Commencing HRT in the Late Menopausal Stage

This advice is based on current guidelines and recommendations which can be subject to change in the future.

Commencing HRT in the late menopausal stage isn't a current criteria to be seen within the Complex Menopause Clinic. Age, in itself, is not a contraindication to HRT use, but there are important counselling points to take into consideration. The late menopausal stage usually refers to more than 10 years from established menopause.

For most women, menopausal symptoms will reduce and resolve over time. The average duration of symptoms is 3-8 years. However, it is recognised that vasomotor symptoms (VMS) will persist into the late menopausal stage for a minority of women with current studies estimating this to be in the range of 10-15%.

If a patient is presenting to you for the first time with VMS, it is important to establish that these are menopausal VMS and alternative causes should be excluded such as haematological, adrenal, or lung pathology.

If other causes are excluded, then there are various ways to improve menopausal VMS such as:

1. Optimising lifestyle and behavioural factors

This is an essential component of management – such as a healthy diet, reducing sugar intake, reducing weight if overweight, stopping smoking as it can be associated with an increased incidence and severity of VMS, and ensuring regular exercise

2. Cognitive behavioural therapy

Cognitive behaviour therapy (CBT) has a proven evidence base in reducing the severity and distress of VMS. This can be self-directed via online resources or books, or delivered via trained practitioners. The Women's Health Concern (WHC) UK have a useful patient information leaflet on CBT on their website. At the end of this leaflet, there are signposts to other written resources. The SSWHG/CKCH Booklet "Let's Talk About the Menopause" also has a section on CBT. The recent NICE Guidelines update on management of the menopause (NG 23) has endorsed the use of CBT as a treatment for menopausal symptoms. The book "Managing hot flushes and night sweats. A cognitive behavioural self-help guide to the menopause" by Myra Hunter and Melanie Smith is also a good resource.

3. Other forms of psychological therapy & acupuncture

Hypnotherapy is listed as an option to treat VMS by The Menopause Society (previously known as NAMS). Acupuncture has shown mixed results in studies but does appear to be useful for some people. There is a small evidence base for its use in helping menopausal symptoms associated with adjuvant therapies used to treat breast cancer.

4. Prescribed non-hormonal therapies

There are many prescribed non-hormonal options that have been shown to help VMS. Clonidine and fazolinetant are licensed to treat VMS. The latter is licensed up to 65 years and therefore initiation >65y would be off-label use. There are many other medications that are commonly used to treat menopausal symptoms and are endorsed in menopause guidelines. These are not licensed to treat VMS, but have been shown to be helpful in studies. Like all meds, it can be trial and error to get the medication that will work best. In general, these medications are used at lower doses than their licensed indication. Example include SNRIs such as venlafaxine; SSRIs such as escitalopram; gabapentinoids; oxybutynin.

Please see our patient information leaflet on Prescribable Alternatives to HRT on the Complex Menopause Section of the CUMH website. https://irelandsouthwid.cumh.hse.ie/women-s-health/menopause/complex-menopause-clinic/

Other useful resources include the BMS Tool for Clinicians leaflet on Prescribable Alternatives to HRT and the ICGP Quick Reference Guide on Management of the Menopause.

5. HRT

If other causes for VMS have been excluded, HRT can be considered once the benefits and risks of use have been discussed. The only indication for its use in this regard is for the persistence of menopausal symptoms. It is not considered a 1st-line option for the treatment of osteoporosis and osteopenia in women > 60. It should not be initiated for the primary prevention of cardiovascular disease.

The **benefits** include:

1. **Symptom improvement** or resolution resulting in an improvement in quality of life and wellbeing. Therefore, if symptoms persist or there is no noticeable improvement after initiation, then the underlying diagnosis should be reconsidered and HRT stopped.

2**. Improvement or stabilisation in bone mineral density**
A DEXA scan could be considered to complete the full benefit/risk analysis if none done to date.

The **risks** include:

1. Small increased risk of breast cancer which increases with duration of use. This risk is largest with combined HRT and less with estrogen-only HRT. The WHI trial showed a reduction in the risk of breast cancer with estrogen-only HRT when initiated in older age groups.

2. Very small increased risk of ovarian cancer which observational studies depict to be in the range of 1 additional case per 1000 women after 5 years of use.

3. Increased risk of VTE/stroke with oral HRT

4. There have been observational studies suggesting a small increased risk of dementia when HRT is started in the late menopausal stage. These studies were mainly utilising older forms of oral HRT.

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In relation to cardiovascular risk: initiating HRT in the late menopausal stage is likely to be neutral overall. It won't provide any benefit or reduction in cardiovascular risk. The BMS 2020 Consensus Statement on the use of HRT in menopausal women states that "evidence from the Cochrane data-analysis as well as that from the long-term follow-up data of the WHI RCT showed no increase in cardiovascular events, cardiovascular mortality, or all-cause mortality in women who initiated HRT more than 10 years after the menopause.

However, there is a lingering concern in relation to women with established atheromatous disease (a confirmed previous event or > 50% occlusion of a major coronary artery) that HRT may increase the risk of cardiac events in the first 1-2 years of use - and this is due to the HERS RCT which looked at the addition of synthetic combined HRT v placebo in women who fulfilled this criteria, and the Canadian Papworth HRT atherosclerosis study which used high dose transdermal & oral estradiol. This increased trend was not evident in the ESPRIT RCT which used oral estrogen-only HRT after a history of a myocardial infarction.

If there are several cardiovascular risk factors, it might be worthwhile availing of additional screening via a coronary artery calcium test for further risk stratification.

Best practice would be for optimisation of any modifiable cardiovascular risk factors prior to starting HRT.

If initiating HRT in the later stages of menopause, a **"low and slow**" transdermal estrogen regime is recommended using low dose HRT.

1. 1/2 of a 25 or 37.5mcg estradiol patch, increasing to 25mcg-37.5mcg estradiol (if required) after 1 month
   Or
2. ½ of a pump of gel, increasing to 1 pump after 1 month
   Or
3. 1 spray of Lenzetto
   And
4. Utilising micronized progesterone (Utrogestan) or dydrogesterone (duphaston) if progestogen is required.

The usual side-effects and complications of HRT would still apply.

If there is no noticeable improvement on commencing HRT, the diagnosis should be revisited and symptoms may not be menopause in aetiology. HRT should not be continued if there is no improvement obtained. The ongoing use of HRT would need to be discussed on an annual basis with a benefit/risk evaluation, as per all patients.

5. Vaginal Estrogen

Symptoms of genitourinary syndrome of menopause (GSM) can start to worsen, or occur for the first time, in the late menopausal stage. There is no age restriction with the initiation and maintenance of vaginal estrogen therapy which can be very effective in treating GSM. This should be considered separately to systemic HRT. Despite what the product information leaflet states, studies have not demonstrated an increased risk of cardiovascular disease, VTE, stroke, breast cancer.

I hope this information is helpful to you and your patient in coming to a shared decision.

References:

1. Hamoda H, Panay N, Pedder H, Arya R, Savvas M. The British Menopause Society & Women's Health Concern 2020 recommendations on hormone replacement therapy in menopausal women. Post Reprod Health. 2020 Dec;26(4):181-209. doi: 10.1177/2053369120957514. Epub 2020 Oct 12. PMID: 33045914. Reviewed March 21
2. Panay N, Ang SB, Cheshire R, Goldstein SR, Maki P, Nappi RE; International Menopause Society Board. Menopause and MHT in 2024: addressing the key controversies - an International Menopause Society White Paper. Climacteric. 2024 Oct;27(5):441-457. doi: 10.1080/13697137.2024.2394950.