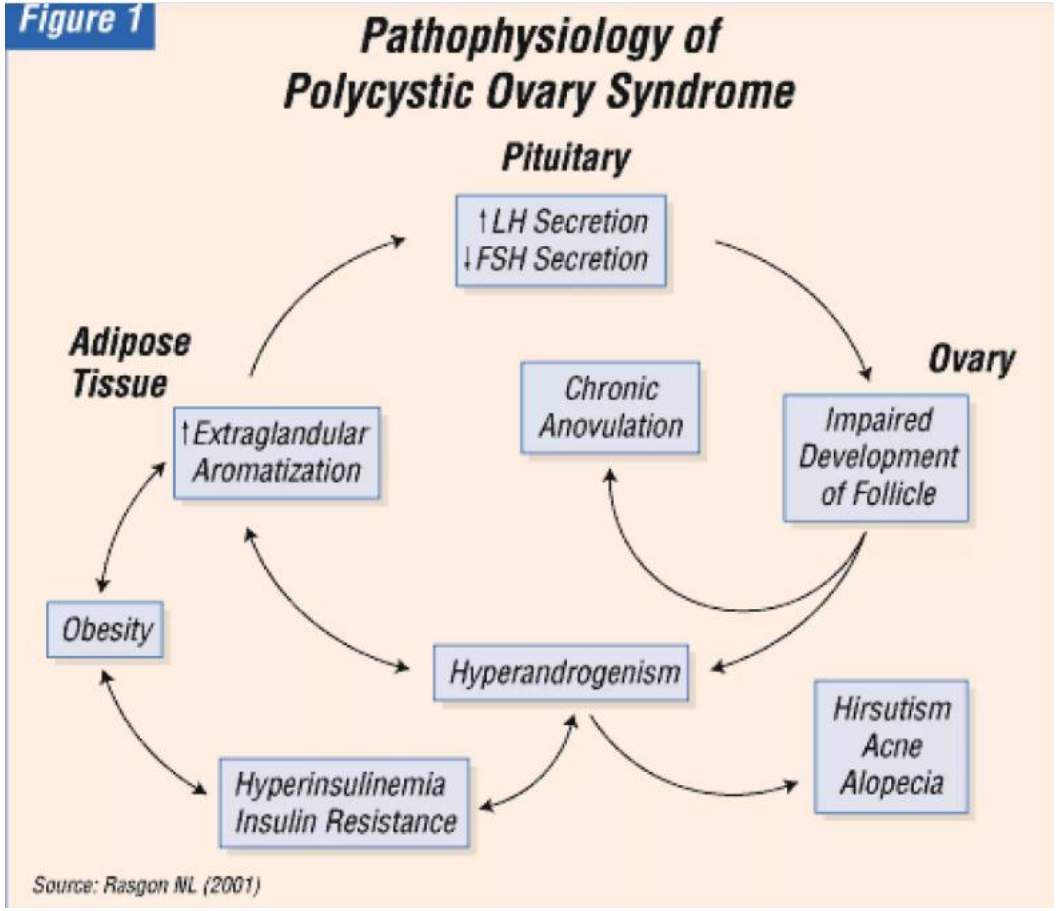
Reproductive, metabolic and endocrine consequences

- Infertility
- Endometrial Ca risk
- Metabolic syndrome in up to 40%
- Type 2 diabetes (3-7X)
- Cardiovascular disease
- Depression and anxiety



Investigations

- Hormonal profile: TFT/prolactin/FSH/LH/Oestradiol – for irregular cycles
- Total testosterone —normal to moderately elevated
- SHBG — normal to low - provides surrogate measurement of the degree of hyperinsulinaemia, risk of DM
- Testosterone
- AMH>4.7
- USS adults

PCOS and weight

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- Higher genetic susceptibility to obesity
- Hyperinsulinaemia – fat storage increased, breakdown decreased
- Impacts on appetite – metabolic and psychological
- Weight escalates from adolescence
- Weight gain predicts metabolic syndrome and CVD
- All symptoms of PCOS (hirsutism, menses, insulin resistance) worse with weight gain (+ disappear after bariatric surgery/natural weight loss)
- Diet and weight management cornerstone of PCOS management and maintained lifelong
- T2DM is 2-3x higher in women with PCOS
- Bariatric surgery - morbidly obese women with PCOS (BMI of 40 kg/m2 or more or 35 kg/m2 or more with a high-risk obesity-related condition) if standard weight loss strategies have failed.

PCOS and hyperandrogenism

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- Excessive production of testosterone
- Clinical hyperandrogenism
  - Hirsutism
  - Acne
  - Alopecia
- Biochemical hyperandrogenism
- Ovarian theca cells stimulated/reduced production SHBG
- Can respond to lifestyle modification
- Pharmacological – COC, anti-androgens - direct, metformin – indirect through insulin sensitivity, topical - eflornithine

PCOS and infertility

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- Anovulation – Gonadotrophin abnormalities, insulin resistance
- Irregular cycles – difficult to predict ovulation
- Obesity – reduces fertility
- Treatments
  - 5-10% weight reduction/exercise can restore fertility
  - Low GI diet – to manage insulin resistance
- Assisted conception
  - Ovulation induction
  - IVF
- High BMI – higher risk pregnancies – gestational diabetes

PCOS and long-term physical health

- Endometrial cancer
- NIDDM and insulin resistance – metabolic syndrome
- BP and other cardiovascular risk factors

PCOS and depression/anxiety

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- Prevalence up to 40-60% with PCOS, relative risk 2-3 X
- Mechanism of depression
  - Direct influence of androgens and metabolic
  - Influence on life goals eg infertility
  - Body image – weight gain, hirsutism, acne
  - Impact of poor body image on social withdrawal and self-esteem
- Impacts – unhealthy behaviours, adherence to treatment

PCOS and other mental health impacts

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Body Image

- Most women dissatisfied with body
- More prevalent with PCOS
- Physical – weight and hirsutism
- Mental health – thoughts and feelings about health, appearance, QoL

Eating disorders

- Risk factors increased
- Have increased body weight plus underlying self-esteem and mood disorder

Psychosexual

- Factors for psychosexual dysfunction increased
- Same desire but poor function
  - Depression
  - Low self esteem
  - Poor body image – sexual attractiveness, body hair, less confident to engage in social contact
  - Impacts of higher weight, infertility

Assessing QoL

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HEALTH PSYCHOLOGY OPEN

Health Psychol Open. 2018 Jul 19;5(2):2055102918788195. doi: 10.1177/2055102918788195

The Polycystic Ovary Syndrome Quality of Life scale (PCOSQOL): Development and preliminary validation

Sophie Williams [1,✉], David Sheffield [1], Rebecca C Knibb [1,2]

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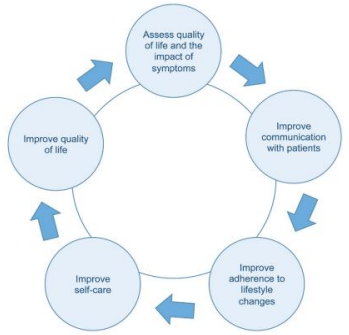
PMCID: PMC6053872 PMID: 30038788

26 Items
5 domains

- Emotional well-being
- Body hair perception and impact
- Weight – concerns and body image
- Infertility – distress related to difficulty conceiving
- Menstrual problems – impact on daily life

7-point likert

Can help to tailor treatment and monitor impacts



Principles of care

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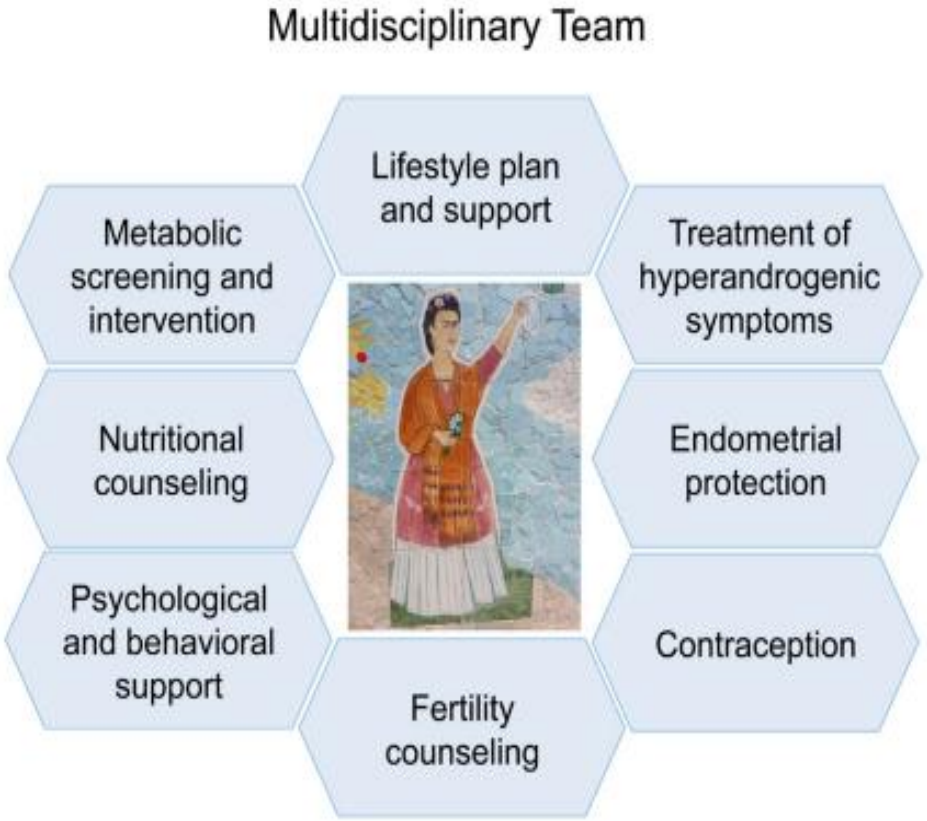

Ms LM – Immediate Management

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Short term

- Hyperandrogenism – Topical, COC, antiandrogens, metformin
- Endometrial protection – withdrawal bleeds, 3-4 per year
- Weight management
- Psychosocial support

Longer term

- Fertility
- Metabolic screening and CV risk factors
- Psychological factors

Psychological Management Strategies for Ms LM

- What would you do in the short and longer term? Interventions/referrals
- How are or could services be organised to optimise multidisciplinary care
- Examples of where this is working well.

What strategies could be considered for NEL?

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- Internal to women's health teams
- Referral pathways into existing mental health teams
- Integrated multidisciplinary team
- Models of care
  - Talking therapies – LTC management
  - Group consultation model

International Evidence-based Guideline for the assessment and management of polycystic ovary syndrome 2023

THANK YOU

[redacted]

Chapter Two

Prevalence, screening, and management of psychological features and models of care

ANY QUESTIONS?