MENOPAUSE 2022

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- Menopause Lead Sheffield,
- Contraception and Sexual Health lead Bassetlaw

- Declarations-
- I have received speakers honoraria from Bayer, Besins, MSD, Pfizer, Organon. COSRT, BSSM

TOPICS

- Menopause fact and fiction
- Menopause symptoms
- Menopause diagnosis
- HRT
- When to stop contraception

• ?testosterone



FACT OF FICTION – YOU DECIDE

- HRT should be stopped after 5 years
- HRT should only be used for the most severe symptoms
- HRT prevents Alzheimers
- HRT treats vaginal and bladder symptoms
- SSRI are better than HRT for menopausal anxiety and depression
- HRT causes an increase in blood pressure
- HRT causes heart disease and stroke
- HRT cause VTE

FACT OR FICTION?

- HRT causes weight gain
- HRT may be continued life long
- Bioidentical HRT are regulated medications
- Women on HRT should not use vaginal estrogen
- HRT reduces the risk of bowel cancer
- HRT started within 10 years of the menopause reduces all cause mortality
- HRT should not be used in diabetics.
- HRT should be continued to 5 lyo in women with premature ovarian insufficiency
- HRT is not suitable for women with a family history of breast cancer

18 WEEKS GESTATION



MENOPAUSE WHAT IS HAPPENING

- Max follicles at 18 w
- Decreasing thereafter
- Greater levels of FSH need to stimulate follicle development
- Follicle produce estrogen, so estrogen levels drop

 Testosterone reducing in all from age 35yo and then ovarian production reduced at menopause

MENOPAUSE NUMBERS!

- Average age menopause 51 yo
- 1% premature menopause age less than 40 yo
- 10% early menopause <45yr
- 80 % have stopped periods age 54 yo

PREMATURE OVARIAN INSUFFICIENCY

I % of women

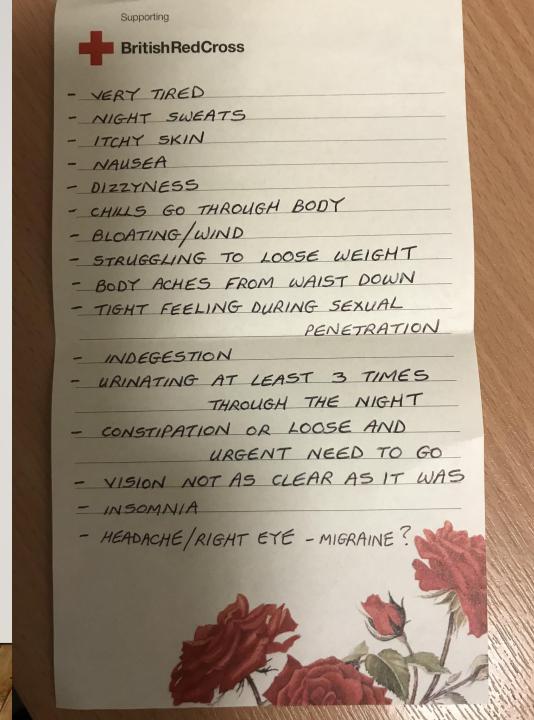
- Linked with surgery, chemotherapy, autoimmune disease, genetic disorders, sterilisation (not combined contraception), smoking but often no cause found.
- Linked with increased risk osteoporosis, CVD, Dementia, Parkinsons disease
- HRT until 50 yo.

IMPACT OF MENOPAUSE

- Bone density reducing with age both sexes- increased loss at menopause
- Vasomotor symptoms
- Atheroma increases in vessels
- Loss of estrogen affects cognition
- Collagen
- Skin
- May change hair growth
- Decreased libido

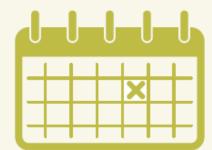
SYMPTOMS?

- 75% experience symptoms
- 25% severe
- Last average 7 years
- I/3 long term symptoms
- 50% say it impacts their home lives



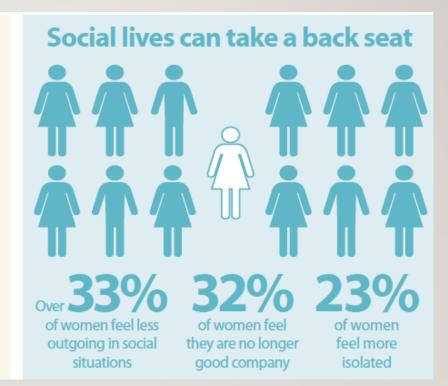
Work can be a struggle

of women say they feel their menopause symptoms have had a negative impact on their work





who have needed to take a day off work due to menopause symptoms say they wouldn't tell their employer the real reason



FLUSHES AND SWEATS- WHAT WOMEN SAY

"I find it difficult to hold a conversation – it is just so embarrassing when I can feel sweat dripping of my nose"



• "I have to sleep on a towel to mop up the sweat"

- Separate beds
- Window open
- Fan in every room
- No bed clothes

MOOD CHANGES

- Increased risk of depressive symptoms pre and perimenopause
- Highest risk age 40-49
- Lowest risk in women over 60yo
- Women with a past history of depression don't see the same reduction in risk post menopause
- Freeman et al longitudinal pattern of depressive symptms around natural menopause jama psychiatry 2014

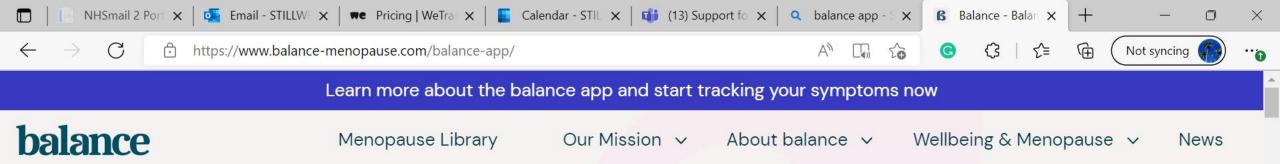
OTHER CAUSES OF "MENOPAUSE" SYMPTOMS

- Thyroid disturbances
- Medication depo, antihypertensives, SSRI
- Skin conditions
- Depression
- Bladder problems
- Cardiac

THE GREENE CLIMACTERIC SCALE

NAME:			В	ATE:	
NUMBER:					
Please indicate the extent to which you a symptoms by placing a tick in the appro	are bother priate bo	red at th	ne mom	ent by any	of these
SYMPTOMS	Not at all	A	Quite a bit	Extremely	Score 0-3
Heart beating quickly or strongly					
2. Feeling tense or nervous					
3. Difficulty in sleeping					
4. Excitable					
5. Attacks of panic				, .	
6. Difficulty in concentrating					
7. Feeling tired or lacking in energy					
8. Loss of interest in most things					
9. Feeling unhappy or depressed					
10. Crying spells					
11. Irritability					
12. Feeling dizzy or faint					
13. Pressure or tightness in head or body					
14. Parts of body feel numb or tingling					
15. Headaches					
16. Muscle and joint pains					
17. Loss of feeling in hands or feet					
18. Breathing difficulties					
19. Hot flushes					
20. Sweating at night					
21. Loss of interest in sex					

P (1–11) =	A (1-6) =
S (12–18) =	D (7-11) =
V (19-20) -	S (21) =



balance app

Looking for knowledge and guidance so you can be certain about what's right for your body during the perimenopause and menopause? You're in the right place.

Brought to you by renowned menopause specialist, Dr Louise Newson and the thousands of people who've shared their perimenopause and menopause insights with us, the free **balance** app allows you to track your symptoms, access personalised expert content, download a Health Report©, share

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DIAGNOSIS OF MENOPAUSE

- Over 45 yo no need any blood tests
- Under 45 yo menopause symptoms consider FSH
- Under 40 yo two FSH at least 6w apart

- OK to do FSH on implant, pop, may be artificially low on depo or estrogen containing meds.
- Don't forget a pregnancy test

RISK OF PREGNANCY

Risk of pregnancy I year of unprotected sex	
Age 40-44yo	10-20%
Age 45-49 yo	12%
Age>50yo	rare

RISKS OF PREGNANCY IN YOUR 40'S

- Miscarriage 50% in women over 45yo
- Increased still birth, perinatal mortality, increased malformations
- Maternal mortality 3 x higher than a 24 yo
- Downs syndrome affects
- 1:909 age 30 yo
- 1:146 age 40 yo
- 1:28 age 45yo

WHEN CAN I STOP CONTRACEPTION?

contraception	40-50yo	>50yo
Non hormonal	2years after last period	I year after last period
Progestagen only pill/implant (Injectable ,CHC pill stop age 50yo)	Continue beyond age 50	Continue to 55yo or stop I year after a raised FSH in a period free woman.
All method		Stop age 55yo

ON LINE TESTING OF HORMONES

- Offered by many companies who may suggest hormone imbalance
- Empowering
- However no evidence knowing these details enhances care

• Remember normal FSH does not exclude menopause as a cause of symptoms

• 41% felt they didn't have enough information about menopause

• 2/3 wanted to learn more

WHAT CAN I DO FOR YOU?

• Health care professionals need to be pro-active asking about sharing information about menopause in women.

To ask about symptoms – especially asking about sex and desire.

Why don't we ask ????

SIGNPOSTING

- <u>www.menopausematters.co.uk</u>
- www.daisynetwork.org
- www.womenshealthconcern
- Managing hot flushes with CBT- Myra hunter
- www. rockmymenopause.com
- Balance app/Newson health
- Menopausedoctor.co.uk
- British menopause society- thebms.org.uk
- Preparing for the perimenopause and menopause
- Managemymenopause

NON HORMONAL TREATMENTS

- Black cohosh
- St Johns wort
- SSRI
- Clonidine
- Gabapentin
- Oxybutynin
- CBT
- Isoflavone/phytoestrogens

- Acupuncture
- Yoga
- Exercise
- Mindfulness
- Vitamin E

HRT - WHO

All menopausal women under 45 yo

Menopausal symptoms who want to try it

There are no absolute exclusions

BENEFITS

- Improved Quality of life
- Control of menopausal symptoms

- Maintenance of bone density, reduced fracture risk
- Reduced risk coronary heart disease
- Reduced risk colorectal cancer, oesophageal cancer
- Reduced risk type 2 diabetes

RISKS OF MEDICATION PER 10,000 PATIENT YEARS COMBINED DATA 3 RCT

	Sympto matic ulcer	GI Bleed	MI	Stroke	Heart failure
baseline	14	7	26	П	5
Naproxen 750mg /day	112	30	26	32	34
ibuprofen	80	30	61	24	34

HRT RISKS/BENEFITS

- VTE
- Ovarian cancer
- Breast cancer
- Cardiovascular disease
- Aches and pains
- Cognition
- Mood

HRT AND THROMBOSIS

- Risk of VTE is increased x 2 by oral HRT background 2/1000
- Transdermal HRT in doses of 50mcg or less no increase in risk
- Consider TD for those with BMI > 30
- Refer to Haematology those with high risk
- Ref: NICE Guidance 23 Menopause 2015

OVARIAN CANCER

- 2015 meta analysis of 52 studies- increased risk E2 and E+P
 - I extra case per 1000 HRT users for 5 y
 - I additional death per 1,700 users

Menopausal hormone use and ovarian cancer risk: individual participant meta-analysis of 52 epidemiological studies. The Lancet.
 Published online February 12 2015

BREAST CANCER

• 1:7 women get breast cancer so inevitably some of your patients on HRT will get breast cancer

HRT AND BREAST CANCER FAST FACTS

- 90% of women have a low life time risk of breast cancer the benefits of HRT for 5 years will outweigh the risks
- Where the background risk is elevated the added risk of HRT is thought to be small
- Risk is not increased in overweight women
- Continuous combined carries a slightly higher risk than sequential but the absolute xs risk is small and the benefits of continuous combined HRT in reducing endometrial cancer, avoiding bleeding etc need to be considered.
- There is little difference in risk incurred by lifestyle factors and current or past use of HRT
- There is no increase in breast cancer mortality for HRT users

Post reproductive health 2021 Marsden and Pedder



LIFESTYLE FACTORS USE AGE 50-59 YO

ABSOLUTE RISK / 1000 5YR

Postmenopausal obesity	Overweight vs healthy weight	+4
	Obese vs healthy weight	+10
Alcohol	4-6 u / day	+8
	>6 u/day	+11
Unopposed estrogen	WHI 2020 NICE 2015 CGHRBC	-6 +3
Combined HRT	WHI NICE CGHRBC	+8 +9 +10

COLLABORATIVE GROUP META ANALYSIS 2019

• 5 years use of MHT starting age 50 would increase risk of breast cancer by I person per

50 users of daily estrogen and progestogen (MPA and NET)

• 70 users of cyclic estrogen and progestogen

200 users estrogen alone

LIVING WITH BREAST CANCER?

Estrogen receptor positive?

• Offer non hormonal treatments- CBT, melatonin, hypnotic, sleep apps

Breast cancer now leaflet

• Systemic HRT can be considered please refer.

DIABETES

• Use of HRT improves insulin resistance and may improve diabetic control

• Suggestion it may reduce the incidence of type 2 diabetes

Use Transdermal preparations

OSTEOPOROSIS

IOF 50 yo woman has 2.8% risk dying related to hip fracture

• Users of HRT have a significant reduction in risk of fracture – risk reduction –0.63 to 0.74

- Zhu et al 2015
- Se e NOGG 2022

HRT AND CARDIOVASCULAR DISEASE

- HRT initiated before the age of 60 or within 10 years of the menopause reduces all cause mortality
- HRT started in this age group prevents coronary heart disease
- HRT started after 60 no reduction but no increase in CV events.

Langer et al HRT where are we now Climacteric 2021

FINNISH REGISTER DATA 2015- RESULTS PER 1000/5YR

- 19 fewer coronary artery disease events and
- 7 fewer stroke events than controls

- Benefits in reduction in CHD were linked positively to duration of HRT usage,
- Risk of death reduction from CHD of 18% by year 10
- All cause mortality reduced by 12 %

WEIGHT

- Women tend to gain at the menopause irrespective of HRT usage
- Reduced insulin sensitivity
- Reduction in physical activity
- Loss of muscle mass reduces metabolic rate
- No evidence HRT causes weight gain
- Occ get fluid retention that usually settles

MOOD

- Anxiety, depression are common perimenopausal symptoms
- SSRI are not recommended first line high discontinuation rate and HRT more effective
- Use HRT- observational data show reduced depression and anxiety symptoms

NICE 2015

DEMENTIA

- Impact of HRT unclear
- WHI no effect of HRT- subgroup analysis suggest increased risk when initiated age > 65Yo
- KEEPS cognitive and affective study no change in cognition
- Finnish 2019 study showed inc risk of Alzheimers when started under and over 60 yo yo

 Reassure HRT unlikely to increase the risk of dementia or effect cognition when started under age of 60

ARTHRITIS AND MUSCULOSKELETAL PAIN

• Estrogen deficiency has a negative effect on connective tissue metabolism in joints, bones, skin, intravertebral discs

- Use of HRT shows a significant reduction in joint aches (WHI)
- Estrogen may reduce changes of muscle aging
- Some studies showing improved muscle power in HRT users.

HRT-

• How to choose ??

What symptoms are a priority?

• How will you measure the outcome? Follow-up plans?

HRT

- Oral/transdermal
- Estrogen only
- Estrogen and progestogen
- Cyclic
- Continuous combined > I year since LMP
- Combination products are less flexible

ORAL VSTRANSDERMAL

Oral	transdermal		
convenient	Patient choice		
Patch non adhesion	Risk factors vte		
Poor symptom control with transdermal	Risk factors CVA		
Patient choice	diabetes		
Under 60 yrs	BMI >30		
Absorption may be poorer an erratic	Age over 60		
Raises shbg	Gall bladder disease/migraine/loss of libido		

TRANSDERMAL ESTROGEN ONLY PATCHES

Pros	cons		
Usually stick well and easy to use	Some get irritation and poor adhesion		
Can swim bathe etc	Sticky mark		
Constant release helpful in migraine			
Can use double or 1/2			
Different brands and dosing			

GELS/SPRAY

pros	cons	
Very flexible dosing	Some find it slow to dry	
Woman can easily adjust	messy	
Can swim bathe	High dose requires multiple applications	
invisible	Irritating	
	Separate progesterone – compliance?	

	Ultra low	low	medium	high
oral	0.5mg	Img	2mg	3mg
Patch	Half 25mcg	25	50	75-100
Gel pump	1/2	I	2	3-4
Gel sachet	½ 0.5mg sachet	0.5mg	Img	1.5-2mg
spray	I	2	3	

ENDOMETRIAL PROTECTION

- The higher the doe of estrogen the more P you need
- Long term sequential HRT may be assoc with increased risk of endometrial hyperplasiadose and duration of P dependent
- Women on high dose e2 ie 75-100patch, 3-4 squirts gel consider mp 300mg 12 days of month or 200mg daily.

Progestagens and endometrial protection tools for clinicans BMS

ESTROGEN ONLY HRT

• For women who have had a total hysterectomy (including cervix)

Estrogen only -No or minimally raised risk of breast cancer

Be cautious of those with a history of endometriosis

COMBINED HRT

- Cyclic /sequential < I yr since LMP
- 12-14 days progesterone /progestogen monthly
- Mirena

• Continuous combined – usually > lyr amenorrhoea or > lyr cyclic and wishes to avoid periods

• Continuous low dose progestogen/progesterone- better endometrial protection

IUS

- 5 year
- Good for those needing constant low dose progestogen
- Good for HMB
- Helpful in PMS
- May be good for migraine
- Contraceptive
- Reinsert as required

MICRONISED PROGESTERONE

- Utrogestan 100mg oral caps
- Utrogestan 200mg 12-14 days cyclic
- Utrogestan 100mg continuous no break
- Take with water
- Take at night
- May be helpful in women with progestagenic side effects
- May have poorer cycle control
- Vaginal use -out of license

PROGESTAGEN MATTERS

Micronised progesterone and dydrogesterone may infer lower risk of breast cancer ???

• Less than 5 year usage showed no increase risk breast cancer

• 5-14 years showed small increase but less than with other progestogens.

No increased risk of VTE

CHOICE OF ORAL HRT

- Combination products -Estradiol and progestogen :
- norethisterone, levonorgestrel, medroxyprogesterone acetate, dydrogesterone and utrogestan
- Suggest dydrogesterone may be the safest progestogen
- But norethisterone combinations commonly used may provide better cycle control and as androgenic some prefer

New estradiol plus micronized progesterone- bijuve

TIBOLONE

- Oral
- Androgenic and estrogenic effects
- Increased risk CVA /breast cancer like HRT
- May be beneficial for libido
- >I year since menopause
- Less effect on breast density than HRT
- No increase VTE

HRT TROUBLE SHOOTING

- Erratic bleeding common first 4-6 months, try increasing progestogen, changing progestogen
- Migraine- start low and use transdermal
- Poor symptom control consider dose and route
- Transdermal measure estradiol 200-800pmol/l rough guide
- Loss libido consider testosterone, change oral to TD
- Progestagen side effects try micronized progesterone

TESTOSTERONE

- Unlicensed
- Effective in 2/3 post menopausal women
- Requires monitoring FAI
- 6 months trial
- Gel formulations
- Usually used with HRT
- Remember to prescribe vag estrogen

TESTOSTERONE FOR HSDD

- No evidence inc. risk vte, cvd, breast cancer, endometrial stimulation
- Side effects unlikely if levels in physiological range
- No effect on liver renal or haematological parameters
- Testogel/tostran/androfemme
- Minimal data on premenopausal women
- Don't forget to look at relationship PST drugs medical and non medical

Sheffield SCP

WIDER BENEFITS OF TESTOSTERONE

- Controversial
- RCT not big enough or long enough to show the effects of T on cognition , MSK health, long term safety

• BMS Testosterone replacement- tools for clinicians.

BMS STATEMENT

- All women should be able to access advise on how they can optimise the menopause transition and beyond.
- There should be a holistic and balanced approach in assessing and advising women with reference to lifestyle and dietary modification
- The decision whether to take HRT, the dose and duration should be individualised,
- No arbitrary limits on duration should be set.

TOP TIPS

- Hormonal changes start long before the last period
- Blood tests are not helpful for the majority of women
- Support from primary care, advice from secondary care
- Signpost
- HRT is easy benefits outweigh risk for the majority
- No restriction on duration of HRT usage
- Don't forget vaginal symptoms
- No absolute contra indications to HRT

