Mental health and the menopause transition

jeanhailes.org.au

Presenters

Professor Rodney Baber AM
B Pharm. MB BS FRCOG FRANZCOG
Clinical Professor of Obstetrics and Gynaecology
Faculty of Medicine and Health, The University of Sydney
Past President IMS
Editor in Chief, Climacteric
Associate Editor ANZJOG

Professor Jayashri Kulkarni AM
MBBS MPM FRANZCP PhD FAHMS
Director HER Centre Australia
Director Monash Alfred Psychiatry research centre (MAPrc)
Head Central Clinical School Department of Psychiatry

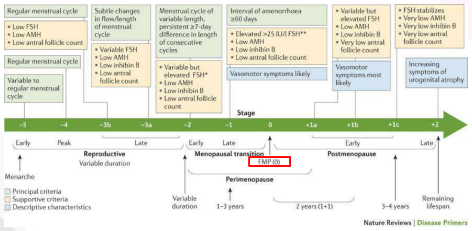
Definitions

Perimenopause
- is the time period preceding the menopause until one year after the last menstrual period
- defined as a change in cycle length of at least 7 days and is often accompanied by symptoms such as hot flushes, night sweats and mood changes

Menopause
- is the date of the last period and can only be diagnosed retrospectively once 12 months has passed since that last period

Postmenopause
- 12 months since a woman's last period they are considered postmenopausal

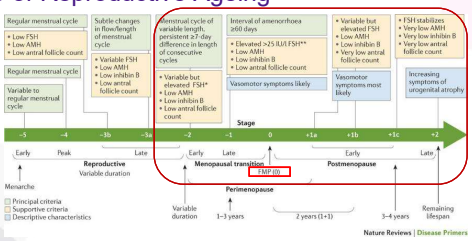
Stages of Reproductive Ageing



- Current data indicate STRAW* + 10 criteria apply to most but not all women
- Criteria cannot be used in PCOS or POI, nor after endometrial ablation or hysterectomy

Davis, S. R. et al. Nat. Rev. Dis. Primers 2015; STRAW + 10. Menopause 2012;19:387-95

Stages of Reproductive Ageing



- Current data indicate STRAW* + 10 criteria apply to most but not all women
- Criteria cannot be used in PCOS or POI, nor after endometrial ablation or hysterectomy

Davis, S. R. et al. Nat. Rev. Dis. Primers 2015; STRAW + 10. Menopause 2012;19:387-95

Changes through perimenopause to postmenopause.

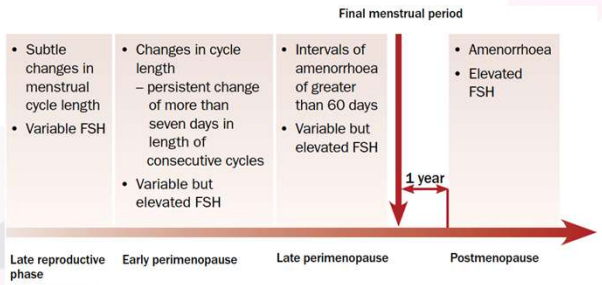


Image Prof. Rod Baber

How to Diagnose Perimenopause and Menopause

- Perimenopause is a clinical diagnosis and can NOT be diagnosed with a blood test. FSH, LH, oestrogen and progesterone levels will fluctuate between pre-menopausal and post-menopausal levels during perimenopause.
- Menopause can be diagnosed clinically and retrospectively once it has been 12 months since a woman's last period
- Blood tests may be helpful in someone with a Mirena in, who has had a hysterectomy, or might have premature ovarian insufficiency.

Screening for Mental Health Issues in the Menopause Transition

- When a woman presents with possible perimenopausal symptoms, it's important to screen not only for hot flushes and night sweats but also specifically ask about mood or cognitive changes
- Also, in a woman presenting with mood complaints whose age indicates that she may be perimenopausal, it is good to ask about cycle length and other perimenopausal symptoms
- Simply asking the question is a good place to start but also the Meno-D is a great screening tool

Assessing Mental Health in the Individual Woman – could it be hormonal?

- When a woman presents with mood changes in perimenopause or menopause it can be difficult to tease out what the causal factor/s are.
- Many women in their late 40s and early 50s are dealing with:
  - Post-pandemic mental health issues in themselves and others within their family
  - Ageing parents
  - Teenage kids with their own challenges and issues
  - Relationship issues
  - Career challenges
  - Health issues
- However, it's important to consider whether hormonal fluctuations may be one or the main causal factor for a change in a woman's mood or mental health

What comes to mind?
Menopause and the midlife brain

Disclosures

- Remuneration for lectures sponsored by Pfizer, Abbott, Viatris and Besins.
- Medical advisory board membership for Pfizer, Besins, Viatris, Theramex and Mayne Health.
- Clinical research funded by Pfizer, Organon, Novartis, Wyeth, Novogen, QUE Oncology and Madorra.
- I am currently Editor in Chief, *Climacteric*

This presentation is based on my own clinical experience, reading and research.

The ageing brain

Normal brain aging (cognitive aging)

Changes associated with age that do not cause dementia.

Abnormal brain aging (minimal cognitive impairment and dementia)

Changes associated with age, usually associated with underlying pathology that may eventually lead to dementia.

Dementia

Cognitive impairment that *interferes with usual occupational and social activities, or with independence.*

Henderson, *Climacteric* 2014;17

Cognitive skills change with normal aging

Some cognitive abilities are well maintained or improve with age

- These are abilities that draw largely on acquired skills, knowledge and experience and are known as **crystallized intelligence**, eg. vocabulary)

Other cognitive abilities decline, beginning insidiously during or before midlife

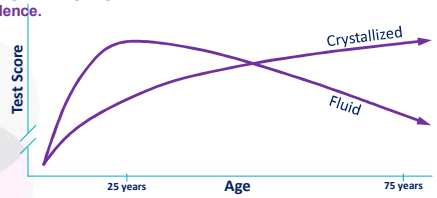
- These are abilities based on new learning, abstract reasoning, and problem solving and are known as **fluid intelligence**.
- These tasks tend to be performed better by young adults than old adults

Henderson, *Climacteric* 2014;17

Cognitive skills change with normal aging

The normal cognitive changes which occur with ageing are thus a combination of improved crystallized intelligence and declining fluid intelligence.

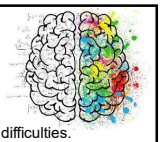
Normal cognitive ageing will not interfere with normal activities or independence.



Henderson, *Climacteric* 2014;17

Brain fog at menopause

Brain fog



The constellation of cognitive symptoms experienced around menopause which most frequently manifest in memory and attention difficulties.

- difficulty in encoding and recalling words, names, stories or numbers
- difficulty in maintaining a train of thought, distractibility
- forgetting intentions (reasons for coming into a specific room)
- difficulty switching between tasks
- the large majority of women with brain fog at menopause *will not* develop dementia although brain fog is associated with mood changes

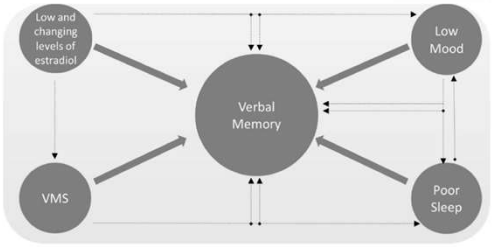
 Maki P and Jaff N Climacteric 2022

What menopause related factors influence cognition?

Cognitive changes at menopause are linked to:

1. changes in estradiol levels
2. vasomotor symptoms
3. sleep
4. mood

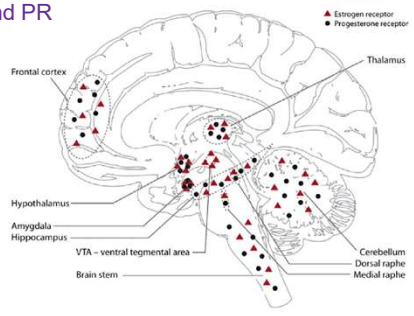
Treating these may benefit cognition



 Maki P and Jaff N Climacteric 2022

Distribution of ER and PR in Human Brain

- Estrogen receptors are widely distributed throughout the brain.
- Key sites include frontal cortex, thalamus and hypothalamus, amygdala, hippocampus and cerebellum.
- **Effects of MHT** will also depend on lifestyle factors, timing of use and genetic factors.



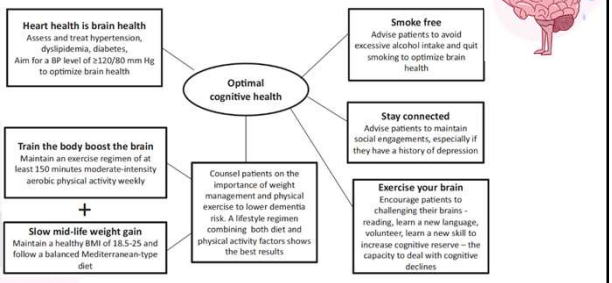
 Boyle C et al Hum Brain Mapp 2021;42:24-35

What is the role of MHT in treating cognitive concerns?

- The effect of MHT on cognitive function in menopause is influenced by timing of therapy, lifestyle factors and genetic factors
- Use of MHT in early post menopause is safe for cognitive function
- Use of MHT in women with early menopause or POI may be helpful in maintaining cognitive function and lowering risk of dementia
- Use of ET in late postmenopause appears safe for cognitive function
- We need more research to determine whether MHT improves cognition in women with bothersome VMS or whether MHT or oral contraceptives improve cognition in perimenopause
- Based on current guidelines MHT is not recommended to treat cognitive concerns at menopause or to prevent cognitive decline or dementia

 Maki P and Jaff N Climacteric 2022

How to optimize brain health



 Maki P and Jaff N Climacteric 2022

IMS Recommendations

- **Normal Menopause is not linked to dementia**
- **MHT should not be used to enhance cognitive function**
- **Healthy lifestyle measures help maintain cognition**
- **Estrogen therapy may confer cognitive benefit after surgical menopause when initiated at oophorectomy**
- **MHT initiated during midlife may be associated with reduced risk of Alzheimer's disease and dementia**
- **MHT may improve depressive symptoms during menopause transition**

1. Weber M, *et al. J Steroid Biochem Mol Biol* 2014;142:90–8; 2. Bromberger JT, *et al. Menopause* 2013;20(5):488–95; 3. Worsley R, *et al. J Womens Health (Larchmt)* 2017;26(7):712–18.; 4. Baber RJ, *et al. Climacteric* 2016;19(2):109–50

Case study one

Case study one: Jennifer

- Age 51
- 2 children, both NVD, now aged 22 and 20
- 4 years of irregular heavy menses
- Had a Lng IUS inserted 3 years ago with good effect
- Menses now infrequent, last menses 8 months ago
- Hot flushes more frequent
- Moody
- Experienced some post natal depression in 1st pregnancy
- No significant medical or family history
- No medications

Case study one: Jennifer

- Mood changes have been more apparent over the past 3 years
- Symptoms include irritability, poor sleep, poor memory poor concentration, forgetfulness
- Experiencing VMS 4-5 times each day and 2-3 at night
- Has also noted increasing weight gain and loss of libido
- Worried about the effects this is having on her and on her family
- BP 130/85, BMI 27

Diagnosis

- What is Jennifer's menopausal stage?
- Jennifer is perimenopausal – LMP 8 months ago

Diagnosis

- What is Jennifer's menopausal stage?
- Jennifer is perimenopausal – LMP 8 months ago
- It is difficult to assess her proximity to menopause because of the presence of the Mirena which has been effective in treating HMB
- Her main complaints are perimenopausal VMS and a worsening mood disorder
- Her libido has declined
- She is also overweight and has borderline hypertension

Diagnosis

- Jennifer's vasomotor symptoms and sleep disturbances are due to fluctuating levels of hormones during the perimenopause
- **Loss of libido** may be attributable to her perimenopausal symptoms or may be associated with her mood disorder
- 30% of midlife women complain of reduced sexual function and around 10% will have hypoactive sexual desire disorder (HSDD)
- **Mood disturbances** may be related to perimenopause, fluctuating hormones and sleep disorders
- Her mood changes share some chronological association with the insertion of LnG IUS

Screening at midlife

- Ideal time for a full midlife check-up
- CVD risk factors
- Ensure her screening tests are all up to date

.

Screening at midlife

Menopausal women are at increased risk of:

- **Cardiovascular disease.** Assess for thyroid disease, type 2 diabetes, iron deficiency, metabolic syndrome. Monitor BP, lipids, blood glucose, waist circumference and weight. Discuss physical activity and nutrition guidelines.
- **Osteoporosis.** Evaluate risk (see bone health section).
- **Mood disorders.** Ask about depression/anxiety symptoms (see emotional wellbeing section).

Also assess:

- **Heavy or abnormal bleeding.** Investigate for iron deficiency and gynaecological pathology.
- **Cervical screening test, breast examination and mammogram.**
- **Risky behaviours.** Assess alcohol intake and smoking.

Management options

- Would you do blood tests to see if she was menopausal?
- Would you treat her with an antidepressant?
- Would you remove her LnG IUS?
- Would you suggest MHT?
- What other advice could you suggest?

Management options

Would you do blood tests to see if she was menopausal?

- LMP 8 months ago
- No, that is a useless investigation in a perimenopausal woman of normal age

Management options

Would you treat her with an antidepressant?

- Antidepressants might help the depression and might also reduce her VMS
- Antidepressants commonly reduce libido so that might not be a good first choice!

Management options

Would you remove her LnG IUS?

- Progestogen IUS are associated with adverse mood changes in around 10% of women and are more likely to do this in women with a history of PMS/ PND
- Removal of the LnG IUS in a perimenopausal woman might also lead to a recurrence of the HMB
- Treatment of the HMB with progestogens might worsen the mood changes

Management options

Would you suggest MHT?

- Jennifer is keen to try MHT, a friend has found conjugated estrogen tablets great.
- CEE very good for alleviating VMS but do not cross the blood brain barrier so no benefit on moods

What other advice?

- Offer her lifestyle advice such as a regular exercise programme?
  - Very good idea for her CVD health and may help moods but will do nothing for VMS.
- Suggest counselling, cognitive behavioural therapy?
  - Both quite effective but neither is as effective as MHT in alleviating menopausal symptoms.

Management

- Jennifer agrees to a trial of transdermal estradiol What dose?
  - Start low and titrate up until satisfactory alleviation of symptoms
  - After initially starting with 1 pump of estrogen gel, this was increased to 2 pumps daily after 6 weeks and after a further 6 weeks her VMS have settled. No bleeding.
- Her mood changes have improved although she is still bothered by an underlying low mood. No longer fluctuating. What will you do?

Management

- Jennifer agrees to a trial of transdermal estradiol What dose?
  - Start low and titrate up until satisfactory alleviation of symptoms
  - After initially starting with 1 pump of estrogen gel, this was increased to 2 pumps daily after 6 weeks and after a further 6 weeks her VMS have settled. No bleeding.
- Her mood changes have improved although she is still bothered by an underlying low mood. No longer fluctuating. What will you do?
  - Options: Increase the estradiol dose, add an antidepressant, remove the LnG IUS.

Management

- Jennifer agrees to a trial of transdermal estradiol What dose?
  - Start low and titrate up until satisfactory alleviation of symptoms
  - After initially starting with 1 pump of estrogen gel, this was increased to 2 pumps daily after 6 weeks and after a further 6 weeks her VMS have settled. No bleeding.
- Her mood changes have improved although she is still bothered by an underlying low mood. No longer fluctuating. What will you do?
  - Options: Increase the estradiol dose, add an antidepressant, remove the LnG IUS.
  - Removing the IUS may be very effective in further reducing the mood changes, but we do not know if Jennifer is yet post menopausal and bleeding may return
  - The antidepressant will probably help the moods, but these are less bothersome, and her libido will likely be reduced by the antidepressant

Management

- I chose to increase her estradiol dose further. A 75ug patch was chosen to facilitate the higher dose and minimize cost.
- Upon review, after a further 6 weeks, Jennifer's mood disorder had settled.
- Her BMI was reduced to 25, she had initiated a moderate exercise programme, and taken up Tai Chi.

Management

- Her libido is still bothering her. What will you do?
  - Conduct a biopsychosocial assessment to exclude other causes of low libido.
  - Consider introducing transdermal testosterone therapy for HSDD
  - Consider changing her MHT from Estradiol to Tibolone
  - Remove the Mirena
  - There is no correct answer. I would trial options 1 and 2 as 75ug patch is a more estrogenic MHT dose than tibolone
  - I would not remove the LnGIUS until its due date (5 years post insertion) unless all else failed.

Menopause and Mental Health

MONASH University

Menopause and Mental Health

"Mental health policy in Australia does not consider women's mental health as a separate and important area of need".

Duggan, M. (2016) Investing in Women's Mental Health. Strengthening the foundations for women, families and the Australian economy.
Australian Health Policy Collaboration Issues paper No. 2016-02. Australian Health Policy Collaboration, Melbourne

MONASH University

62%

of individual submitters to the Royal Commission into Victoria's Mental Health System were women.

Despite this, the interim-report remains silent in response to many concerns identified as critical to women and girls. **The report does not propose actions that address the specific experiences of women and girls in the mental health service system.**

#RCMENTALHEALTH

MONASH University

Mental illness in Australian women

- Mental disorders represent the leading cause of disability and the highest burden of non-fatal illnesses for women in Australia
- 47% of women (3.5 million) have experienced mental illness at some time
- COVID impacted women's mental health enormously, increasing the number of women with depression, anxiety, PTSD, Eating Disorders and alcohol use disorder

AIHW 2019

MONASH University

The cost of mental illness in women

- The economic impact of depression/anxiety in women in Australia due to direct lost productivity is estimated to be $32 billion per year (ABS 2018 data)
- Add in costs of treatments, lost earnings, cost of loss of effective parenting of children, divorce, loss of care of elderly and other……

MONASH University

So – Where to now for Women's Mental Health?

MONASH University

Adopt a holistic model for women with mental ill-health

- **SOCIAL:** Violence, poverty, gender inequities in wages, power imbalance, social roles
- **BIOLOGY:** Hormone impacts, gender differences in drug metabolism systems, brain circuitry and genetic transmission
- **PSYCHOLOGY:** Psychiatric illnesses may present very differently in men and women because of gender differences in psychological responses

Urgently need neurobiological research into women's mental illnesses

- Most other fields in Medicine have made huge advances through greater understanding of biology – oncology, stroke management, vaccine development, cardiology, anaesthetics, obstetrics
- Then add on the extra social care aspects e.g.: better breast cancer support services – but this builds on biological advances in breast cancer treatments
- **Psychiatry struggles with the lack of neurobiological knowledge**
- In the absence of neurobiology, psychiatry has focussed on psychosocial therapies, support services
- Issues – poor diagnoses, missed diagnoses due to euphemisms (e.g.: 'baby blues', 'personality disorders'), no biomarkers

NEUROBIOLOGY & WOMEN'S MENTAL HEALTH

Many Aspects Yet to be Explored…

Gonadal hormones impact women's mental health
(Not news for many women!)

MONASH University

Hormones and the brain

- Estrogens, progesterones, androgens – are all potent neurosteroids
- Significant evidence for modulation of dopamine, noradrenaline, serotonin, glutamate and acetylcholine by estradiol, progesterones and androgens
- Longstanding clinical / anecdotal evidence for biological hormone impact on mental state

MONASH University

Perimenopausal depression
Under recognised and underrated

MONASH University

Depression

outlook

The misunderstood female factor

Menopausal depression takes a huge toll, but is underfunded and under-researched, says Jayashri Kulkarni.

Depression affects almost 300 million people worldwide, and women are twice as likely to experience it than are men. Notably, the incidence of depression in women peaks in the years around menopause[1].

Menopause is a long process that generally begins in a person's mid-40s and can continue for more than a decade. Depression caused by menopause can be more severe than that experienced by pre- and post-menopausal women (or by men of any age). Not coincidentally, suicide rates for women also are highest in the 45–64 age group[2].

Remarkably, these sad and shocking statistics have not created serious concern in society at large.

There are several reasons for the lack of attention. One is

"Too few women are benefiting

menopausal depression often respond inadequately to standard antidepressants.

The good news is that hormone treatments such as oestrogen therapy can be an effective way to treat the condition — either as an adjunct to antidepressants[3] or as a solo first-line treatment[3,4]. Yet there remains considerable reluctance to use them; in many cases, a diagnosis of any form of depression still leads to an automatic prescription of an antidepressant. This practice is particularly inexplicable given that the guidelines from both the North American Menopause Society and the International Menopause Society highlight the safety of hormone therapy in women during and up to 10 years after menopause.

There was a clear starting point for this automatic jump to antidepressants. In the early 2000s, a study[5] by the Women's Health Initiative on hormone replacement therapy (HRT) during menopause received sensational media attention. In 2002, the investigators suddenly stopped the combined (oestrogen and progestogen) HRT arm of the study because of an increased risk of breast cancer, heart disease, stroke and blood clots. The preliminary data were widely reported, and many people and their physicians became alarmed about the safety issues of HRT.

Since then, many of the study's results have been refuted. Furthermore, new menopause hormone medications are being developed, including synthetic selective oestrogen-receptor modulators, which should improve the safety of hormone therapy. But many health-care professionals do not recognize menopause as the underlying causal factor in women with mid-life depression, and so do not prescribe hormone therapy. As a result, too few

Nature **608**, S54 (2022)
doi: https://doi.org/10.1038/d41586-022-02213-w

Perimenopausal depression

- Very high incidence of first onset depression in perimenopause. Even higher relapse risk of depression in women with past history
- Overall depression rates increase up to sixteen times in 42–52-year-old women
- **Second highest completed suicide demographic group – in Australia – women aged 45-52** (highest is men >84)
- Declining / chaotic gonadal hormone function occurring from age 43-55. CNS changes first – up to 5 years before hot flushes, amenorrhoea

Kulkarni et al. *Translational Psychiatry* (2018)8:123
DOI 10.1038/s41398-018-0172-0

Translational Psychiatry

ARTICLE Open Access

Development and validation of a new rating scale for perimenopausal depression —the Meno-D

Jayashri Kulkarni[1], Emorfia Gavrilidis[1], Abdul-Rahman Hudaib[1], Caitlin Bleeker[1], Roisin Worsley[1] and Caroline Gurvich[1]

MONASH University

Perimenopausal depression symptoms THE MENO-D

- Plummeting self – esteem
- Paranoid ideation
- Aggressive
- Disconnection
- No libido
- Irritable / agitated
- Weight gain
- Poor sleep (compounded by hot flushes)
- Memory / concentration changes
- Anxiety / Panic

MONASH University

MENO- D

A rating scale to detect depression in menopause

Professor Jayashri KULKARNI
Monash Alfred Psychiatry research centre
Melbourne

Subject's name or code: ..... Date: .....

A – LOW ENERGY
0 No change in energy, feel active all day
1 More tired after activity than previously
2 Decreased activity because of tiredness
3 Feel tired most of the time despite resting, decreased activity
4 Continually feeling exhausted, even small tasks such as brushing hair feel draining. 'Bone weary, mind weary'.

B – PARANOID THINKING
0 No Paranoid thinking
1 Increasingly worried that others think badly of you
2 Suspicious that people at work or home think badly of you
3 Convinced that others have a low opinion of you and are trying to replace you

C – IRRITABILITY
0 No irritability
1 Mild irritability
2 Increased irritable response to minor incidents
3 Anger expressed by "snapping", verbal outbursts over minor incidents
4 Rage, major verbal outbursts over minor incidents

D – SELF ESTEEM
0 Good self esteem or no change in self-esteem
1 Slight decrease in self-esteem
2 Poor self-esteem with no reality base
3 Very poor self-esteem in all life domains, with marked self-denigratory comments
4 No self-worth at all to the point of believing that the world would be better off without you. (NB – this rating must then lead to further questioner about suicide planning, actions and deliberate self harm)

E – ISOLATION
0 Socialising normally
1 Decreased socialising
2 Disinterested in socialising
3 Social and occupational withdrawal
4 Feeling isolated, "in a bubble" even when with others

©Kulkarni 2011

F – ANXIETY
0 No new anxiety
1 Increased anxiety when performing in public
2 Highly anxious when doing new tasks
3 Heightened anxiety when doing routine and familiar tasks
4 Panic attacks, highly anxious when doing ordinary and familiar tasks

G – SOMATIC SYMPTOMS
0 No physical symptoms
1 Increased muscle aches, joint pains on exercise
2 Increased leg, back and joint pains with little exertion
3 Frequent headaches, muscle and joint pains limiting activity
4 Severe aches and pains requiring pain relief and preventing activity

H – SLEEP DISTURBANCE
0 No sleep problems
1 Sleep broken by brief waking once or twice per night, but easily return to sleep
2 Sleep broken by waking several times per night, but easily return to sleep
3 Waking up three or more times per night due to hot flashes and sweating, plus difficulty returning to sleep
4 Sleeping two or less hours per night consistently. Sweating, hot flushes, feeling hot then cold, interrupting sleep all night

I – WEIGHT
0 No change in weight
1 Mild weight gain (1-2kg)
2 Moderate weight gain despite no change in diet or exercise (3-6kg)
3 Continuing weight gain and abdominal fat deposition, despite dietary restrictions and increasing exercise
4 Major weight gain (>6kg) with abdominal, breast, hip and thigh fat deposition

J – SEXUAL INTEREST
0 No change in libido
1 Mild decrease in libido
2 Diminished libido
3 Decreased libido and discomfort with sexual activity
4 Loss of interest in all sexual activity

K – MEMORY
0 No change in memory
1 Mild problems remembering names and numbers
2 Need to make lists to function at work or home
3 Impaired memory leading to dysfunction
4 Severe loss of memory leading to inability to function

©Kulkarni 2011

Drugs & Aging (2022) 39:607–618
https://doi.org/10.1007/s40266-022-00962-x

REVIEW ARTICLE

Hormonal Agents for the Treatment of Depression Associated with the Menopause

Megan Herson[1] · Jayashri Kulkarni[2]

Accepted: 14 June 2022 / Published online: 30 July 2022

Abstract
Perimenopause marks the transition from a woman's reproductive stage to menopause. Usually occurring between 42 and 52 years of age, it is determined clinically by the onset of irregular menstrual cycles or variable cycle lengths. Women are at an increased risk of depression and anxiety during perimenopause and the menopausal transition. Depressive symptoms experienced in perimenopause are often more severe compared to pre- and post-menopause. During menopausal transition, the impact of fluctuating estrogen in the central nervous system (CNS) can have negative psychological effects for some women. Traditional first-line management of menopausal depression involves antidepressants, with modest outcomes. The positive effects of estrogen treatment in the CNS are becoming increasingly recognised, and hormonal therapy (HT) with estrogen may have a role in the treatment of menopausal depression. In this review we will outline the prevalence, impact and neurochemical basis of menopausal-associated depression, as well as hormone-based approaches that have increasing promise as effective treatments.

MONASH University

Mechanisms for menopausal depression

- Estrogen modulates serotonin via serotonin receptor expression
- Estrogen levels fluctuate during menopause, causing destabilizing effects on mood and levels of serotonergic neurotransmitters
- Changes in major neuropeptide pathways can also affect mood in menopause

MONASH University

Mechanisms for menopausal depression

- Dehydroepiandrosterone sulphate (DHEAS) is an endogenous steroid hormone and neuroregulator of serotonergic and γ-aminobutyric acid (GABA) neurotransmitter signalling
- Levels of DHEAS decline with ageing and there may be a relationship between lower levels of DHEAS in older women and increasing symptoms of depression
- Similarly, a decline in GABAergic inhibitory function is seen in postmenopausal depression
- Endogenous opioid dysfunction may be involved in the pathophysiology of major depressive disorder and perhaps the change in neuronal opioid activity during menopause may be involved in the pathophysiology of associated depression

MONASH University

Menopausal depression

- 2 groups of menopause related depression
  1. Exacerbation in women with a history of mood disorders - especially history of premenstrual and postnatal mood-related symptoms or a female family history of mood disorders related to hormone events
  2. Women with no previous history of mood disorders at all with severe menopausal depression de novo
- Not found with usual hormone lab investigations – this is brain estradiol fluctuation

Menopausal depression management

- Depression in middle aged – multifactorial
- Antidepressants or MHT? Usually both, but, if possible, better to start with MHT
- Sleep regulation
- Natural medicines
- Psychotherapy

How To Treat Perimenopausal Depression
J.Kulkarni
Aus Doc 14 April 2017

New approaches to menopausal depression

Our research

- Recognition of the condition
- Develop biomarkers for this depression
- Safe, shorter – term hormone treatment eg: new E2, E3, SERMs
- Different antidepressant approach (on/off)
- Physical health overview – tackle weight gain, wine consumption, lack of exercise
- Working with natural medicines too

New ways forward are urgently needed in women's mental health

MONASH University

Case study two

CASE STUDY –PERIMENOPAUSAL DEPRESSION

- Anne is a 49-year-old ICU nurse
- No previous mental health issues
- Over 2 weeks – presents with panic attack for first time ever. Happened at work, during a handover. Worked in same ICU for 10 years, senior and respected ICU NUM
- Increasing 'brain fog' – felt overwhelmed, unable to perform tasks, several panic attacks per week. Depression symptoms included – rapid onset of sadness, tears, rage
- Gained 5 kg without change in food intake or exercise
- No new issues in work or home
- After 6 weeks, Anne sees her GP – saying she feels 'not right', then bursts into tears and says 'can't live like this'

MONASH University

Case Study cont..

- Lifestyle approaches suggested – yoga, 2 weeks time off work, eat more healthy food, walk more
- 3 months later – Anne feeling fluctuating sadness, rage, on/off confusion, in bed a lot, arguing with husband a lot, angry with 14- and 11-year-old sons, not socializing with friends or family
- Fluoxetine 20mg/day prescribed by GP. Increased to 40mg/day a week later
- Rage increased; Anne has major argument with ICU Consultant & storms out of ward, leaving her shift. Disciplinary processes started
- Referred to Psychiatrist. Mood stabilizer added (LiCO3), with diagnosis of Bipolar Disorder
- Poor response to antidepressant + LiCO3. Olanzapine added
- Anne gains 20 kg over 5 weeks, deemed unfit for work
- Spouse sees same GP and says – *'we can't go on like this as a family'*
- WHAT DO YOU DO NOW?

MONASH University

MONASH University

Management of mood changes in menopause

- As a GP if a woman presents with perimenopausal symptoms like hot flushes, night sweats + mood or cognitive changes and it's safe to start MHT or the COCP then these are good first line options
- Then you can review to see how their symptoms (including their mood symptoms) have improved after a period of time

MHT – some key information for GPs

- It's difficult as a GP to remember all the different MHT products
- As a GP a good place to start is either with Zoely as your COCP or for MHT start with:
  1. Transdermal oestrogen
     - This is safer from a VTE perspective than oral oestrogen
     - Start with low to medium dose so either 25 or 50mcg estradiol patch OR 1-2 pumps of estradiol gel daily

  2. Micronised progesterone
     - Is the safest progesterone to use from a breast cancer perspective
     - 1 tablet daily for women who are post-menopausal
     - For women still having periods even if they are irregular, it's 2 tablets on the same 12 days per month.
     - Sometimes oral progesterone can worsen mood symptoms, so consider LnGIUS or other progesterone alternatives.

Alternatives to MHT

- Other options where MHT isn't the safest or most appropriate option in a woman with vasomotor plus mood symptoms are:
  - Escitalopram
  - Citalopram
  - Fluoxetine

  NB: only 35-60% efficacy as per eTG for treatment of vasomotor symptoms

Key messages

Key messages – Tessa

- Cognitive and mood changes are common symptoms of perimenopause and menopause and just like VMS can be directly caused by the hormonal fluctuations during this time.
- It's important to specifically ask about mood and cognitive changes during perimenopause and menopause as women won't always volunteer this information
- Just like vasomotor symptoms, mood changes can respond positively to MHT

Key messages - Rod

- All women should receive individual assessment prior to treatment
- Make sure you correctly diagnose the stage of menopause transition
- In a perimenopausal or recently post menopausal woman with menopausal symptoms including VMS and mood changes, MHT should be considered as first line therapy after appropriate evaluation of mental health
- When the only symptoms are mood disorders MHT may also be appropriate
- Progestogen containing IUS may induce mood disorders in a small number of women and is more likely if PMS / PND have been identified previously
- Pharmacological interventions should be a part of an overall plan to maximize the health of women in midlife and beyond

Key messages – Jayashri

- Estrogen, progesterone, testosterone and their pituitary & hypothalamus related hormones are potent neurosteroids and impact on mental health
- Mental health changes of the perimenopause can occur from the mid 40's onwards, well before the body symptoms of hot flushes and others
- Women with previous PMDD, perinatal depression or psychosis are more likely to experience menopausal depression
- Women with significant early life emotional/ physical/sexual abuse/trauma and subsequent significant life stress are more likely to experience menopausal depression
- MHT can improve mood symptoms

Questions

Resources

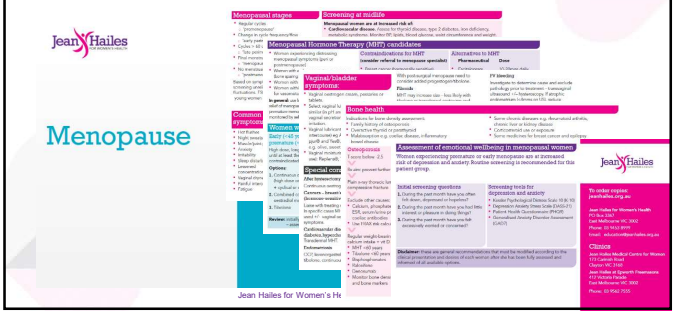
Jean Hailes health professional resources

Health professional tools

Health professional education

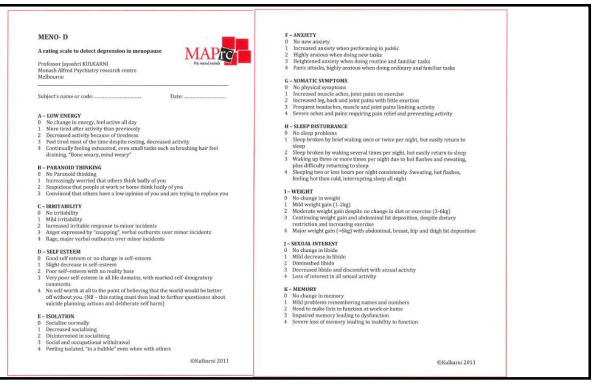
- E-learning course
  - Managing menopause
  - Fertility, infertility and preconception care
  - Diagnosis and management of PCOS
- Webinars
  - Ask an Expert: menopause management
  - MHT cases
  - Using natural therapies in the menopause transition
  - Postmenopausal health

Health professional menopause tool



Consumer booklets and multilingual fact sheets

Jean Hailes for Women's Health | **jeanhailes.org.au**



MENO- D

A rating scale to detect depression in menopause

MAPrc

Professor Jayashri KULKARNI
Monash Alfred Psychiatry research centre
Melbourne

Subject's name or code: ..... Date: .....

A – LOW ENERGY
0 No change in energy, feel active all day
1 More tired after activity than previously
2 Decreased activity because of tiredness
3 Feel tired most of the time despite resting, decreased activity
4 Continually feeling exhausted, even small tasks such as brushing hair feel draining. 'Done weary, mind weary'

B – PARANOID THINKING
0 No Paranoid thinking
1 Increasingly worried that others think badly of you
2 Suspicious that people at work or home think badly of you
3 Convinced that others have a low opinion of you and are trying to replace you

C – IRRITABILITY
0 No irritability
1 Mild irritability
2 Increased irritable response to minor incidents
3 Anger expressed by "snapping", verbal outbursts over minor incidents
4 Rage, major verbal outbursts over minor incidents

D – SELF ESTEEM
0 Good self esteem or no change in self-esteem
1 Slight decrease in self-esteem
2 Poor self-esteem with no reality base
3 Very poor self-esteem in all life domains, with marked self-denigratory comments
4 No self worth at all to the point of believing that the world would be better off without you. (NB – this rating must then lead to further questioner about suicide planning, actions and deliberate self harm)

E – ISOLATION
0 Socialising normally
1 Decreased socialising
2 Disinterested in socialising
3 Social and occupational withdrawal
4 Feeling isolated, "in a bubble" even when with others

©Kulkarni 2011

F – ANXIETY
0 No new anxiety
1 Increased anxiety when performing in public
2 Highly anxious when doing new tasks
3 Heightened anxiety when doing routine and familiar tasks
4 Panic attacks, highly anxious when doing ordinary and familiar tasks

G – SOMATIC SYMPTOMS
0 No physical symptoms
1 Increased muscle aches, joint pains on exercise
2 Increased leg, back and joint pains with little exertion
3 Frequent headaches, muscle and joint pains limiting activity
4 Severe aches and pains requiring pain relief and preventing activity

H – SLEEP DISTURBANCE
0 No sleep problems
1 Sleep broken by brief waking once or twice per night, but easily return to sleep
2 Sleep broken by waking several times per night, but easily return to sleep
3 Waking up three or more times per night due to hot flushes and sweating, plus difficulty returning to sleep
4 Sleeping two or less hours per night consistently. Sweating, hot flushes, feeling hot then cold, interrupting sleep all night

I – WEIGHT
0 No change in weight
1 Mild weight gain (1-2kg)
2 Moderate weight gain despite no change in diet or exercise (3-6kg)
3 Continuing weight gain and abdominal fat deposition, despite dietary restriction and increased exercise
4 Major weight gain (>6kg) with abdominal, breast, hip and thigh fat deposition

J – SEXUAL INTEREST
0 No change in libido
1 Mild decrease in libido
2 Diminished libido
3 Decreased libido and discomfort with sexual activity
4 Loss of interest in all sexual activity

K – MEMORY
0 No change in memory
1 Mild problems remembering names and numbers
2 Need to make lists to function at work or home
3 Impaired memory leading to dysfunction
4 Severe loss of memory leading to inability to function

©Kulkarni 2011

Thank you

Jean Hailes FOR WOMEN'S HEALTH jeanhailes.org.au

References

- AIHW 2007 (**National Survey of Mental Health and Wellbeing: Summary of Results, 2007**) Vic Health Ref "Preventing violence against women" http://www.vichealth.vic.gov.au
- ABS (2012). Personal Safety Data
- Sex Differences in Stress Response Circuitry Activation Dependent on Female Hormonal Cycle Jill M. Goldstein, Matthew Jerram, Brandon Abbs, Susan Whitfield-Gabrieli and Nikos Makris The Journal of Neuroscience, 13 January 2010, 30(2): 431-438; doi: 10.1523/JNEUROSCI.3021-09.2010
- Weaver, I.C.G, Cervoni, N., Champagne, F.A., D'Alessio, A.C., Sharma, S., Seckl, J.R., Dymov, S., Szyf, M., & Meaney, M. (2004). Epigenetic programming by maternal behavior. Nature Neuroscience, 7, 847-854
- Kulkarni J Australasian Psychiatry 2017, Vol 25(4) 333–335

MONASH University

References

- Jankard, R., & Herman, J.P. (2008). Limbic regulation of hypothalamo-pituitary-adrenocortical function during acute and chronic stress. Stress, Neurotransmitters, and Hormones: Annals of the New York Academy of Science, 1148, 64-73.
- Horesh N, Ratner S, Laor N, & Toren P. (2008). A comparison of life events in adoles- cents with major depression, borderline personality disorder and matched controls: a pilot study. Psychopathology. 41(5):300-6. Epub Jul 1.
- Tyrka AR, Wyche MC, Kelly MM, Price LH, & Carpenter LL. (2009). Childhood maltreat- ment and adult personality disorder symptoms: influence of maltreatment type. Psychiatry Res. Feb 28;165(3): 281-7. Epub.
- Ball JS & Links PS (2009). Borderline personality disorder and childhood trauma: evi- dence for a causal relationship. Current Psychiatry Reports, 11, 63-68.
- Zanarini, M. C., Frankenburg, F. R., Reich, D. B., Marino, M. F., Lewis, R. E., Williams, A. A., & Khera, G. S. (2000c). Biparental failure in the childhood experiences of bor- derline patients. Journal of Personality Disorders, 149, 264–273.
- Zanarini, MC; Yong, L; Frankenburg; FR et al (2002). Severity or reported childhood sexual abuse and its relationship to severity of borderline psychopathology and psy- chosocial impairment among borderline inpatients. Journal of Nervous and Mental Disease.190: 381-387.
- Grant BF, et al. Prevalence, correlates, disability, and comorbidity of DSM-IV borderline personality disorder: results from the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry. 2008;69(4):533-45.

MONASH University

References

- Zanarini MC, et al. Attainment and Stability, of Sustained Symptomatic Remission and Recovery Among Patients With Borderline Personality Disorder and Axis II Comparison Subjects: A 16-Year Prospective Follow-Up Study. Am J Psychiatry. 2012;169(5):476-83.
- Black DW, et al. Suicidal behavior in borderline personality disorder: prevalence, risk factors, prediction, and prevention. J Pers Disord. 2004;18(3):226-39.
- Fertuck EA, et al. Cognitive disturbance in borderline personality disorder. Curr Psychosis and Therapeutics Reports. 2006;4(3):105-11.
- Commonwealth of Australia. Clinical practice guideline for the management of borderline personality disorder. 2012.
- Grosjean B, et al. NMDA neurotransmission as a critical mediator of borderline personality disorder. J Psychiatry Neurosci. 2007;32(2):103-15.
- Battle CL, et al. Childhood maltreatment associated with adult personality disorders: findings from a Collaborative Longitudinal Personality Disorders Study. J Pers Disord. 2004;18(2):193-211.
- Stern A. Psychoanalytic investigation and therapy in the borderline group of neuroses. Psychoanal Q. 1938;7:467-89.
- Lupien SJ, et al. Effects of stress throughout the lifespan on the brain, behaviour and cognition. Nat Rev Neurosci. 2009;10(6):434-45.
- Javitt DC. Glutamate as a therapeutic target in psychiatric disorders. Mol Psychiatry. 2004;9(11):984-97

MONASH University