Premenstrual Syndrome
Latest Definitions, Management Guidelines & Research
Premenstrual Syndrome - History

Hippocrates’ Aphorisms – (370BC) ’shivering, lassitude and heaviness of the head denotes onset of menstruation….’

Henry Maudsley (1873) - First to make connection between PMS & cyclical ovarian activity
Frank (1931) - First use of term “Premenstrual tension”
Greene & Dalton (1953) – “Premenstrual syndrome”
Studd (1988) - Ovarian cycle syndrome – “menstruation not an essential feature of PMS”
Fashionable 19th Century Disorders in Women

- Neurasthenia
- Insanity
- **Menstrual madness**
- Nymphomania
- Masturbation
- Moral insanity
- Hysteria

all often due to reading serious books or playing music
Have views on PMS changed??
Up to a million British women may suffer from psychosis due to PMS, gynaecologist warns

'I got psychosis and started seeing things which weren’t there. It happened just like that,' one woman told The Independent

Dr Panay says women are being let down by a toxic mix of “poor education of the public regarding the condition; poor education of health professionals at university and postgraduate level; social stigma/taboo and prejudice that this is not a ‘real’ condition.”
Development of consensus and guidelines on PMS essential to encourage acceptance of condition by patients/health professionals and regulatory authorities

“Management of Premenstrual Syndrome”
- 2007 RCOG Green-Top Guideline No 48
  - Panay et al.
- 2016 RCOG Green-Top Guideline No 48
  - Baker L, Panay N, Craig M, O’Brien PMS

*guidelines systematically developed using standardised evidence-based methodology
Management of Premenstrual Syndrome

Green-top Guideline No. 48
February 2017

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www.rcog.org.uk www.pms.org.uk
Core Premenstrual Disorders (PMDs): Classic PMS: Ovulatory cycles, functional impairment, post menstrual resolution

Variants

- Premenstrual Exacerbation e.g. epilepsy, migraine
- Non Ovulatory PMDs: ovarian activity (perimenopause)
- Progestogen Induced: side effects of OCP / HRT
- PMDs without Menstruation: post TAH / ablation
Definitions: PMS or PMDD?

- NAPS will change its name to the National Association for Premenstrual Syndromes from “…Syndrome” to reflect the variation in definitions and severities of this disorder.

- Current PMS terminology should be maintained because PMDD refers to only one type of severe form of PMS. PMDD excludes some women with severe PMS due to the strict definition criteria.

- Education of public and HCPs is the key issue going forward.

- It is vital that there is universal recognition of the severe impact that PMS can have, whatever terminology is used.
PMS Patient Quotes – emotional symptoms are the most distressing.

- “Jeckyll and Hyde personality”
- “My… body is taken over / mind is not my own”
- “I don’t recognise myself”
- “The mist descends”
- “The demons take over”
- “I love my husband / children but I’m about to kill him / them!”
PMS 2.2 Aetiology & Prevalence

- **Prevalence**
  - Peak prevalence of severe PMS in 40-50y age group
  - Moderate PMS: 24% in SWS\(^1\)
  - Severe PMS (PMDD) 5-8%\(^2\) in general population v 23% in perimenopausal women\(^3\)

- **Aetiology**
  - Likely to be multiple aetiologies (E2/serotonin, Progesterone-allopregnanolone/GABA)
  - (Cyclical) ovarian activity / hormonal fluctuations play an essential role in the genesis of symptoms, also in VMS
  - Probable genetic predisposition – unique ESR1 gene polymorphisms in PMDD sufferers v controls.\(^3\)

“This is a big moment for women’s health, because it establishes that women with PMDD have an intrinsic difference in their molecular apparatus for response to sex hormones – not just emotional behaviors they should be able to voluntarily control,” said Goldman.
Proof that ovarian activity integral to PMS Aetiology
Stages with no symptoms
4. How is PMS diagnosed?

When assessing women with PMS, symptoms should be recorded prospectively, over two cycles using a symptom diary, as retrospective recall of symptoms is unreliable.

There are many symptom diaries available but the Daily Record of Severity of Problems (DRSP) is well-established and simple for patients to use (See Appendix 1).
5. How should severe PMS be treated?

**Good Practice Points**

When treating women with PMS:

- General advice about exercise, diet and stress reduction should be considered before starting treatment

- Women with underlying psychopathology as well as PMS should be referred to a psychiatrist (ideally in MDT)

- The most efficacious treatments for PMS are evidence based but unlicensed for that indication!
PMS
6.2 Algorithm – Management GTG

Figure 1. Possible treatment regimen for the management of severe PMS

| First Line | Exercise, cognitive behavioural therapy; agnus castus, red clover, calcium
Combined new-generation pill, such as Yasmin®, Cilest®, Eloine®,
(cyclically or continuously)
Continuous or luteal phase (day 15-28) low-dose SSRIs |
| Second Line | Estradiol patches (100 micrograms) + oral/vaginal progesterone such as
utrogestan 100 mg D17-D28 or Mirena®
Higher-dose SSRIs continuously or luteal phase |
| Third Line | GnRH analogues + addback HRT (continuous combined estrogen +
progesterone or tibolone) |
| Fourth Line | Total abdominal hysterectomy and bilateral oophorectomy + HRT (including
testosterone) |

How do I approach a PMS patient?

1) **Listen!**

2) **Confirm the diagnosis** – charts if necessary  
   …..NB: prior diagnosis of bipolar disorder!

3) **Judge intervention** according to  
   • **Patient wishes** – consider all interventions  
   • **Previous treatments** – treatment algorithm  
   • **Severity of PMS** – may need to **start** with GnRHa if lives are at risk – please refer urgently.

4) **Review at 3 months** but remain available

5) **Don’t place arbitrary limits** on treatment duration
“Evidence Free” Complementary Therapies for PMS

She found if administered correctly, evening primrose oil had a remarkably calming effect.

Purchase More Shoes
PMS
9. Management with SSRIs/SNRIs

- Modulating levels of serotonin with SSRIs improves psychological PMS symptoms. [A]

- When treating women with PMS, both luteal and continuous dosing with SSRIs can be recommended. [B]

- Well tolerated: Escitalopram 10 – 20mg in luteal phase or even symptom phase dosing [Personal Experience]

- In perimenopause, short term treatment of symptoms until cycle stabilisation achieved hormonally [Personal view]

Premenstrual Syndrome
Treatment - SSRI’s

- Practical messages

Women should be warned of the possible adverse effects such as nausea, insomnia, fatigue and reduction in libido. [GPP]

When discontinuing treatment of SSRIs, therapy should be withdrawn gradually to avoid withdrawal symptoms if continuous.

This is unnecessary if treatment is with low-dose luteal-phase dosing. [GPP]
‘WHY WOULD I BE INTERESTED IN THAT?’
10. Management with cycle modifying agents

10.1 The combined oral contraceptive pill

When treating women with PMS, newer contraceptive pill types may represent effective treatment for PMS and should be considered as one of the first-line pharmaceutical interventions.

10.2 Should use of combined oral contraceptive pill be continuous or cyclical?

When treating women with PMS, emerging data suggest that consideration should be given to use of the contraceptive pill continuously rather than cyclically.
Moderation of Hormonal Fluctuations

**Menstrual Cycle**
- **Estrogen**
- **Progesterone**

**Traditional Cyclic Contraceptive**
- **Estrogen**

**Continuous / Long Cycle Contraceptives**
- **Estrogen**
- **Progesterone**
PMS
10. Management with cycle modifying agents – OC cyclical regimens

- Cochrane review of five RCTs with 1920 participants.\(^1\)

- OCs: Drsp(3 mg)/EE v Plbo v Deso(150mcg) v Levo(150mcg)

- Drospirenone-containing OCs used for 3 months were beneficial in reducing severity of symptoms in PMDD.
  - (MD –7.92; 95% CI –11.16 to –4.67)

- Problems with OCs in PMS: 7/7 HFI & prog. side effects

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Yaz vs. SSRIs in PMDD
Standardized mean difference 95% CI on overall symptoms

SSRIs pooled data from 13 RCTs
844 patients
(Wyatt et al. Cochrane Library 2002)

Yaz cross-over study

SSRIs pooled data from 13 RCTs
844 patients
(Wyatt et al. Cochrane Library 2002)

OC v SSRI for PMS –
Similar efficacy so let women decide according to preference!

PMS
10. Management with cycle modifying agents - HRT

- Estradot 75-100mcg twice weekly or...

- Oestrogel 2 pumps twice daily, with

- Utrogestan 100-200mg 7-12 days / cycle pO / pV

- or Mirena IUS (also contraception)
Transdermal estrogens in peri-menopausal depression

50 depressed peri-menopausal women
26 Major depressive disorder, 11 dysthymic
13 Minor depressive disease

100 μg estradiol patches in 12 week placebo controlled study

Remission of depression in 17/25 (68%) of E2 patients and in 5/25 (20%) of placebo patients

Soares et al 2001 Arch Gen Psych
Role of LNG IUS (Mirena®)

Rx of PMS is “off label” with or without E2

- Prog side effects / bleeding possible first 3 - 6 months
- 12mcg* system (3y) in PI women?
  - Jaydess*

Some data for use of Mirena alone – needs confirmation.¹

If GnRH analogue therapy does not result in elimination of premenstrual symptoms, this suggests a questionable diagnosis rather than limitation of therapy. *Evidence level 1++*

When treating women with severe PMS using GnRH analogues for > 6 months, *add-back hormone therapy* should be used. [A]

Women on long-term treatment should have annual measurement of bone mineral density (ideally by dual energy X-ray absorptiometry). [A]
PMS

10. Management with cycle modifying agents – GnRH analogues

- Start with nasal GnRHa if patient uncertainty re Rx
- Minimum 3 cycles to assess response
- Transdermal E2 50 / Utrogestan 100 best ccHRT
- DEXA scans baseline & annually if long term use
PMS
12. Surgical approach (Hysterectomy and BSO)

- Hysterectomy and bilateral salpingo-oophorectomy is of benefit. [C] NB: BSO alone not ideal!

- TAH BSO if on long-term GnRHα or other gynaecological conditions indicate surgery e.g. fibroids/bleeding. [GPP]

- Preoperative GnRH analogue test mandatory to ensure adequate efficacy / HRT is tolerated. [GPP]

- Adequate E2 +/- T essential post operatively!

Cronje et al Hum Reprod 2005
Severe PMS – time for a new approach!

Severe premenstrual syndrome (PMS) or premenstrual dysphoric disorder (PMDD) remains a poorly understood, poorly diagnosed and poorly treated condition. The severest symptoms occur in 5–10% of women in whom their personal, social and professional lives are disrupted, occasionally leading to suicide and homicide attempts. Whilst physical symptoms are common, e.g. breast tenderness, weight gain, headaches...

the levonorgestrel intrauterine system, they do not menstruate.

Awareness of the condition and training in its management are essential. Although primary care should deal with most cases of mild to moderate PMS, women with severe PMS should ideally be managed by a multidisciplinary team within a specialist setting, which might comprise of a gynecologist.
Universal adoption of ISPMD diagnostic criteria vital to facilitate recognition and treatment of PMS (WHO-ICD 11)

Training of Health Professionals should be addressed by Universities & Royal Colleges

Management of severe PMS should ideally be by multidisciplinary teams with ref. to evidence based guidelines

Best evidence thus far is for 24/4 or continuous OC, Estradiol (TD), SSRI & GnRHa.

?Role of Ulipristal Acetate (Esmarty – promising but need data!)

PMS – Key Messages (approach to menopause)

- PMS and VMS often coexist in perimenopause
- PMS symptoms often predict severity of VMS in perimenopause (and progestogen intolerance with HT)
- Both symptoms triggered by fluctuations in hormone levels in genetically vulnerable women
- Optimum management in perimenopause is with cycle stabilising ET + P or LNG IUS if contraception required

National Association for Premenstrual Syndrome NAPS – A Charitable Organisation for more than 30 years!

- New Website Planned [www.pms.org.uk](http://www.pms.org.uk) (>1000 hits per day)
- Ask the Experts
- Discussion Forum (Blog)
- PMS Guidelines
- Annual scientific meetings
- NAPS PMS awareness week
If PMS symptoms affect physical, psychological, social and economic wellbeing, this should be regarded as being clinically significant PMS, warranting prompt diagnosis, appropriate recognition and evidence based medical care.

Some cases of PMS will qualify for a PMDD diagnosis, but in non-PMDD cases of severe PMS, symptoms may have an equally or even more serious impact on the sufferer.
Thank you for listening...questions?

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