Menopause and Libido: Evidence-Based Insights into Sexual Health and Testosterone

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Disclosures and disclaimers

- Session sponsored by Lawley
- Chair of Menopause Guideline Development Group, Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)
- Board member of WHEN (Women's Health Education Network), a non-profit

Content is my own (not representing any organisation)

Information is of a general nature and you should see your doctor if you have any health concerns

Gender-inclusive language

A case study: Samira*

- Samira is a 52 year old woman referred by her GP
- Menopause symptom score sheet completed
- Her demeanour is flat; she seems quite guarded initially and then tearful
- She says that she has tried everything and “I need some help!”

*Case deidentified

Menopause symptom score checker

- 4 categories of symptoms: vasomotor, psychological, musculoskeletal, urogenital
- Self score as 0= none to 3 = severe
- Scores of 20-50 common in symptomatic women
- Usually reduce to <10 on 3-6 months with personalised treatment

BUT

Not all symptoms can be directly attributed to oestrogen deficiency

Symptom	Not at all 0	A little 1	Quite a bit 2	Extremely 3	Comments
Hot flushes					
Feeling lightheaded					
Headaches					
Irritability					
Depression					
Unloved feelings					
Anxiety, panic					
Mood changes					
Difficulty sleeping					
Unusual tiredness					
Backache					
Joint pains					
Muscle pains					
New facial hair					
Dry skin					
Crawling feelings under the skin					
Loss of interest in sex					
Dry vagina					
Uncomfortable sex					
Urinary symptoms					

Samira’s key symptoms

- Hot flushes – “It’s embarrassing when I’m in a meeting”
- Insomnia – “I fall asleep quickly but wake up during the night”
- Unusual tiredness – “I’m tired all the time”
- Low libido - “I have no interest in sex at all”
- Painful sex – “If we do have sex it burns”
- Dry and itchy skin – “My skin used to be oily”
- Weight gain – “I’ve tried everything and can’t shift the weight”
- Feels anxious and doesn’t feel like herself – “I feel like a hypochondriac”

Menopause symptom score =29

GP has undertaken investigations to exclude other causes of symptoms

Samira’s medical history

- LMP 14 months ago
- Obs/gyn - 2 vaginal births, sons 19 and 23 years. Husband has had a vasectomy and she also has an LNG-IUD inserted 3 years ago for heavy periods
- Medical history- migraine with aura, recently her BP and cholesterol are borderline, no regular meds and no allergies
- Family history- CVS disease, grandmother had breast cancer aged 76 years
- Screening – breast, CST, bowel, up to date and normal, (bone?)
- BP 140/82mmHg
- Height 165cm, weight 84kg, BMI 31

Samira’s social history

- Works fulltime in marketing
- Married for 26 years and lives with husband and 2 sons
- Carer for elderly mother
- Non-smoker, seldom drinks alcohol
- Previously enjoyed hiking and walking the dog
- Has a gym membership but doesn’t go very much as too tired

What has Samira tried so far?

- Soy rich foods to her diet
- Some “happy tablets” advertised on her social media stream
- Black cohosh
- Acupuncture
- Yoga
- Venlafaxine 75mg (antidepressant)
- Lubricants for sex

Hasn’t tried hormonal therapy because worried about breast cancer risk

Next Steps

- Discussed evidence we have and evidence we don’t have for treatment
- Discussed other non-hormonal drug options e.g. Fezolinetant
- Explored her concerns about menopause hormone therapy (MHT) including risks and benefits
- Used evidence based resources and infographics
- Explained genitourinary syndrome of menopause (GSM) and its treatment

Medicine/ Therapy	Symptom	Comments	Recommendation
Botanical/herbal/vitamin supplements			
Vitamin E	Hot flushes	May decrease the number of hot flushes by 1-2 per day.	
St John's Wort	Mood symptoms	Can improve mood and may help with mild depression. This therapy interacts with many prescription medicines.	
Soy isoflavones or phyto-oestrogens	Menopausal symptoms	May help hot flushes. Not helpful for sleep.	
Wild yam cream or progesterone cream	Endometrial (lining of the uterus) protection	No evidence that it is effective.	
Red clover	Menopausal symptoms	Can slightly reduce the frequency of hot flushes. Post menopausal women may see a greater reduction.	
Omega-3 supplements	Hot flushes	No evidence that effective for menopausal symptoms but can lower high triglycerides.	
Black cohosh	Menopausal symptoms	There are different forms of Black Cohosh and some extracts (isopropanolic) may be beneficial. There are possible safety concerns.	
Evening primrose oil	Hot flushes	1000mg twice a day may reduce night sweats, but not hot flushes.	
Ashwagandha	Menopausal symptoms	Insufficient evidence of benefit and concerns for gastrointestinal and liver side-effects.	

Medicine/ Therapy	Symptom	Comments	Recommendation
Mind-body therapies			
Acupuncture	Hot flushes	May be effective at reducing frequency and severity of hot flush versus a placebo, but not compared to sham acupuncture.	
Cognitive behavioural therapy	Menopausal symptoms	Can help some women with menopausal symptoms (sleep/ hot flushes/mood).	
Hypnosis	Menopausal symptoms	May be helpful for some women.	
Yoga	Menopausal symptoms	May be helpful for some women.	
Homeopathy	Menopausal symptoms	No evidence that is it effective.	
Other			
Bioidentical compounded hormone therapy	Menopausal symptoms	Do not take it if you can't take prescribed menopausal hormone therapy (MHT) or hormone replacement therapy (HRT) for safety reasons.	

Information obtained from The North American Menopause Society (The 2023 nonhormone therapy position statement of The North American Menopause Society).

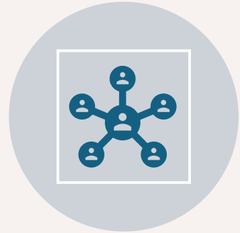
The Pillars of Health

SLEEP

MOVEMENT

NUTRITION

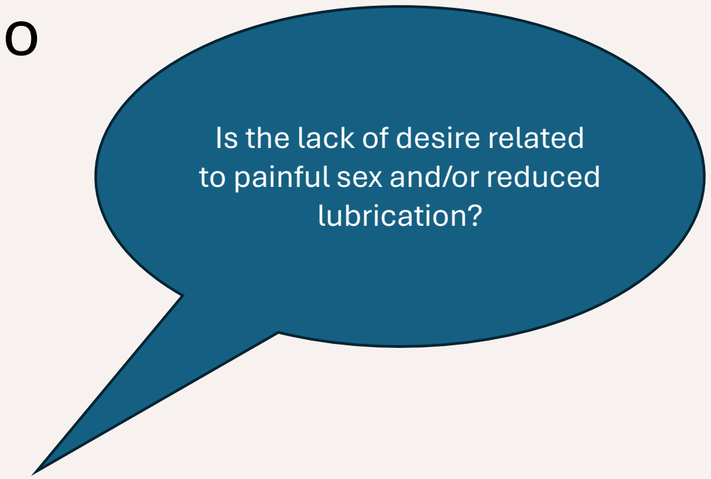
MINDFULNESS/MEDITATION



SOCIAL CONNECTION

Outcome & Progress

- Samira decided to try MHT
- Commenced transdermal oestrogen gel
- Started with 1 pump of Estrogel® for 1 month
- No increase in migraine but still some symptoms so escalated to 2 pumps daily
- On review at 3 months VMS almost completely resolved, sleep improved, less tired and anxious.
- Menopause symptom score 12
- Outstanding concern: “my sex drive is still in my boots!”



Genitourinary syndrome of menopause (GSM)

- Very common – at least 50% of women (likely many more)
- Vulval and vaginal dryness, itch, irritation, pain, urinary tract infections
- Easily and safely treated with:
  - Local vaginal oestrogen (cream or pessary)
  - Local vaginal DHEA pessary (prasterone)
  - Vulval care, moisturisers and lubricants

Sexual Difficulties in the menopause

- Multifactorial and often complex
- Difficulties may be longstanding vs recently acquired
- Investigate relationship issues & dynamics, medications, co-morbidities, biopsychosocial elements
- Relationship between hormones and sexual function
  - Low oestrogen responsible for GSM* → dyspareunia
  - Poor sleep (+/- VMS**) → reduced libido
- MHT (E2 + P) improves sexual functioning independently of effect on VMS

* Genitourinary syndrome of menopause

**Vasomotor symptoms

Medical conditions impacting sexual function

- Hypertension, diabetes, metabolic syndrome, CVS disease
- Hypothyroidism, pituitary tumour/hyperprolactinemia, primary ovarian/adrenal insufficiency
- Parkinson's disease, spinal cord injury/multiple sclerosis/neuromuscular disorders
- Malignancy, (breast, anal, bladder, colorectal, gynaecological)
- Major depression
- Gynaecological: lichen sclerosus (and other dermatosis), GSM, urinary incontinence, pelvic and vulval pain syndromes

Hypoactive Sexual Desire Disorder (HSDD)

The International Society for the Study of Women's Sexual Health (ISSWSH), 2016 defines HSDD as manifestations of *any* of the following for a minimum of 6 months[1] :

- Lack of motivation for sexual activity as manifested by decreased or absent:
  - Spontaneous desire (sexual thoughts or fantasies); or
  - Responsive desire to erotic cues and stimulation or inability to maintain desire or interest through sexual activity;
- Loss of desire to initiate or participate in sexual activity, including behavioural responses such as avoidance of situations that could lead to sexual activity, that is not secondary to sexual pain disorders;
- And is combined with clinically significant personal distress that includes frustration, grief, guilt, incompetence, loss, sadness, sorrow, or worry.

HSDD can be lifelong or acquired, and generalised or situational

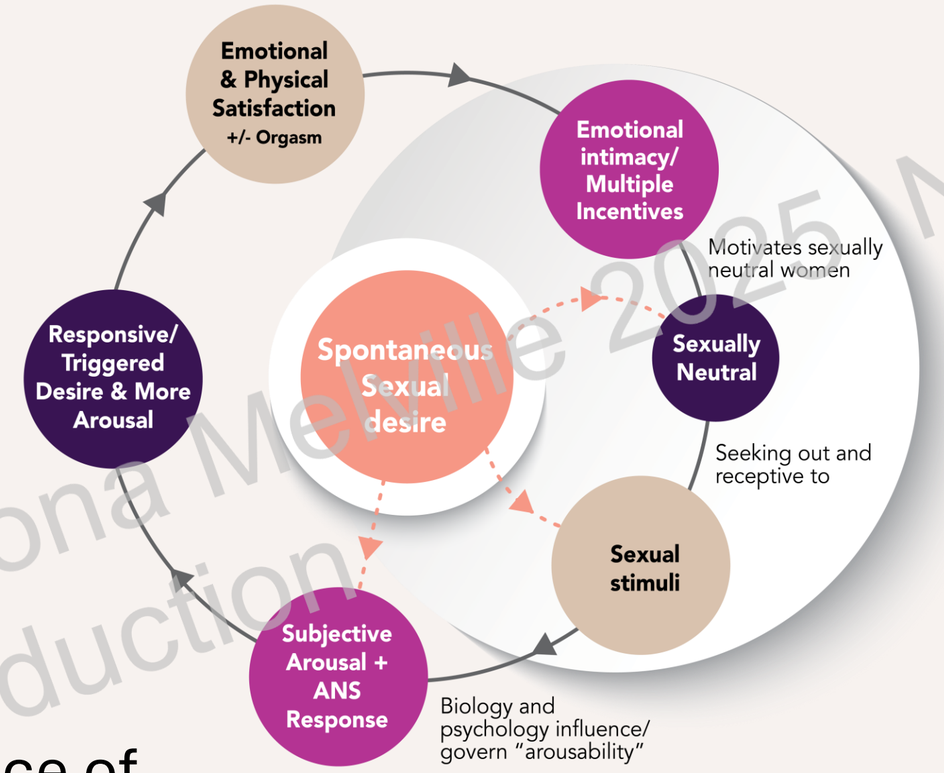
HSDD is the most common form of sexual dysfunction in women affecting 1 in 3 Australian women aged 40-64 years [2]

1. Clayton AH, Goldstein I, Kim NN, et al. The International Society for the Study of Women's Sexual Health Process of Care for Management of Hypoactive Sexual Desire Disorder in Women. Mayo Clin Proc 2018;93(4):467–87.

2. Worsley R et al. Prevalence and predictors of low sexual desire, sexually related personal distress, and HSDD in a community-based sample of midlife women. J Sex Med; 14:675-686.

Circular incentive-based model

- Desire for intimacy may motivate a sexually neutral woman to seek out or be receptive to sexual stimuli



- Female sexual desire is a balance of excitatory and inhibitory signals regulated by key neuromodulators

Basson. J Sex Martial Ther 2001.

Evaluation of low sexual desire

Decreased Sexual Desire Screener: DSDS

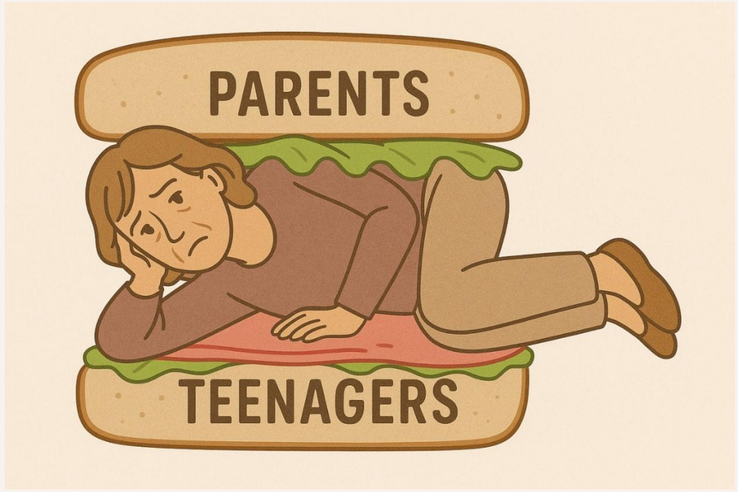
Results are to be discussed with your health care provider. Each question is answered Yes or No.		
1. In the past, was your level of sexual desire or interest good and satisfying to you?	☐ Yes	☐ No
2. Has there been a decrease in your level of sexual desire or interest?	☐ Yes	☐ No
3. Are you bothered by your decrease level of sexual desire or interest?	☐ Yes	☐ No
4. Would you like your level of sexual desire or interest to increase?	☐ Yes	☐ No
5. Please mark all the factors that you feel may be contributing to your current decrease in sexual desire or interest:		
a. An operation, depression, injuries, or other medical condition	☐ Yes	☐ No
b. Medications, drugs, or alcohol you are currently taking	☐ Yes	☐ No
c. Pregnancy, recent childbirth, or menopausal symptoms	☐ Yes	☐ No
d. Other sexual issues you may be having (pain, decreased arousal, or orgasm)	☐ Yes	☐ No
e. Your partner's sexual problems	☐ Yes	☐ No
f. Dissatisfaction with your relationship or partner	☐ Yes	☐ No
g. Stress or fatigue	☐ Yes	☐ No

- Validated screening tool for generalised acquired HSDD
- “Yes” to questions 1-4 = criteria met for generalised acquired HSDD
- “No” to question 5 = no modifiable factors

Clayton AH, Goldfischer ER, Goldstein I, Derogatis L, Lewis D’Agostino DJ, Pyke R. Validation of the Decreased Sexual Desire Screener (DSDS): a brief diagnostic instrument for generalized acquired female hypoactive sexual desire disorder (HSDD). J Sex Med. 2009;6(3):730-738

Management of Sexual problems in the menopause transition

- Psychological and interpersonal issues: address modifiable biopsychosocial factors
  - Consider psychosexual therapy
- Treat co-existing medical issues e.g. thyroid dysfunction, iron deficiency
- Consider side effects of current medications
- Optimise oestrogen (+/- PV)
- Testosterone treatment [1]
  - ⇧ sexual function
  - ⇩ distress in women with HSDD



1.Islam RM, Bell RJ, Green S, Page MJ, Davis SR. Safety and efficacy of testosterone for women: a systematic review and meta-analysis of randomised controlled trial data. Lancet Diabetes Endocrinol 2019;7(10):754–66.

Testosterone therapy: approved use

- AndroFemme®1 for management of HSDD in postmenopausal women (with or without MHT)
- Pre-treatment total testosterone levels within normal ref range
- 1% transdermal testosterone cream (0.5 ml dose = 5 mg testosterone)
- Contraindications:
  - Breast cancer (current or remission), hormone dependent cancers
  - Women of reproductive age
  - Nephrotic syndrome
  - H/O thromboembolism
  - Allergies to testosterone or tree nuts (e.g. almond oil) or any excipients

Testosterone therapy

Bloods

- Baseline total testosterone, SHBG*
- Repeat in 3-6 weeks, 12 weeks, 6 months, 24 months
- Check lipids, LFTs, FBC

Treatment

- AndroFeme®1 (1% testosterone cream
- 0.5mls (5mg) daily to upper outer thigh or buttock
- Adjust in 0.25ml increments
- Max dose 1.0 ml (10mg)

*Sex hormone binding globulin

Testosterone levels

- The initial testosterone level is to ensure women with high levels are not inappropriately treated
- Measure total testosterone rather than free testosterone because evidence that “free” testosterone is the biologically active fraction is lacking
- The aim of treatment is to achieve total testosterone levels that were normal in pre-menopause
- LC-MS* assay is the gold standard lab test but not widely available
- Most labs use the less accurate immunoassay and reference ranges vary e.g.
  - Postmenopausal reference ranges are often 0.2-1.0nmol/L [1,2]
  - Premenopausal adult women reference range often 0.5-2.2nmol/L [1,2]

*Liquid Chromatography-Mass Spectrometry

1. S. L. Davison et al. Androgen Levels in Adult Females: Changes with Age, Menopause, and Oophorectomy, *The Journal of Clinical Endocrinology & Metabolism*, Volume 90, Issue 7, 1 July 2005, Pages 3847–3853, https://doi.org/10.1210/jc.2005-0212

2. Haring R, Anke Hannemann A, et al. Age-Specific Reference Ranges for Serum Testosterone and Androstenedione Concentrations in Women Measured by Liquid Chromatography-Tandem Mass Spectrometry, *The Journal of Clinical Endocrinology & Metabolism*, Volume 97, Issue 2, 1 February 2012, Pages 408–415, https://doi.org/10.1210/jc.2011-2134

Follow up and monitoring

- Levels up to 50% above normal range acceptable
- No blood testosterone level treatment target
- Adjust in 0.25ml increments and re-test in 6 weeks
- If no improvement in 6 months, cease treatment
- Recommend 6 mthly and annual lipids, LFT and FBC

Side effects and safety of testosterone therapy

Side effects: minor and temporary if levels kept within premenopausal range

- Mild acne, oily skin
- Increased hair growth application site or face
- Serious side effects rare at physiological doses e.g. clitoral enlargement, deepening voice

Safety

- No increase in breast density
- No stimulation of endometrium
- Transdermal route does not adversely effect lipid profiles
- No association with increases in BP, blood glucose or HbA1C

Testosterone therapy for postmenopausal women, in doses that approximate physiological testosterone concentrations for premenopausal women, is not associated with serious adverse events

Islam RM, Bell RJ, Green S, Page MJ, Davis SR. Safety and efficacy of testosterone for women: a systematic review and meta-analysis of randomised controlled trial data. Lancet Diabetes Endocrinol 2019;7(10):754–66.

Current and future research

- Effect of testosterone therapy on muscle mass, bone, mood

Mohamad NV, Soelaiman I-N, Chin K-Y. A concise review of testosterone and bone health. Clin Interv Aging 2016;Volume 11:1317–24.

Hua JT, Hildreth KL, Pelak VS. Effects of Testosterone Therapy on Cognitive Function in Aging: A Systematic Review. Cognitive and Behavioral Neurology 2016;29(3):122–38.

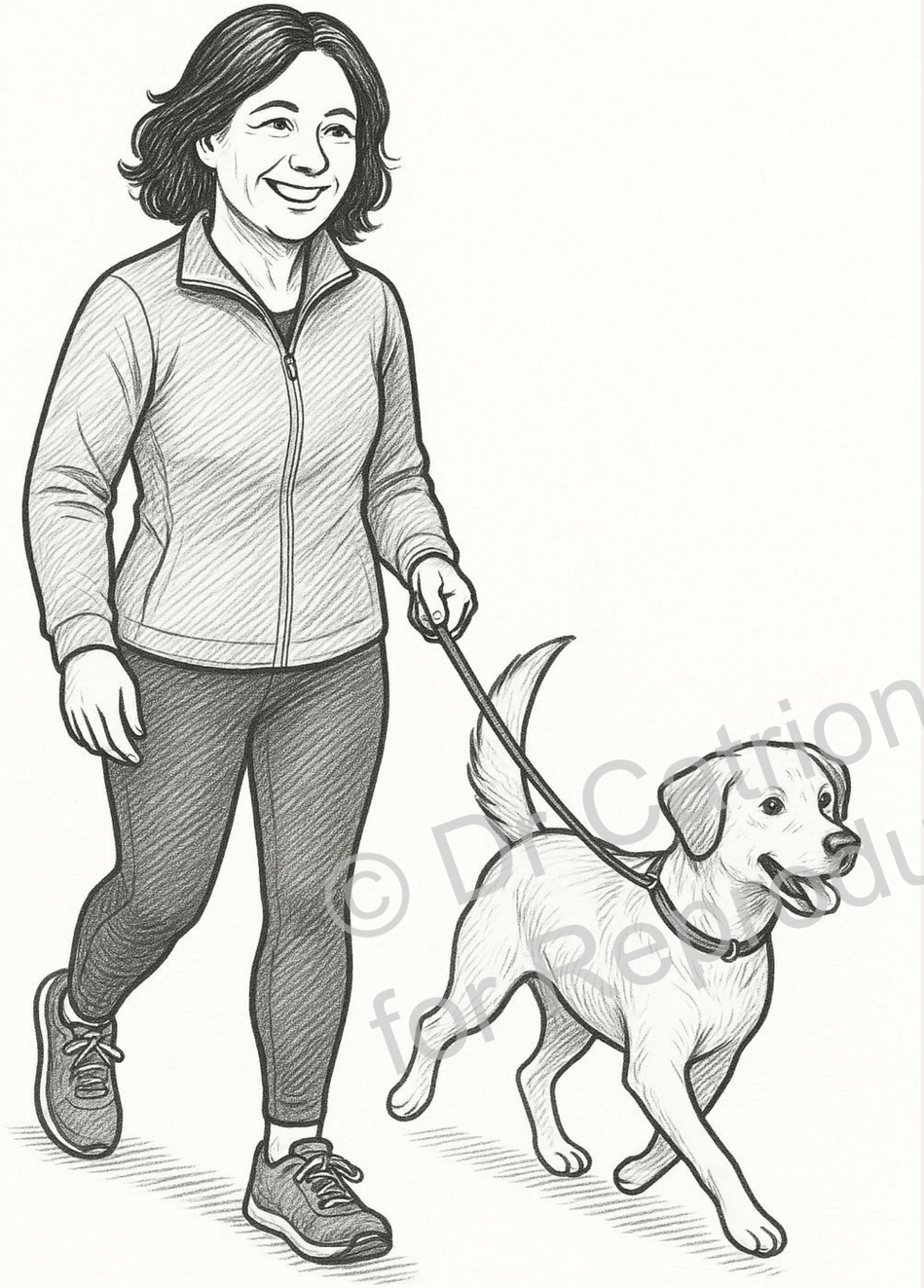
- Studies in pre- and peri-menopausal women

Goldstat R, Briganti E, Tran J, Wolfe R, Davis SR. Transdermal testosterone therapy improves well-being, mood, and sexual function in premenopausal women. Menopause 2003;10(5):390–8.

- The PAMELA study: Prevention of Muscle Loss After Menopause Using Testosterone; Monash RCT
- ETHEL Study: Evaluating Testosterone Therapy to Prevent Heart Failure in Women; Monash
- ESTEEM trial: Evaluating the clinical and cost-effectivenesS of TEstosteronE to improve Menopause-related quality of life; RCT, NIHR, Cardiff UK

Coming soon!!

- PBS listing for AndroFeme®1 : PBAC consultation phase
- Pump applicator: TGA submission end of 2025; if approved will be mid-2026
- LC-MS/MS testosterone testing in pre-menopausal women:
  - Proposal to establish standardised, commercially available assay range
  - Meanwhile request: “LCMS Testosterone (State specific centre)”, directing samples to:
    - Pathology QLD (QLD)
    - POW – Prince of Wales Hospital (NSW)
    - Monash Pathology (VIC)
    - PathWest (WA)
  - Request premenopausal range (QLD and NSW automatically include it)



Key Points

- Sexual problems are a common presentation at menopause
- Aetiology is often multifactorial
- Declining oestradiol correlates with declining sexual function: remember GSM!
- Holistic approach critical to management
- Transdermal testosterone therapy is safe at physiological doses
- Testosterone therapy improves sexual functioning/desire and decreases sexually related distress in postmenopausal women with HSDD

Resources

- “Where did my Libido go?” Rosie King
- “Come as you are” Emily Nagoski
- Australian Menopause Society: Factsheet https://www.menopause.org.au/hp/information-sheets/sexual-difficulties-in-the-menopause
- A Practitioner’s Toolkit for managing Menopause; Monash University https://www.monash.edu/__data/assets/pdf_file/0011/3476072/menopause-toolkit-update.pdf
- The International Society for the Study of Women's Sexual Health Process of Care for Management of Hypoactive Sexual Desire Disorder in Women. Mayo Clin Proc. 2018 Apr;93(4):467-487.
- Sexual well-being after menopause: An International Menopause Society White Paper, Climacteric, DOI: 10.1080/13697137.2018.1482647
- Global Consensus Position Statement on the Use of Testosterone Therapy for Women, The Journal of Clinical Endocrinology & Metabolism, Volume 104, Issue 10, October 2019, 4660–4666, https://doi.org/10.1210/jc.2019-01603

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